Annual Activity Report 2019

In accordance with Article 17 of the Statutes of IMI2 JU annexed to Council Regulation (EU) No 557/2014 of 6.05.2014 and with Article 23 of the Financial Rules of IMI2 JU adopted by the IMI2 JU Governing Board on 27.05. 2020.

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

Annex 1 to the Decision of the IMI2 Governing Board no. IMI2 GB-DEC-2020-19 approved by the Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking on 19.06.2020

Contents

Factsheet – IMI2 JU 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)** Irene Norstedt, Director (acting) in the People Directorate of the Directorate-General for Research and Innovation Carlo Pettinelli, Director in the Consumer, Environmental and Health Technologies Directorate of the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs Andrzej Jan Rys, Director in the Health systems, medical products and innovation Directorate of the Directorate-General for Health and Food Safety Maria Pilar Aguar Fernandez, Head of Unit 'Health Innovations' in the People Directorate of the Directorate-General for Research and Innovation Barbara Kerstiëns, Head of Unit 'Combatting Diseases' in the People Directorate of the Directorate-General for Research and Innovation **Representatives of the European Federation of Pharmaceutical Industries and Associations (EFPIA)** Olivier Laureau, President of Servier group Nathalie Moll, Director General of EFPIA Salah-Dine Chibout Global Head Discovery and Investigational Safety, Novartis, Chairman of the EFPIA Research and Innovation Strategy Working Group Jacky Vonderscher, CEO of Enyo Pharma S.A., member of the European Biopharmaceutical Enterprises Board

	Paul Stoffels, Chief Scientific Officer at Johnson & Johnson, Worldwide Chairman of Janssen Pharmaceutical Companies of Johnson & Johnson
Other bodies	States Representatives Group (SRG): 28 European Union (EU) Member States and 16 countries associated to the Horizon 2020 Framework Programme Scientific Committee: 13 members including ad hoc members Stakeholder Forum: 365 registrations in 2019 Strategic Governing Groups (SGGs): 7 groups
Staff	Total posts: 56 (39 Temporary Agents, 15 Contract Agents, 2 Seconded National Experts) Posts filled: 53 (38 Temporary Agents, 14 Contract Agents, 1 Seconded National Expert)
2019 budget	Commitment appropriations: EUR 261 371 750 Payment appropriations: EUR 231 316 906
2019 budget implementation	Commitment appropriations: EUR 259 212 582 (99.17 %) Payment appropriations: EUR 222 821 258 (96.33 %)
Grants	29 grants signed in 2019 for a total value of EUR 820 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 2019.
Call implementation in 2019	Calls launched: 3 Proposals submitted under two-stage Calls: ▪ Short proposals submitted: 36 ▪ Eligible proposals submitted: 36 ▪ Full proposals submitted: 15 ▪ Proposals selected for funding: 14 Proposals submitted under single-stage Calls: ▪ Proposals submitted: 5 ▪ Eligible proposals submitted: 5 ▪ Proposals selected for funding: 2 Global project portfolio in 2019: 99 projects running during 2019 (16 under IMI1, of which 5 ended by 31 December 2019; and 83 under IMI2, of which 4 ended by 31 December 2019)
Participation, including SMEs	Beneficiaries receiving EU funding in IMI1 and IMI2 projects represent a range of different types of organisations, including universities, research organisations, small and medium-sized enterprises (SMEs) and patient organisations. IMI2: SMEs account for 15.8 % of beneficiaries and receive 10.3 % of EU funding. IMI1: SMEs account for 15.9 % of beneficiaries and receive 14.3 % of EU funding

Unless stated otherwise, all data in this factsheet reflects the situation as of 31 December 2019.

Foreword

As we enter the final year of the Horizon 2020 programme, it is interesting to reflect on Europe's position regarding its innovation ecosystem. This ecosystem has been criticised for decades as being fragmented, underfunded, and inefficient, and constant comparisons are made between funding pots available from the United States or China, which are indeed impressive. However, money is not everything, and if we look collectively at the European Joint Undertakings (JUs), we can be proud of what has been achieved in a relatively short period of time.

The public-private partnership (PPP) networks that have been developed in fields as diverse as healthcare, advanced rail systems, new generation aircraft and air traffic control systems, electronic systems, clean energy and so on, are world class and have been developed at a scale that are the envy of the world. These PPP networks are challenging to create, develop and maintain and indeed the European JU model has not been replicated elsewhere (attempts have been made in the US but have not reached anywhere near the scale that has been possible in the EU). Why is that? Well, in my view, it's because of the European model, the existence of Europe, and the culture of collaboration which is by nature cross border, cross institutional and cross disciplinary.

Thus in the Innovative Medicines Initiative (IMI[1]), we have been able to create a neutral platform where the relevant actors can collaborate, co-create and accelerate the knowledge needed to advance fields of innovation, whether that be in dementia and other neurological conditions, diabetes, infectious diseases, cancer, etc. IMI has driven private sector collaboration to a new level that has enhanced the private sector research and development (R&D) landscape, enabling industry resources to be mobilised for the public good. In doing so IMI has attracted many new partners: 32 Associated Partners (who are well on their way to reaching and surpassing the target of EUR 213 million in contributions), and over 20 Partners in Research who contribute through EFPIA. IMI has become a partnering machine and we are truly at the cutting edge of 'radical collaboration'.

No wonder therefore the IMI project portfolio is full of high-risk projects. Europe needs these PPPs in order to share risk and in turn incentivise investment in the most scientifically complex areas – but which are so important for public health and thus for the European citizen.

In 2019, we have seen some remarkable achievements directly attributable to IMI projects. A vaccine for Ebola and several rapid diagnostic kits are in field trials in the Democratic Republic of the Congo (DRC) and neighbouring countries. A new anti-microbial from our ENABLE project has entered into clinical assessment. For the first time ever, IMI launched a project designed by the diagnostic industry, validating that the IMI platform can indeed be used by industries outside the pharmaceutical industry (the VALUE-Dx project targets rapid diagnostics for anti-microbial resistance).

IMI has also launched new projects that take advantage of the digital revolution. Our first projects in artificial intelligence (AI) and blockchain technology are taking shape with the engagement of many specialised SMEs in this area. Our RADAR–CNS project for example has created a generic IT platform to capture remote monitoring data using smart phones or wearables from people with major depressive disorder, epilepsy, and multiple sclerosis and this platform is now being used in other studies on Alzheimer's disease, Parkinson's disease and autism.

Indeed in the current IMI portfolio we have around 250 SMEs involved, and this diverse collection of innovators is fuelling new inventions and applications at the digital biology interface.

Where else but IMI could we tackle the issues around the use of medicines in pregnant women and lactating mothers? There is a massive public health need in this area and of course, because of the thalidomide catastrophe, women have been excluded from benefiting from potentially safe and efficacious medicines during this critical part of their lives. This situation has to change, but how does society create a trustworthy platform for advancing this agenda? This is yet another topic where a public-private venture is the only way to go, and in 2019 IMI launched the 'first in the world' project called ConcePTION in order to make progress. We

1 A note on nomenclature: to avoid confusion, we use the term 'IMI' throughout to refer to the IMI initiative in general. We 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.

have assembled 15 pharmaceutical companies, over 30 of Europe's top institutions and five SMEs to address this topic.

We have also added an important pillar to our patient engagement strategy. In 2019, IMI launched a call for expressions of interest for patients (or informal carers) to become members of the IMI pool of patient experts. We wish to engage patients and involve them at each stage of our core business processes from topic definition, through project evaluation, to helping us to disseminate project results to citizens. In evaluating projects for example, we treat patient comments on proposals with the same weight as a scientific expert, thus the terminology of 'patient expert'. This pool of now more than 150 patients and carers are getting involved more strategically in IMI's business.

I would like to thank all of those who support IMI in its duties as the implementing body of the world's largest public-private partnership in innovative medicines R&D. Firstly all of the researchers, clinicians, industrialists, patients, regulators and health economists who are delivering amazing results in our projects. Secondly, IMI benefits from dedicated individuals who are the members of our governing bodies, the IMI Governing Board, the Scientific Committee, the States Representatives Group and the Strategic Governing Groups. We also enjoy productive interactions with our day-to-day contacts in the European Commission and the European Federation of Pharmaceutical Industries and Associations who make this partnership work. Finally, I would like to thank my colleagues in the IMI office who go well beyond the call of duty every day to make IMI successful.

Pierre Meulien

IMI Executive Director

Executive summary

IMI2 JU highlights in 2019

- Launched three Calls for proposals including IMI's first topics on advanced therapy medicinal products (ATMPs), as well as further topics in the fields of big data and digital health; patient engagement; and environmental issues.
- Signed 29 new Grant Agreements for projects with a total combined budget (i.e. EU + EFPIA + Associated Partner commitments) in excess of EUR 800 million, bringing the total IMI portfolio to 148 projects.
- The new projects focus on both IMI's traditional areas (e.g. infectious diseases, neurodegenerative diseases, and autoimmune diseases) as well as other industry sectors (e.g. diagnostics, digital health, big data, and imaging).
- Further improved IMI's operational performance, leading to exceptional results on the execution of the operational budget and the achievement of all key targets relating to the management of Calls and grants and payments to projects.

IMI continues to expand into new areas

In 2019, IMI launched 3 Calls for proposals with a total of 10 topics, and signed 29 Grant Agreements for new projects. A glance at the topics and projects reveals that IMI continues to expand into new areas within the pharmaceutical industry while also increasing its ties with other sectors involved in health research and innovation.

One highlight was the launch of the first two IMI Call topics in the field of advanced therapy medicinal products (ATMPs). One topic aims to accelerate research and innovation for ATMPs for rare diseases, while the second topic focuses on the development of engineered T cells to fight cancer. This is a relatively new, fast-moving area where competition between the companies is particularly fierce. Without a neutral platform like IMI, the companies behind these ATMP topics would not have been able to come together and identify the shared challenges where collaboration is the only way forward.

IMI's 2019 Calls also included a topic on the environmental impact of medicines – a hot topic considering the European Commission's ongoing work in this specific area, and more broadly the public's ever-increasing concerns about the health of the environment. One output of the project resulting from this topic will be a publicly available database to make environmental data on human medicinal products more transparent to all stakeholders.

Another achievement was the start of the CONCEPTION project, which is tackling the challenge of providing women who are pregnant or breastfeeding with reliable information on what medicines are safe for them and their child. Currently, just 5 % of medicines come with adequate safety information on this, yet 90 % of women are exposed to a prescription medicine at some time during pregnancy. The project brings together 88 organisations, including regulators, drug manufacturers, universities, hospitals, and public health organisations, and it is hard to imagine that this diverse consortium could have formed without IMI's assistance.

IMI in 2019 at a glance

New projects

29 Grant Agreements signed launching new projects with a combined budget of **EUR 820 million** from…

EU: EUR 397 million

EFPIA: EUR 346 million

Associated Partners: EUR 77 million

Disease areas

Infectious diseases

AB-DIRECT
COMBINE
ERA4TB

Other industry sectors are increasingly involved in IMI. In 2019, work started on the VALUE-Dx project, which is led by companies from the diagnostics industry and is working to generate evidence on the medical, economic, and public health value of diagnostics in treating antimicrobial resistance (AMR).

In the data and computing field, the new MELLODDY project places IMI at the cutting edge of work on the use of machine learning for drug discovery, while PharmaLedger aims to bring blockchain technologies into healthcare. Meanwhile a new Call topic in 2019 is set to apply artificial intelligence to the analysis of digital images and pathology.

In the digital health space, Trials@Home and IDEA-FAST are testing how digital technologies such as wearable and mobile devices can improve clinical trials by making it possible to collect more and better data as participants go about their daily lives. As well as making life easier for clinical trial participants by reducing the number of times they need to visit the clinic, these projects will gather more reliable information that is relevant to patients' quality of life.

All of these achievements amply demonstrate that a cross-sector partnership with partners from multiple industries can and does work in practice.

In 2019, IMI also created a pool of patient experts to further strengthen the role and voice of patients in IMI activities at both strategic and operational levels. The pool counts over 150 patients and informal carers from across Europe and covering the different disease areas highlighted in IMI's Strategic Research Agenda.

IMI is delivering results in areas of public health need

IMI maintains a strong focus on areas where there is a major public health need, including antimicrobial resistance (AMR), Alzheimer's disease, and diabetes.

Antimicrobial resistance

The goal of IMI's ENABLE project was to help universities and small and medium-sized enterprises (SMEs) to advance promising potential antibiotics through the highly challenging early stages of antibiotic development. 2019 saw the project launch its first clinical trial, and select its second candidate drug; if the final pre-clinical tests go well, it could also enter clinical trials. Meanwhile ENABLE is still working on a further 10 potential antibiotics that are at earlier stages of development.

When setting up a clinical trial of a new antibiotic, one major challenge is finding enough patients with the resistant infection under study. IMI's COMBACTE projects have established a network of over 900 hospitals and 800 laboratories across Europe that are ready to participate in clinical trials of novel antibiotics. In 2019, the project announced the results of some of the first trials to take place thanks to the network.

Tackling emerging epidemics

IMI's ZAPI project is working to ensure the world is prepared to respond to disease outbreaks. In 2019, the project demonstrated that certain antibodies can stop the MERS (Middle East respiratory syndrome) coronavirus from infecting new cells. The project is now assessing whether the antibodies could also be effective against severe acute respiratory syndrome

GNA NOW
RespiriNTM
RespiriTB
TRIC-TB

Neurodegenerative diseases

NeuroDeRisk
NEURONET
PD-MIND
PD-MitoQUANT

Autoimmune diseases

BIOMAP
3TR
ImmUniverse
imSAVAR

Diabetes

CARDIATEAM

Cancer

IMMUcan

Rare / orphan diseases

STOPFOP

Other sectors

Diagnostics

VALUE-Dx

Big data and knowledge management

MELLODDY (machine learning)
PharmaLedger (blockchain)

Digital health

Trials@Home
IDEA-FAST

coronavirus 2 (SARS-CoV-2), the virus responsible for the outbreak of COVID-19 that started in China at the end of 2019.

ZAPI has also advanced the development of a biomanufacturing platform that means production of vaccines or therapeutic antibodies can be rapidly scaled up. Finally, they have compiled a master file to facilitate the fast-track regulatory approval of vaccines and therapeutics in emergency situations. This has been shared with regulatory and other authorities.

Alzheimer's disease

Many of IMI's Alzheimer's disease projects are shedding new light on the detailed workings of the genes and misfolded proteins that play such a key role in the development of the disease. This information is essential for the development of targeted treatments that tackle the root causes of the disease.

In a similar vein, the EPAD project has recruited almost 2 000 people across Europe aged 50 and over for a long-term study that will help to improve our understanding of the very earliest stages of Alzheimer's dementia – before people have any symptoms. Participants undergo multiple assessments including regular health checks, standardised tests and brain scans over several years. Now, the project is making data from the first visit of the first 500 participants available to the scientific community. The data has been de-identified to protect participants' privacy, and quality controlled. As the project progresses, further data will be made available to the wider research community.

Diabetes

In 2018, IMI projects played a key role in identifying a new classification of diabetes, with five major subtypes instead of the traditional two. In 2019, the projects confirmed these initial findings and started working on a tool that would help doctors to identify each patient's diabetes subtype and indicate the most appropriate treatments.

Turning stories into numbers: measuring IMI's performance

Stories such as those outlined above paint a rich picture of the diversity of work taking place in IMI projects. However, anecdotes alone are not enough to demonstrate that the EU and pharmaceutical industry's joint investment in IMI is well spent.

The IMI Programme Office has worked hard to revise and streamline the key performance indicators (KPIs) that put numbers on how IMI2 JU projects are delivering on the ambitious, long-term objectives set out in the IMI2 legislation. IMI reported on the new KPIs for the first time in the AAR 2018, and in 2019 this triggered valuable discussions with stakeholders on IMI's work and outputs.

The good news is that the results from 2019 show that IMI is indeed making good progress towards its objectives, as evidenced by the fact that many KPI targets for IMI2 have already been, or are close to being, met. For example:

- IMI2 projects have generated 54 assets (e.g. tools, methodologies, processes, services, etc.) that completed a significant milestone during the project lifecycle (versus a target of 50);

Imaging
Immune-Image

Cross-cutting issues

Stem cells
EBiSC2

Ageing-associated diseases
MOBILISE-D

Paediatrics
ConcePTION

Medicines safety
TransBioLine

Clinical trial design
EU-PEARL

New Call topics

3 Calls for proposals launched with a total of 10 topics and a budget of:
EU: EUR 136 million
EFPIA: EUR 117 million
Associated Partners: EUR 11 million

Advanced therapy medicinal products (ATMPs)
Accelerating research & innovation for ATMPs for rare diseases
Supporting the development of

- IMI2 projects are impacting the regulatory framework, with projects reporting 10 completed procedures (versus a target of 10);
- 44 IMI2 project results (including animal models, standards, biomarkers, standard operating procedures (SOPs), screening platforms, clinical trial networks, etc.) are being implemented by industry participants; the target for this KPI is 50.

Although the KPIs are officially aligned with the IMI2 programme, IMI also collects data on IMI1 projects where relevant. This shows that IMI projects continue to deliver results and impacts long after the IMI funding period has finished, and also tells the long-term story about the partnership between the EU and the pharmaceutical industry.

A focus on sound financial management

In all its activities, the IMI Programme Office ensures adherence to sound financial management principles and effective internal control, and always strives to improve and maintain high levels of operational excellence. This is recognised by the European Court of Auditors (ECA), which again gave IMI an unqualified ('clean') opinion on the reliability of the 2018 accounts as well as on the legality and regularity of revenue and payments underlying the annual accounts.

In 2019, the IMI Programme Office achieved exceptional results on the execution of its operational budget – the result of steps taken in previous years to improve the budgetary planning and monitoring process.

The execution rate for operational commitment appropriations reached 99.84 %, meaning the annual budget has effectively been fully executed. On operational payment appropriations, execution hit 97.33 %, far higher than the rate in 2018 (87 %) and 2017 (72 %).

The Programme Office also hit all key targets on the management of Calls and grants and payments to projects:

- Time to inform (TTI) applicants of evaluation results: 73 days (target: 153 days)
- Time to grant agreement signature (TTG): 210 days (target: 245 days)
- Time to pay (TTP)
  - pre-financing: 9 days (target: 30 days)
  - interim payments: 57 days (target: 90 days)
  - final payments: 65 days (target: 90 days).

1 Implementation of the Annual Work Plan 2019

1.1 Key objectives in 2019

The key objectives for IMI in 2019 were set out in the Annual Work Plan (AWP) 2019 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 1: Execute Strategic Research Agenda priorities by initiating competitive Calls for proposals bringing together the different stakeholders involved in health research (including SMEs, regulators and patient organisations) and by fostering cross-project collaboration.

- Launched three Calls for proposals:
  - IMI2 – Call 17 (two stages, 3 topics, launched 22 January) covered the AWP priorities of diabetes / metabolic disorders and other enablers of research topics.
  - IMI2 – Call 18 (two stages, 6 topics, launched 26 June) covered the AWP priorities translational safety; big data, digital health, clinical trials and regulatory research; oncology; and facilitating the translation of advanced therapies to patients in Europe.
  - IMI2 – Call 19 (one stage, launched 26 June) was a Restricted Call to maximise the impact of IMI2 JU objectives and specific priorities.
- 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.
- Launched a pool of patient experts to further increase patient involvement in IMI's activities and strategic and operational level.

Objective 2: Ensure sound budget implementation through the effective and efficient management of Calls for proposals, grant award process, close monitoring of projects and error rate.

- 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 97.93 %, an improvement over previous years.
- On Call and grant management, IMI achieved the official targets for:
  - Time to inform (TTI): 73 days out of a target of 153 days
  - Time to grant (TTG): 210 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: 57 days out of a target of 90 days
  - TTP final payment: 65 days out of a target of 90 days.

  This was achieved thanks to the continued use of the Horizon 2020 IT management tools, 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 2019, IMI held 22 interim review meetings of its ongoing projects. During these meetings, external experts reviewed the performance of the projects against their original objectives and were able to provide advice and guidance to the project consortia and feedback to the IMI office.

Objective 3: Demonstrate the EU added value of IMI2 JU through assertive communication to target audiences with emphasis on the openness, transparency, relevance, and coherence of IMI2 JU activities.

- Built on the engagement generated during our 10th anniversary by increasing our production of success stories, and by boosting the diversity of our output to include written articles in different styles as well as short, accessible videos for promotion via social media.
- Setting up and implementing an editorial calendar to highlight the links between IMI research and some of the biggest health challenges facing society today.
- IMI's Stakeholder Forum focused on brain health and disease in the digital era, and brought together diverse stakeholders in an open, wide-ranging conversation that resulted concrete ideas for new IMI projects in this exciting new field.

Objective 4: Involve industry from related sectors other than the pharmaceutical industry (diagnostics, medical technologies industry, imaging, digital industry, food and nutrition, etc.) in IMI2 JU projects through proactive outreach strategies.

- IMI continued to attract new Associated Partners from other sectors. These include Datapharm, a company specialising in digital platforms to improve the accessibility and usefulness of medicines information, which contributes to the IMI2 - Call 18 topic on improving patient access, understanding and adherence to healthcare information, an integrated digital health project.
- Diamond Light Source, a not-for-profit limited company funded as a joint venture by the UK Government, and in partnership with the Wellcome Trust contributes to Call 17 topic on open access chemogenomics library and chemical probes for the druggable genome).
- Medicines for Europe is a trade association representing generic and biosimilar manufacturers and it contributes to IMI2 Call 18 Health Outcomes Observatory – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes.
- A number of companies from other sectors opted to contribute to IMI as EFPIA Partners in Research. In total, 6 companies committed EUR 3.4 million to IMI Calls for proposals in 2019, including bioMérieux, Lonza, Medidata, Medtronic, Nanostring Technologies, Transgene.
- IMI continued to work closely with ECSEL, the joint undertaking on electronic components and systems, to exploit obvious synergies. Both IMI and ECSEL have continued to present at each other's strategy meetings.

Objective 5: Ensure IMI2 JU internationalisation and build productive linkages to major international efforts to address Global Challenges (AMR, Alzheimer and other dementias, autism, cancer, diabetes, 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.
- The JDRF, the leading global organisation funding type 1 diabetes (T1D) research, has continued its engagement and support of IMI projects by contributing to two new topics launched in 2019 – the IMI2 - Call 17 topic 'Optimising future obesity treatment', and the IMI2 - Call 18 topic 'Health Outcomes Observatory – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes'.
- The Obesity Action Coalition (OAC) is a US non-profit organisation with the mission to elevate and empower those affected by obesity through education, advocacy and support. It is contributing to the IMI2 - Call 17 topic 'Optimising future obesity treatment'.
- Trial Nation is a partnership offering a single, national entry point for global companies, patient organisations and clinical researchers wishing to conduct clinical trials in Denmark. It is contributing to IMI2 - Call 18 topic 'Health Outcomes Observatory – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes'.
- The power of collaboration is reflected in that a growing number of academic or research institutions from across the globe wish to participate in IMI and not necessarily to receive funding. The IMI2 - Call 17 topic 'Open access chemogenomics library and chemical probes for the druggable genome' has attracted three

academic institutions to join as associated partners two from Canada (McGill University and the Ontario Institute of Cancer Research) as well as the KTH Royal Institute of Technology from Sweden.
- The European Hematology Association is a European non-governmental and not for profit membership society of medical specialists in the field of haematology and it is contributing to the IMI2 – Call 18 topic supporting the development of engineered T cells.
- In Alzheimer's disease (AD) the project EPAD continued its positive interaction with the Global Alzheimer's Platform (GAP) to ensure learning and harmonisation of procedures for clinical trials in secondary prevention of AD.
- In autism, the project AIMS-2-Trials worked to leverage emerging global standards with a newly-pledged resource to guide progress in ensuring maximal benefits of AIMS-2-TRIALS data to autistic people by becoming a founder member of the Global Alliance for Genomics and Health Autism Sharing Initiative.
- An existing Memorandum of Understanding (MoU) between the European Lead Factory and the EU-OpenScreen, Science for Life Laboratory (ScilifeLAB) and the Spanish Network of Excellence in Drug Discovery (REDEFAR) was reviewed and renewed under the IMI2 project ESCulab. In the MoU, the parties declare to exploit the complementarity and synergistic potential between their activities.
- The BEAT-DKD project expanded its collaboration efforts to secure access to external cohorts that would allow testing and validation of biomarkers, and initiated very productive discussions with the chronic kidney disease biomarker consortium CKD BioCon (National Institute of Diabetes and Digestive and Kidney Diseases, US).
- 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.

Objective 6: Improve and broaden access to IMI project outcomes in collaboration with IMI2 projects by embedding dissemination in all stages of the project lifecycle.

- Carried out field work for a study of the socio-economic impacts of 44 IMI1 JU projects that had finished. The report will be published in 2020.
- Ran an event for IMI projects to help them boost their communications efforts and share best practice with one another.
- During 2019, IMI held close-out meetings on 16 projects that had finished. The results and impacts were summarised on the IMI website and promoted.
- Participated in European Commission working groups on project dissemination.
- Ongoing and increased communication on IMI project results through the IMI website (including the catalogue of project tools) and other channels.

1.2 Research & innovation activities

The overarching goal of IMI1 JU 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 JU, 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 classifies 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 IMI's KPIs. The categories 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); and more broadly addressing ongoing challenges in medicines research and drug development.

1.2.1 Infectious diseases

Infectious diseases have been a priority area for IMI throughout our existence; we now have over 40 projects in the area, covering antimicrobial resistance (AMR), Ebola and related diseases, vaccines, tuberculosis, diagnostics, respiratory infections and zoonoses (diseases transmitted between animals and humans).

A public-private partnership like IMI is a logical place to work on infectious diseases. Firstly, there is a clear and growing public health need; AMR is on the rise, and the linked-up nature of our world means that outbreaks of new or re-emerging diseases like the novel coronavirus COVID-19 or Ebola can rapidly spread around the planet. Secondly, addressing AMR and disease outbreaks involves numerous scientific, regulatory and practical challenges, and we will only succeed if we bring all stakeholders together around the same table. As a PPP, IMI is well placed to do this, and the successes of our projects show the benefits of this global, cross-disciplinary, collaborative approach.

Be prepared! Getting ready for the next disease outbreak

The outbreak of a novel coronavirus (now named COVID-19) in China at the end of 2019 put the spotlight on this large family of viruses which includes the common cold as well as more serious diseases such as SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome). Coronaviruses are also found in many animals, and outbreaks occur when a virus jumps from animals to humans and mutates to allow direct transmission between humans.

IMI's ZAPI project was set up to deliver a platform and technologies to facilitate a rapid response to future disease outbreaks. One of the diseases chosen by ZAPI as a case study is MERS, which is closely related to COVID-19. MERS is mainly transmitted to humans from camels and has infected around 2 500 people since it was first identified in 2012.

The surface of the MERS virus features so-called 'spike proteins' which help the virus to break into cells and infect them. ZAPI developed a number of antibodies that block the MERS spike proteins; tests in animals showed that these could be effective as treatments for MERS. The team also drew on a MERS spike protein to create a vaccine; again, tests in animals showed that it appears to be effective.

ZAPI has also advanced the development of a biomanufacturing platform that means production of vaccines or therapeutic antibodies can be rapidly scaled up. Finally, they have compiled a master file to facilitate the fast-track regulatory approval of vaccines and therapeutics in emergency situations. This has been shared with regulatory and other authorities.

ZAPI is now running tests to see if the MERS therapeutic antibodies are also capable of blocking the spike proteins on COVID-19, and the initial results are promising.

Early antibiotic development gets a much-needed boost

The goal of IMI's ENABLE project is to advance the development of potential antibiotics against Gram-negative bacteria, such as *Escherichia coli*. The ENABLE project has set up a platform that gives universities and small and medium-sized enterprises (SMEs) the opportunity to advance promising potential antibiotics through the highly-challenging early stages of antibiotic development.

One goal of the project was to get at least one drug candidate into Phase I clinical trials, when the drug is tested in humans for the first time. In 2019, it achieved this goal with Juvabis' apramycin. In pre-clinical tests, apramycin proved effective against a variety of drug-resistant bacteria, classified as priority pathogens by the World Health Organisation (WHO).

Another highlight in 2019 was the selection of Mutabilis's oral combination including MUT485 as a candidate drug. This means that if the results of the final pre-clinical tests are positive, it can be advanced to a Phase I clinical trial. This drug candidate could be used to treat urinary tract and kidney infections caused by bacteria that are resistant to other antibiotics.

In this battle against antimicrobial resistance, European small and medium-sized enterprises (SMEs) such as Juvabis and Mutabilis are playing an increasing role.

Meanwhile ENABLE is still working on 10 further potential antibiotics that are at earlier stages of development. The ENABLE portfolio is managed by a Portfolio Management Committee, which screens applications to the ENABLE programme and decides which molecules are ready to pass to the next stage of development, and which should be stopped. 'With its different platforms and well-functioning expert bodies, ENABLE has created a unique ecosystem that has proven effective in bringing promising compounds forward,' said the committee's chair, Frederik Deroose, CEO of Asclepia. 'Further, ENABLE has educated a generation of scientists in academia and SMEs in the scientific, commercial and regulatory realities of antibiotic discovery and development.'

Clinical trials of novel antimicrobials offer hope in fight against drug-resistant bugs

When setting up a clinical trial of a new antibiotic, one major challenge is finding enough patients with the resistant infection under study. IMI's COMBACTE family of projects has established a network of over 900 hospitals and 800 laboratories across Europe that are ready to participate in clinical trials of novel antibiotics. So far, over 350 sites have participated in 23 trials involving 21 000 patients; the first trials delivered initial results in 2019.

Patients in intensive care units (ICUs) who are breathing with the help of ventilating machines are at high risk of contracting pneumonia. The *Staphylococcus aureus* bacteria make their way into healthy lungs by attaching to the medical tubing that connects to the outside world. *S. aureus* is extremely virulent and increasingly resistant to antibiotics. COMBACTE's SAATELLITE study was a Phase II trial to see if patients whose lungs are already colonised by *S. aureus* could avoid pneumonia by being dosed with a one-off injection of a monoclonal antibody designed to block the bacteria's virulence, i.e. the potential for infection.

The results were promising. The researchers enrolled about 200 ventilated ICU patients in a double blind, placebo controlled trial. The percentage of people in the placebo arm that contracted pneumonia was 26 %, while for those who had received the monoclonal antibodies injection, the figure was 18 %. This is a relative reduction of 31 %. Bruno François from the University Hospital of Limoges, who was involved in the SAATELLITE study, is cautiously optimistic about the results.

'This was the first trial with this type of drug to be used as a preventative,' says Dr François. 'This could represent a true opportunity to decrease the number of pneumonia infections in the ICU without needing any antibiotics. Of course it's only a phase two so you would need a confirmatory trial, but it's completely innovative.'

Elsewhere, the REJUVENATE study was a Phase II trial of aztreonam-avibactam (ATM-AVI), which is designed to treat complicated intra-abdominal infections. The results were positive, and work has started on a Phase III trial.

Building capacity in Africa to deal with Ebola outbreaks

Two major Ebola outbreaks have struck Africa in recent years. In 2014-2016, the outbreak in western Africa infected over 28 000 people and killed 11 000. Throughout the outbreak, IMI's Ebola+ programme played a major role in supporting clinical trials of Ebola vaccine regimens and the development of rapid diagnostic tests. In 2018, a new outbreak was declared in the Democratic Republic of the Congo (DRC); by the end of 2019, over 3 000 people had been infected and 2 200 had died of the disease. In 2019, both the DRC and Rwanda started using the Johnson & Johnson Ebola vaccine regimen which had been developed with significant support from IMI.

IMI's Ebola+ projects have always devoted a lot of energy to building the capacity of local scientists and healthcare workers to run clinical trials. In 2019, the EBOVAC 1, 2 and 3 projects ran over 130 training courses in the DRC, Guinea, Liberia, Mali and Sierra Leone covering a range of topics relating to clinical trials, including protocol amendments, data protection, serious adverse event reporting, sample transport, quality control, safety, and informed consent.

In addition, the EBODAC project trained close on 10 000 people in DRC, Rwanda, Sierra Leone, and Uganda in community engagement tools and techniques, including the use of biometric tools and rumour management.

1.2.2 Alzheimer's disease and other neurological disorders

Brain diseases affect millions of people worldwide, yet there is a dire lack of treatments for these diseases. This is not for want of trying; pharmaceutical companies spent years, and upwards of EUR 10 billion, looking for an effective treatment for Alzheimer's disease, without success. And while treatments do exist for other diseases such as depression, they do not work in all patients. The brain is a highly complex organ, and we still have a lot to learn about how it works. IMI is a neutral platform that allows companies, universities, patients and others to share knowledge, ideas and resources and so make progress in this vital area.

New tools to study the role of ApoE in Alzheimer's disease

We know that people with the ApoE4 version of the ApoE gene have a considerably higher risk of developing Alzheimer's disease and are also more likely to develop the disease much earlier in life. However, we don't know why this is, and IMI's ADAPTED project is working to change this. The project has developed tools to make it easier to study the role and activity of the ApoE gene in the lab. These include nerve cells derived from human induced pluripotent stem cells with different versions of the ApoE gene, and a method to study the effect of ApoE on inflammation in Alzheimer's disease.

Unravelling the role of misfolded proteins in dementia associated with head injuries

Scientists have unravelled the structure of the abnormal tau filaments associated with chronic traumatic encephalopathy (CTE), a type of dementia associated with repeated blows to the head. Furthermore, the tau filaments associated with CTE are different to those found in people with Alzheimer's disease. The findings add to our understandings of how different forms of dementia develop, and could pave the way for future treatments for CTE and other diseases associated with abnormal tau filaments.

The work, which was published in the prestigious journal Nature, was funded in part by IMI through the IMPRiND project.

Study reveals complex role of TREM2 gene in Alzheimer's disease

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. 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. A study published in Nature Neuroscience, funded partly through IMI's PHAGO project, sheds new light on how TREM2 influences the progression of Alzheimer's disease in different ways in the early and later stages.

TREM2 codes for the TREM2 protein, which activates immune cells in the brain called microglia. Microglia play a vital role in the removal of amyloid plaques. In this study, the researchers showed that in mice with early signs of plaque deposition (and a functioning TREM2 gene), microglia cluster around small plaques and cause them to disintegrate. In mice lacking a functional TREM2 gene, the microglia were not able to break up the amyloid plaques. This suggests that in early stage Alzheimer's disease, activating TREM2 could help to prevent the build-up of toxic amyloid plaques.

However, the results of a similar test in mice with more advanced plaque deposition paint a different picture. There, the amyloid plaques grew faster in mice with a functioning TREM2 gene than in mice without it. Further analyses showed that in the microglia, TREM2 also stimulates the production of a protein called ApoE, which is by far the strongest genetic risk factor for developing sporadic Alzheimer's disease, and is thought to promote the aggregation of amyloid plaques. 'Our findings indicate that future therapies will need to be applied in a stage-specific manner,' says Christian Haass of DZNE Munich and Ludwig-Maximilians University, who led the research. 'Based on the outcome of our study, activation of microglia by TREM2 would be a useful strategy to apply during the early phase of the condition.' Professor Haass and his colleagues are now working on antibodies that could stabilise the TREM2 protein, increasing its ability to activate microglia.

Alzheimer's project EPAD releases first wave of data to research community

IMI's EPAD project is recruiting people across Europe aged 50 and over to participate in a long-term study that will help to improve our understanding of the very earliest stages of Alzheimer's dementia – before people have any symptoms. Participants undergo multiple assessments including regular health checks, standardised tests and brain scans over several years. Now, the project is making data from the first visit of the first 500 participants available to the scientific community. The data has been de-identified to protect participants' privacy, and quality controlled. Access is provided via secure online tools; researchers who want to use it have to apply via the EPAD website.

According to project coordinator Craig Ritchie of the University of Edinburgh, the research participants are enthusiastic about the move to make their data available to researchers. 'Research participants love and expect it - they want as much knowledge to be gained as possible from their contribution,' he says. So far, EPAD has recruited almost 2,000 people through 28 study sites in 8 European countries. As the project progresses, further data will be made available to the wider research community.

- Find out how to access the EPAD data: http://ep-ad.org/erap/

ROADMAP Data Cube allows interactive visualisation of Alzheimer's data

IMI's ROADMAP project has released its Data Cube, an online, three-dimensional 'heat map' that allows users to visualise how different data sources capture different Alzheimer's disease outcomes at different disease stages. Furthermore, users can switch between the perspectives of people with dementia, carers, and health professionals. The Data Cube makes it easy to see what data sources are available, and where there are gaps. It comprises information from 65 data sources, including electronic health records, clinical trials, and cohorts, but does not provide access to any underlying data. According to the project, 'Enabling the visualisation of the AD-related data availability in different types of European data sources and the intrinsic gaps has proven to be a powerful tool for the design, planning and validation of the models and strategies used to guide future recommendations to enhance AD research.' ROADMAP is part of IMI's Big Data for Better Outcomes programme.

- View the ROADMAP Data Cube: https://datacube.roadmap-alzheimer.org/

Uncovering clues on autism

Autism spectrum disorders (ASD) affect around 1 % of the population and are characterised by difficulties in social interactions and communication as well as repetitive behaviours. The precise symptoms and their severity vary widely from one person to another; some are only mildly afflicted and can lead relatively independent lives, while others are severely disabled and require a lot of specialist care. IMI's autism projects aim to add to our understanding of the underlying causes of ASD and pave the way for treatments designed specifically for ASD – currently, people with autism are treated with drugs designed for other conditions.

EU-AIMS has found that when adolescents with autism watch scenes of human interactions, the way their pupils dilate predicts their social cognitive performance. This information will add to the ways researchers can study how autistic and non-autistic people process social or sensory information. In another study, AIMS-2-TRIALS researchers worked with industry partners and autistic individuals aged from 6 to 45 years to develop a wearable device to measure symptom change. The involvement of people with autism ensures it is acceptable to them and the project plans to use it in a clinical trial.

1.2.3 Diabetes

According to the International Diabetes Federation, diabetes currently affects 463 million adults, and by 2045 this will rise to 700 million. Despite decades of research, there is still no cure for diabetes, and many patients still have to inject themselves with insulin to manage their condition. IMI has a strong diabetes project portfolio, with 11 projects addressing different aspects of the disease.

IMI projects refine new classification of diabetes subtypes and pave way for use in the clinic

In 2018, IMI's BEAT-DKD and RHAPSODY projects published a revised classification of diabetes, with five major subtypes. In 2019, the projects validated these initial findings in additional patient populations and uncovered new clues as to the best treatment options for the different groups. For example, one study demonstrated that patients with 'severe insulin resistant diabetes' (SIRD) who undergo bariatric surgery show the best recovery from diabetes and the greatest improvement in kidney function. This is important as kidney disease is a common complication in diabetes.

Now, BEAT-DKD is working on a software package that would allow doctors to identify which diabetes subtype a patient has. The doctor would simply have to enter information on the six variables used for clustering. As well as indicating the subtype that is the best match for the patient, the tool would generate information on the best choice of treatment. The tool is under development and will be formally tested as a medical device for use in clinics.

New tool could predict risk of diabetes drugs for kidneys

People with diabetes are already at greater risk of heart and kidney problems. Now, the BEAT-DKD project has developed a tool that indicates whether long-term use of a drug could harm the heart or kidneys. The tool, which is built on earlier work, could prove helpful to those developing new drugs. It could also be used by doctors to assess which patients would benefit from certain medicines and which patients should use alternative treatments.

INNODIA identifies genes behind destruction of insulin-producing cells

Type 1 diabetes occurs when the immune system attacks the beta cells in the pancreas responsible for producing the hormone insulin, which regulates blood sugar levels. Writing in the journal Nature Genetics, scientists from the INNODIA project explain how they have identified some of the genes involved in the beta cells' response to attacks by the immune system. The findings add to our understanding of the molecular basis of the disease and could pave the way for future treatments.

1.2.4 Cancer

According to the European Journal of Cancer, in 2018 there were an estimated 3.9 million new cases of cancer in Europe. And although advances in treatments mean survival rates are on the up, the disease killed 1.9 million people in Europe in the same year. IMI's cancer portfolio is growing steadily, and includes projects from IMI's big data programme, as well as projects working on new tools to study the disease, including childhood cancers.

First steps on the path to new treatments for colon and skin cancers

IMI's European Lead Factory project has created a vast library of over 500 000 compounds that were contributed to the project by large pharmaceutical companies as well as other organisations. Researchers from universities and SMEs can apply to access the compound collection to hunt for compounds that could be useful in their own drug development projects. Scientists at the German Cancer Research Centre (DKFZ) had discovered that a protein called kallikrein-related peptidase 6 (KLK6) appears to be involved in the development and spread of some cancers, including colon cancer and melanoma (skin cancer).

The team turned to the European Lead Factory in their hunt for potential drugs that could block the activity of KLK6. With the help of the project, they screened the collection and identified a number of compounds that could fit the bill. Further work on the 'hit list' narrowed the list down, and one of the compounds blocked the spread of the cancer in laboratory tests. The findings were published in the journal ChemMedChem.

Carrying on the legacy of an innovative cancer project

Today, many cancer patients have to undergo biopsy surgery to provide doctors with the cell samples they need to diagnose the disease, determine the treatment needed, and then monitor how well a treatment is working. Needless to say, doctors cannot carry out biopsies too often because they are invasive, costly, and risky to the patient. Yet cancer is a dynamic disease, and patients would benefit immensely from more regular analyses of their condition.

Cancerous tumours shed cells and fragments of DNA into the bloodstream, and IMI's CANCER-ID project was set up to see if these 'circulating tumour cells' (CTCs) and DNA could be detected and analysed in blood samples – a so-called 'liquid biopsy'. The project picked two cancers as case studies: lung cancer (where biopsies are particularly hard to obtain on a regular basis) and breast cancer (where there is an urgent need for tests that detect early on when a tumour has become resistant to certain medicines).

The project has developed and validated a range of methods and protocols to extract these cells and fragments of genetic material from blood samples and then analyse them. This is no mean feat. The levels of tumour cells and DNA in the blood are low. The levels of rare genetic mutations in the circulating tumour DNA are even lower, and detecting them requires a special, faster centrifuge that is not available in all clinical labs. In addition, even small changes in the way a blood sample is handled can affect the results. The CANCER-ID team validated its methods and protocols by testing them in different laboratories.

In 2019, the project coordinator set up the European Liquid Biopsy Society (ELBS) to continue the work of the project once the IMI funding period is over. The ELBS brings together many project partners and already has strong ties with the global liquid biopsy research community.

1.2.5 Other challenges in health research and drug development

Many IMI projects do not focus on specific diseases, but seek to address broader challenges in health research and drug development. Projects here are working on issues such as big data, digital health, and medicines safety, to name just a few. In many cases, project outputs are made accessible to the wider research community.

Want to make your data FAIR? Follow the recipes in the FAIRplus cookbook!

The vast amounts of data generated in life science research have the potential to add to our understanding of disease and help advance drug development. Yet most data is hidden away in proprietary databases and stored in different formats. The goal of FAIRplus is to deliver guidelines and tools to facilitate the application of 'FAIR' principles to data from certain IMI projects and datasets from pharmaceutical companies. FAIR stands for 'findable, accessible, interoperable, reusable'. In 2019, the project published a FAIR 'cookbook', an open

access resource designed to help researchers ensure their data is 'FAIR'. The cookbook, which will continue to evolve throughout the project, sets out step-by-step 'recipes' on what researchers need to do. The project has already used the 'recipes' in the cookbook to FAIRify datasets from four IMI projects, and their data is now in the IMI data catalogue:

- View the FAIR 'cookbook' fairplus.github.io/the-fair-cookbook/intro.html
- View the IMI Data Catalogue: datacatalog.elixir-luxembourg.org/?query=&sort_by=dataset_created&order=desc&groups=IMI%20Projects&page=1

RESOLUTE opens up treasure trove of materials on understudied proteins

Transport proteins are the gatekeepers of our cells, effectively controlling the flow of nutrients and other molecules across the cell membrane. With over 400 members, solute carriers represent the largest class of transport proteins. Yet although they have been implicated in diseases ranging from Alzheimer's disease and amyotrophic lateral sclerosis (ALS) to schizophrenia, solute carriers have never been studied in detail.

Enter IMI's RESOLUTE project, which aims to deliver knowledge and resources on these under-studied proteins, and making the information available to the scientific community.

For example, the consortium has made available the DNA sequence of approximately 400 solute carrier transporters. The RESOLUTE plasmid repository is available via Addgene.org, a not-for-profit repository for this kind of material. Within weeks of the material becoming available, several labs worldwide had placed orders. In the future, more DNA sequences will be added to this collection.

The project has also published the RESOLUTE 'knowledgebase', which brings together in one place high quality, reliable information on solute carrier proteins from publicly available sources. The RESOLUTE knowledgebase is freely accessible and the project will add information to it from both public sources as well as the project's own results.

- Visit the RESOLUTE 'knowledgebase': re-solute.eu/knowledgebase

RADAR-CNS study reveals factors influencing digital technology use for depression

IMI's RADAR-CNS project is working to develop new ways of monitoring major depressive disorder, epilepsy, and multiple sclerosis using wearable devices and smartphone technology. The hope is that these technologies would make it possible to detect changes in behaviour, sleep, or mood before the individual themselves is aware of it. This could help them to predict – or even avoid – a relapse.

The project is working with patients to discuss their attitude towards the use of these technologies to monitor their condition. In a recent study, the project discussed the technologies with adults with experience of depression from Spain, Italy and the UK. In all three countries, the patients raised issues regarding their motivation levels, the potential impact of the technologies on mood and anxiety, aspects of inconvenience, and ease of use. These findings will help the project to deliver technologies that fit in with patients' lives.

Underlying much of the project's work with mobile and wearable devices is the RADAR-BASE software platform, which integrates data from different sources, stores it, and makes it available to those who need it, all while respecting users' privacy and security. The platform has been open source since 2018 and is now being used by over 13 additional studies involving more than 13 500 participants. These include a study on emerging infectious diseases in Africa, and a study to track how recovery from poor mental health 'unfolds' over time.

- RADAR-BASE: radar-base.org

Getting to grips with pharmaceuticals in the environment

When we take a medicine, much of it will be broken down by the body. However, very often some of the active ingredient will remain intact and is excreted when we go to the toilet. After that, it travels in the sewage system to a wastewater treatment plant (WWTP), and if it is not removed during the sewage treatment process, it is released into the environment. Although the concentrations of medicines in the environment are generally low, in some cases they could potentially be harmful to wildlife and ecosystems. A first step in assessing the environmental risk of chemicals is estimating the levels of the chemical in the environment. IMI's iPiE project has developed a technical model that draws on national drug consumption data to estimate the concentrations of pharmaceuticals in the environment across Europe.

- Download the model: http://i-pie.org/epie/

Can real world data replicate a clinical trial? EHDEN study suggests yes

IMI's EHDEN project has dramatically demonstrated the power of using clinical data in research by replicating, during a five-day 'study-a-thon', the results of a systematic review covering 20 years of research, and a multi-year clinical trial. The findings, which focus on the pros and cons of different types of knee replacement surgery, are published in the journal Lancet Rheumatology. They show that it is possible to harness clinical data (such as electronic health records) from different sources and use it to generate information that could help patients and doctors to make better decisions about their care.

'Randomised controlled trials remain the gold standard for establishing efficacy,' the EHDEN team concludes in the paper. 'However, we feel that this study shows the value of real world evidence for complementing the evidence produced from randomised trials.'

WEB-RADR medicines side effects reporting apps go global

Traditionally, reporting a suspected side effect of a medicine entails filling in a paper form. However, thanks to the WEB-RADR project, patients and healthcare workers alike can now report side effects quickly and easily via an app. Interest in the app is on the rise, and in 2019 Armenia, Botswana, Cote d'Ivoire, Ethiopia and Ghana had brought the number of countries using the app to 11.

Meanwhile the project has also published its findings on the usefulness of social media for detecting medicines safety issues. Writing in the journal Drug Safety, the project team explains that generally speaking, social media is not currently suitable for detecting potential safety issues. Nevertheless, it may be beneficial in certain specific circumstances, and advances in technology could mean that social media could be used as a source of information on side effects in the future.

Stem cell bank on track for sustainability

Induced pluripotent stem cells (iPSCs) are key tools for early drug development and disease modelling. IPSCs are mature adult cells that have been reprogrammed to make them 'pluripotent', i.e. able to differentiate into any type of cell found in the human body. IMI's EBiSC project was established to provide researchers across academia and the pharmaceutical industry with disease-relevant, quality-controlled, research-grade iPSC lines, data and cell services. Now, the EBiSC2 project is building on the work carried out under EBiSC to ensure the long-term sustainability of the infrastructure. During 2019, EBiSC2 continued to add new cell lines to the catalogue, and distributed cell lines to over 20 users in more than 10 countries. These numbers show that the iPSC repository is expanding, and is therefore well placed to meet future demands from both the industry and the wider research community.

- Visit the EBiSC catalogue: https://cells.ebisc.org/

1.2.6 Collaboration among consortia and with external bodies and other sectors

Promoting data sharing globally in autism

The project AIMS-2-TRIALS is leading together with Autism Speaks the 'driver project' Autism Sharing Initiative in the Global Alliance for Genomics and Health. The initiative brings together the world's most ambitious efforts in autism to create the first federated, global network for sharing genomics and clinical data to accelerate discoveries and the development of precision therapeutics in autism. This will underpin the project efforts to develop: 1) state-of-the-art openness *and* privacy with community endorsement; and 2) a practical path to global 'precision recruitment' using stratification/enrichment markers (and therefore sustainability). See: www.autismspeaks.org/press-release/autism-sharing-initiative-named-2019-ga4gh-driver-project

Coordinating and supporting IMI neurodegenerative disorders projects

NEURONET is a Coordination and Support Action (CSA) that started on 1 March 2019 and aims to support and better integrate projects in the IMI neurodegenerative disorders (ND) portfolio and share their learnings. The signature of a Memorandum of Understanding between NEURONET and each of the 15 projects is ongoing to allow data sharing for integrated portfolio analysis and impact analysis. NEURONET organised the first annual networking and communication event for the projects at the Alzheimer Europe Conference in The Hague on 24-25 October 2019: www.imi-neuronet.org/2019-event-the-hague/.

Collaborating on antibiotic stewardship

The COMBACTE project's network EPI-Net is collaborating with the Joint Programming Initiative on Antimicrobial Resistance funded projects ARCH (bridging the gap between human and animal on surveillance data, antibiotic policy, and stewardship) and GAP-ON€ (global antimicrobial resistance platform for one burden estimates) to develop practical tools for the implementation of antibiotic stewardship programs in both human and veterinary fields based on surveillance data as well as a strategic research agenda (SRA) highlighting priority topics for future research and funding.

Advancing biological concepts into drug discovery projects

The existing Memoranda of Understanding (MoU) between the European Lead Factory and the EU-OpenScreen, ScilifeLAB and REDEFAR were reviewed and renewed under the IMI2 project ESCulab. EU-OpenScreen (European Infrastructure of Open Screening Platforms for Chemical Biology) and ELF have a common deep interest in the discovery and development of small molecule compounds that specifically modulate the biological function of target proteins. SciLifeLab (Science for Life Laboratory) and ELF share a deep interest in the discovery and development of small molecule therapy and serving the needs of basic, applied and pharmaceutical-directing research. The REDEFAR network (Spanish Network of Excellence in Drug Discovery) and ELF share a deep, common interest in the discovery and development of small molecule compounds that specifically modulate the biological function of target proteins. In the MoU, the parties declare to exploit the complementarity and synergistic potential between their activities.
www.europeanleadfactory.eu/search/node/memorandum

Leveraging worldwide collaborations to progress research in diabetic kidney disease

BEAt-DKD project is expanding its collaboration efforts to secure access to external cohorts that would allow the testing and validation of BEAt-DKD biomarkers. So far, the project has had very productive discussions with the chronic kidney disease biomarker consortium, BioCon, of the National Institute of Health – National

Institute of Diabetes and Digestive and Kidney Disease. BioCon is a US consortium that brings together numerous cohorts and trial populations to study biomarkers of chronic kidney disease (CKD). BioCon explores a large set of targeted biomarkers and has generated vast metabolomics and proteomics data in selected subsets of their cohorts using techniques and platforms that are harmonised with the methodologies used in BEAt-DKD. In addition, the project is already collaborating with KPMP, DYNAMO, IMI2 RHAPSODY and IMI DIRECT. All these partnerships are fundamental for the two remaining years of the project, at which stage the consortium will cross-validate their results in other cohorts and populations of different ethnicities.

BEAt-DKD project is also collaborating with the H2020-MSCA-COFUND Personalised Medicine in Diabetic Chronic Disease Management (PROMINENT) educational training programme. This partnership will contribute to the education of 16 early stage researchers by providing them training in: 1) disease mechanism; 2) drug development; 3) drug registration; and 4) drug application for personalised medicine in diabetic chronic disease management. The 16 PhD students were appointed at the University of Groningen and at UMCG.

Collaboration with ECSEL

In 2019, IMI2 JU and ECSEL JU (www.ecsel.eu) further explored possibilities for cooperation between both JUs in the domain of smart health. A meeting focussing on brain health took place in March 2019. It showcased that the combination of digital technology and medical treatment can have a highly valued impact on European citizens. As a result, the JUs agreed to highlight the following themes at the IMI2 Stakeholder Forum 2019: digital recording and monitoring of early biomarkers of dementia; digital pathology; remote patient monitoring; models and simulation of function/disease. As from October 2019, ECSEL JU and IMI2 JU identified a concrete opportunity for synergies between the IMI2 Trials@Home project and a future ECSEL project to be selected following an open call for proposals to be launched by ECSEL in 2020.

In parallel, the Executive Directors presented the proposed activities to the respective Governing Boards, ECSEL JU was invited to the IMI2 SGG Digital Health, and the Programme Office attended the meetings of the ECSEL Lighthouse Initiative Health.E.

Collaborations and connections with other EU initiatives in the health cluster

IMI continues to maintain and strengthen many additional collaborations and connections with several existing EU initiatives for synergistic and/or sustainability purposes. These include:

- JPND (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.

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 2019, the review of all Call texts to ensure expected SME participation is highlighted was continued. In addition, the proposal template and evaluation criteria were updated to put more emphasis on the importance of the projects' results impacting on SMEs. All Strategic Governing Groups (SGGs) were also informed of the importance of embedding SME participation in all IMI topics.

- Communications: As in previous years, 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 2019, attracting a total of 149 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.

- Outreach: The programme of outreach established in 2016 was continued and enhanced. This included promoting SME impact in project meetings as well as giving presentations at SME events including BIO-Europe 2019; the Nordic Life Science Days partnering event; BioData World Congress and the ELIXIR Innovation and SME Forum. Opportunities in IMI were also promoted 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 project ENABLE and the IMI2 European Lead Factory (ELF) provided open platforms that allow SMEs to progress interesting drug targets and candidate molecules. The ENABLE project continued to support SME Juvabis in their evaluation of apramycin as a new antibiotic in a Phase I randomised, double-blind, placebo-controlled single ascending dose study in healthy volunteers. This is a first-in-human study to evaluate the safety, tolerability, and pharmacokinetics of apramycin, an aminoglycoside antibiotic that has demonstrated encouraging efficacy against a variety of WHO priority pathogens

In addition, the EHDEN project offers training and certification to SMEs so that they can harmonise data to the OMOP common data model. In 2019, the project ran its first data harmonisation service providers call which resulted in 11 SMEs receiving training and certification. These SMEs are now eligible to harmonise the data of the data partners identified in the data partner call. The directory of certified SMEs is available at www.ehden.eu/business-directory. Further SME calls will be held in 2020 and future years.

For the IMI2 programme, SMEs account for 15.8 % of EU funded beneficiaries (by participations), 22.5 % of EU funded beneficiaries (by participants), and receive 10.3 % of EU funding so far.

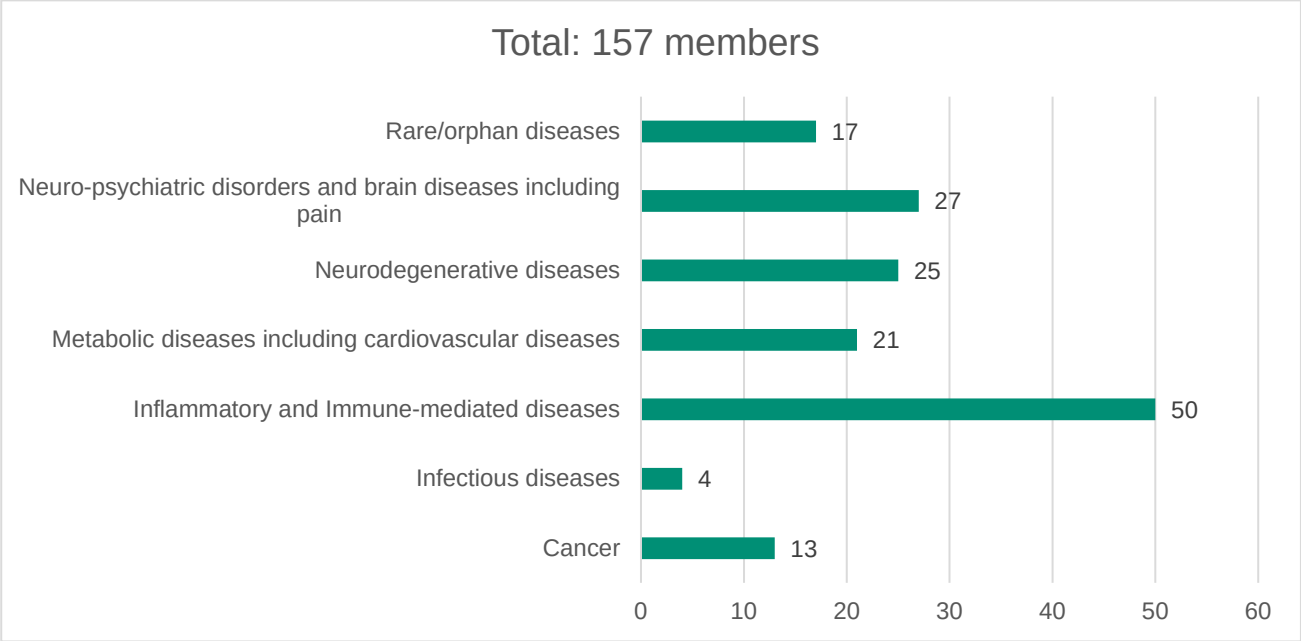
1.3.2 Patient involvement

IMI has involved patients in its projects and activities since the very beginning – as project partners, as members of the IMI Scientific Committee, and as speakers in events. As of the end 2019, close to 56 % of all IMI1 and IMI2 projects have patient organisations either as partners in the consortium or represented in advisory boards, ethics advisory boards, or being consulted for topics of relevance, while this percentage rises to almost 64 % for IMI2 projects alone.

In order to enhance the involvement of patients in its activities, in 2019 IMI established the IMI pool of patient experts. The aim of this new initiative is to provide in a rigorous and systematic way, patients' perspectives, needs and priorities within IMI2 JU activities, both at strategic and operational levels, and subsequently, improve the relevance, quality and validity of its projects.

In April 2019, IMI launched a Call for expressions of interest to identify patients and informal carers with a strong interest in fostering patient-centred innovation who would like to be part of the pool.

This exercise resulted in a pool of 157 experts coming from 26 countries. The majority (118) are patients, while 39 are informal carers, and 57 % are female. The chart below shows the breakdown of the experts by disease area.



Members of the pool are now invited on an ad hoc basis to:

- contribute to shaping the IMI2 JU portfolio and improving the quality of IMI2 JU projects from the patient perspective through early & meaningful engagement;
- support and enhance patient involvement in IMI2 JU projects;
- support the identification of patient relevant results and, where appropriate, provide input on their implementation in research, regulatory and medical practice.

These roles provide pool members with the opportunity to work alongside experts from other sectors (academia, industry, regulatory, etc.); raise the profile of patients as equal partners in research in the IMI community and beyond; and learn first-hand about the latest research developments in their disease area.

By the end of 2019, the programme office had patient experts participating in project review panels (1), and close out meetings (1), and had confirmed additional participations of patient experts in future project review panels (3).

Moreover, all the patients in the IMI pool were invited to participate in the European Commission's online survey on the strategic plan and priorities for Horizon Europe's first four years (2021-2024). They were also invited to participate in the public consultation launched by industry associations representing Europe's pharmaceutical, biotech and medical technologies industries with regard to the future research agenda of the potential European public-private partnership (PPP) in health.

In order to deploy the full potential of the IMI pool of patient experts, the Programme Office introduced in late 2019 a series of interactive sessions to take place on a regular basis. The purpose of these sessions is to build capacity, provide support and training to patients, but also to collect qualitative data to feed in to the development of IMI's patient engagement strategy. This interactive way of engaging with patients enables a two-way flow of information as all participants have the opportunity to add their comments, suggestions or questions after the completion of each session. The first session of these online series, held in November 2019, was attended by 81 patient experts and featured a general introduction on IMI2 JU's operational framework.

Furthermore, patients, carers and patient advocates participated as speakers or panellists in this year's IMI Stakeholder Forum on 'Brain health and disease in the digital era'. By bringing their unique perspective and experience, patients enriched the discussion and provided significant input on ideas for IMI Call topics that converge around the brain health / digital technologies space.

In addition, as part of IMI's efforts to share best practices and experiences on patient engagement, IMI held meetings with patient organisations at the European, international and national level as well as leading international organisations like the OECD, as well as regulatory authorities (EMA) and national health organisations (NICE).

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 continued to maintain in 2019 a close collaboration with regulators, mainly the European Medicines Agency (EMA) and FDA (US Food and Drug Administration). 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.

In addition, the IMI2 JU programme office organised in collaboration with the EMA and FDA the 6th IMI-EMA-FDA Regulatory Science Summit in December 2019. The aim of this meeting was to discuss the regulatory science challenges and opportunities that, if unblocked, would be game-changers for the use of digital research and development tools in drug development, and for the development of digital health products as well as for the development of advanced therapy medicinal products (ATMPs).

Around 50 representatives from the regulatory agencies [EMA, FDA, EU national competent authorities, Health Canada], health technology assessment bodies (EUnetHTA), notified bodies, industry, the European Commission, the IMI2 Scientific Committee and IMI Programme Office participated in the meeting. The meeting was an opportunity to discuss the key research questions relevant to advance regulatory science and from a public health perspective that would benefit from being addressed collaboratively to be step changing. The key messages from the meetings are available on the IMI website.

Interaction with the EMA and other national regulatory agencies in the EU occurred also through the Scientific Committee, and via participation in meetings like the Stakeholder Forum.

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 and FDA. This year a number of projects benefited from these services, in particular through briefing meetings at EMA for input on the project plan, and the EMA's qualification advice of novel methodologies for drug development.

1.4 Calls for proposals and grant information

1.4.1 Launch and management of IMI2 JU Calls in 2019

In 2019, three Calls for proposals were launched (IMI2 - Calls 17, 18 and 19) and two Calls were at various stages of the evaluation and granting process (IMI2 - Calls 14 and 15). The evaluations for IMI2 - Calls 13 and 16 were completed in 2018 but grant preparation and Grant Agreement signature were completed in 2019.

Each single stage and stage 2 evaluation encompasses ethics screening of the full proposals performed by a separate ethics experts' panel. In 2019, the following evaluations were concerned: IMI2 Call 14 – stage 2, IMI2 Call 15 – stage 2, IMI2 Call 17 – stage 2 and IMI2 Call 19 – 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 2019 (AWP2019) were addressed through Calls launched in 2019.

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

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

The chart also provides information on the consultation period of the IMI2 JU advisory bodies (the States Representatives Group – the SRG, and the Scientific Committee – the SC), as well as of the European Commission (EC).

There were two redress cases following the evaluation of Calls in 2019. The review committee evaluated the complaints and found no grounds to re-evaluate the two proposals.

Chart showing overview of Call processes in 2019

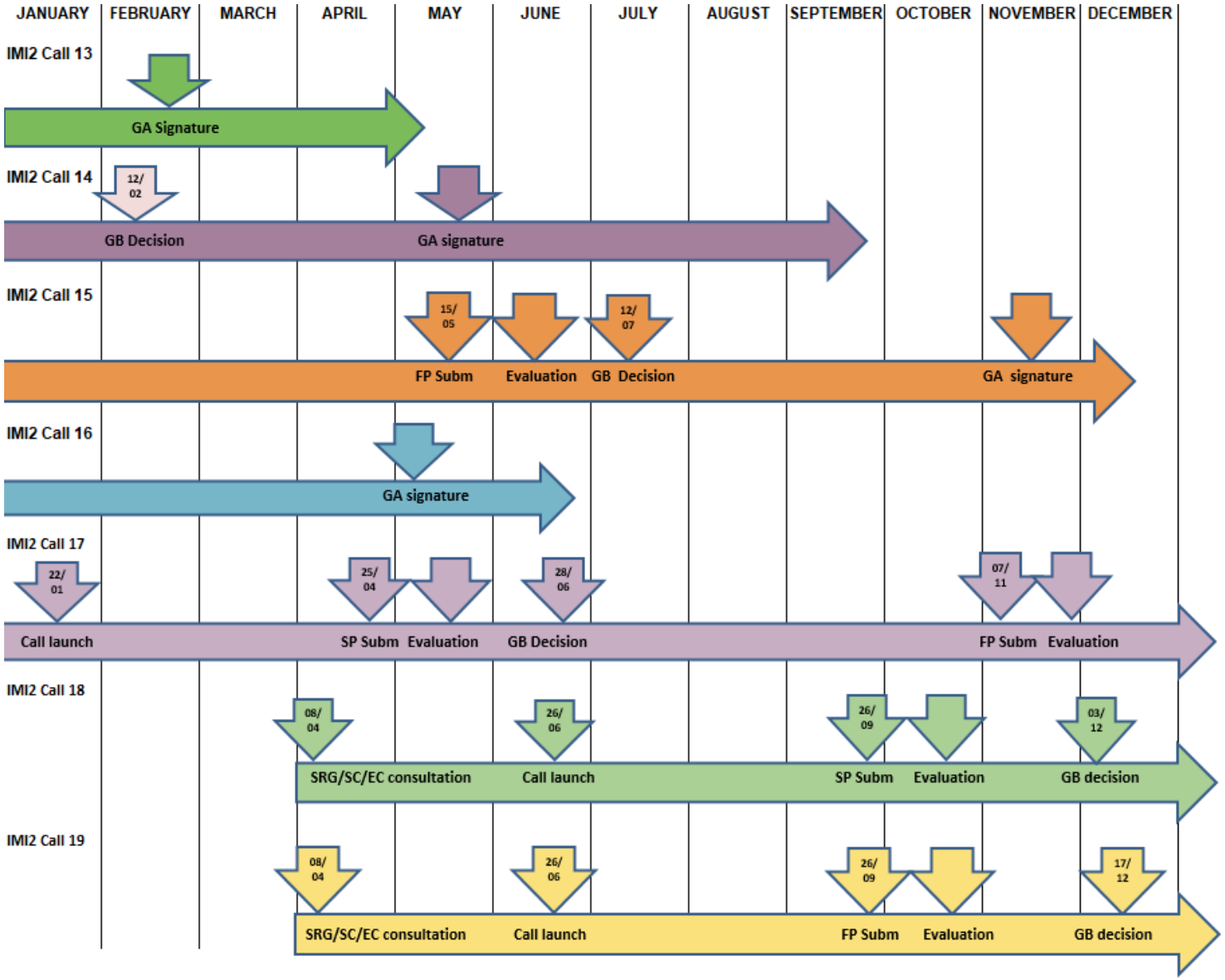


Table summarising key information related to IMI Call launches, submission deadlines and Grant Agreements signed in 2019

IMI2 Call	Topic title	Call process	Launch date	Deadline for submission of SPs	SPs received	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2019
13	▪ Assessment of the uniqueness of diabetic cardiomyopathy relative to other forms of heart failure using unbiased pheno-mapping approaches ▪ Genome-Environment Interactions in Inflammatory Skin Disease ▪ The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use ▪ Mitochondrial Dysfunction in Neurodegeneration ▪ Support and coordination action for the projects in the neurodegeneration area of the Innovative Medicines Initiative (CSA) ▪ A sustainable European induced pluripotent stem cell platform ▪ 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	Two stage	30/11/2017	28/02/2018	38	500	13	13	13

IMI2 Call	Topic title	Call process	Launch date	Deadline for submission of SPs	SPs received	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2019
	▪ 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 ▪ Centre of excellence – remote decentralised clinical trials	Two stage	15/03/2018	14/06/2018	28	384	7[2]	4	4
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	Two stage	18/07/2018	24/10/2018	42	570	8	7	7

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

IMI2 Call	Topic title	Call process	Launch date	Deadline for submission of SPs	SPs received	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2019
	▪ 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								
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 ▪ 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))	Single stage	18/07/2018	24/10/2018	6	42	5	5	5

IMI2 Call	Topic title	Call process	Launch date	Deadline for submission of SPs	SPs received	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2019
	caused by Gram(-) bacteria (Enterobacteriaceae +/- Pseudomonas and/or Acinetobacter)								
17	▪ Optimising future obesity treatment ▪ Open access chemogenomics library and chemical probes for the druggable genome ▪ Intelligent prediction and identification of environmental risks posed by human medicinal products	Two stage	22/01/2019	25/04/2019	10	136	3	3	open
18	▪ Central repository of digital pathology slides to support the development of artificial intelligence tools ▪ Health Outcomes Observatories – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes ▪ Improving patient access, understanding and adherence to healthcare information: an integrated digital health information project ▪ Establishing international standards in the analysis of patient reported outcomes and health-related quality of life data in cancer clinical trials ▪ Accelerating research & innovation for advanced therapy medicinal products ▪ Supporting the development of engineered T cells	Two stage	26/06/2019	26/09/2019	26	437	6	open	open
19	▪ Restricted Call to maximise impact of IMI2 JU objectives and specific priorities	Single stage	26/06/2019	26/09/2019	5	128	5	2	open

Table summarising IMI2 Calls for proposals launched in 2019, highlighting the priorities of Annual Work Plan 2019 implemented, the date of Call launch and budget available per Call

Call number	Call type	Number of topics	Annual Work Plan 2019 Priorities implemented	Launch date	Budget		
					EU (in EUR)	EFPIA (in EUR)	Associated Partners (in EUR)
IMI2 Call 17	Two stage	3	Diabetes/Metabolic disorders Other enablers of research topics	22/01/2019	40 786 000	35 450 000	7 658 139
IMI2 Call 18	Two stage	6	Translational safety Big data, digital health, clinical trials and regulatory research Oncology Facilitating the translation of advanced therapies to patients in Europe	26/06/2019	74 866 000	82 036 760	3 835 000
IMI2 Call 19	Single stage	1	Restricted Call	26/06/2019	20 000 000	See note	See note

Note re IMI2 – Call 19: 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 2019, IMI2 JU used 134 experts from 30 countries in the evaluation of IMI2 - Calls 14, 15, 17, 18 and 19. Most of the experts (99.25%) came from EU and Horizon 2020 associated countries. Half of the experts (67) came from academia (49) and research organisations (18). Other experts came from private for-profit entities (25), public bodies (18) and other type of organisations (24).

IMI2 JU Call	Total no. experts	Science evaluation	Ethical screening	Observers	Gender Female	Gender Male
Call 14 stage 2	27	22	4	1	10	17
Call 17 stage 1	18	17	0	1	9	9
Call 15 stage 2	52	46	4	2	27	25
Call 18 stage 1	37	36	0	1	16	21
Call 19 single stage	14	9	4	1	6	8
Call 17 stage 2	20	15	4	1	9	11

Progress / activities by Call in 2019

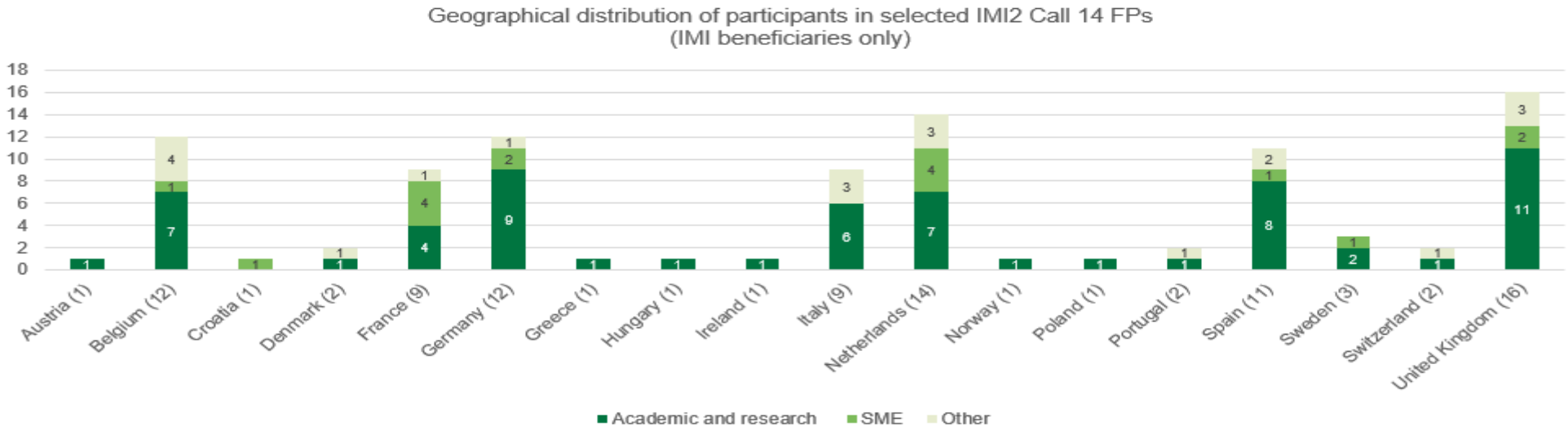
In 2019 IMI2 JU organised 6 evaluation sessions – 4 sessions for the 3 Calls launched in 2019 (IM2 - Calls 17 – stage 1 and stage 2), IMI2 - Call 18 (stage 1) and IMI2 - Call 19 (single stage) and 2 sessions for Calls launched in 2018 (stage 2 of IMI2 - Calls 14 and 15). The six evaluation sessions were completed successfully, according to the IMI rules and procedures.

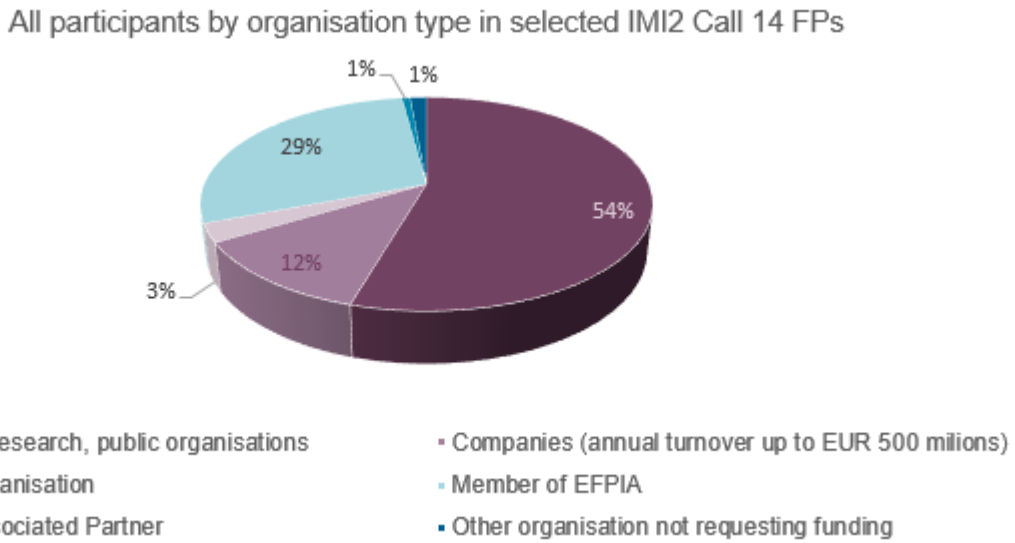
The table below presents the Calls in different stages of the process in 2019, from the Call launch until sending the letters to start GAP.

IMI2 JU Call	Call process	Number of topics	Launch date	Submission deadline S1 (or SS)	Approval of evaluation results in S1	Invitation to prepare FP in S2	Submission deadline S2	Approval of evaluation results in S2	Invitation to start GAP
Call 14	Two stage	4	15/03/2018	14/06/2018	03/08/2018	10/08/2019	11/12/2018	12/02/2019	19/02/2019
Call 15	Two stage	8	18/07/2018	24/10/2018	18/12/2018	08/01/2019	15/05/2019	12/07/2019	16/07/2019
Call 17	Two stage	3	22/01/2019	25/04/2019	28/06/2019	04/07/2019	07/11/2019	Open	Open
Call 18	Two stage	6	26/06/2019	26/09/2019	03/12/2019	06/12/2019	26/03/2020	Open	Open
Call 19	Single stage	1	26/06/2019	26/09/2019	17/12/2019	N/A	N/A	N/A	18/12/2019

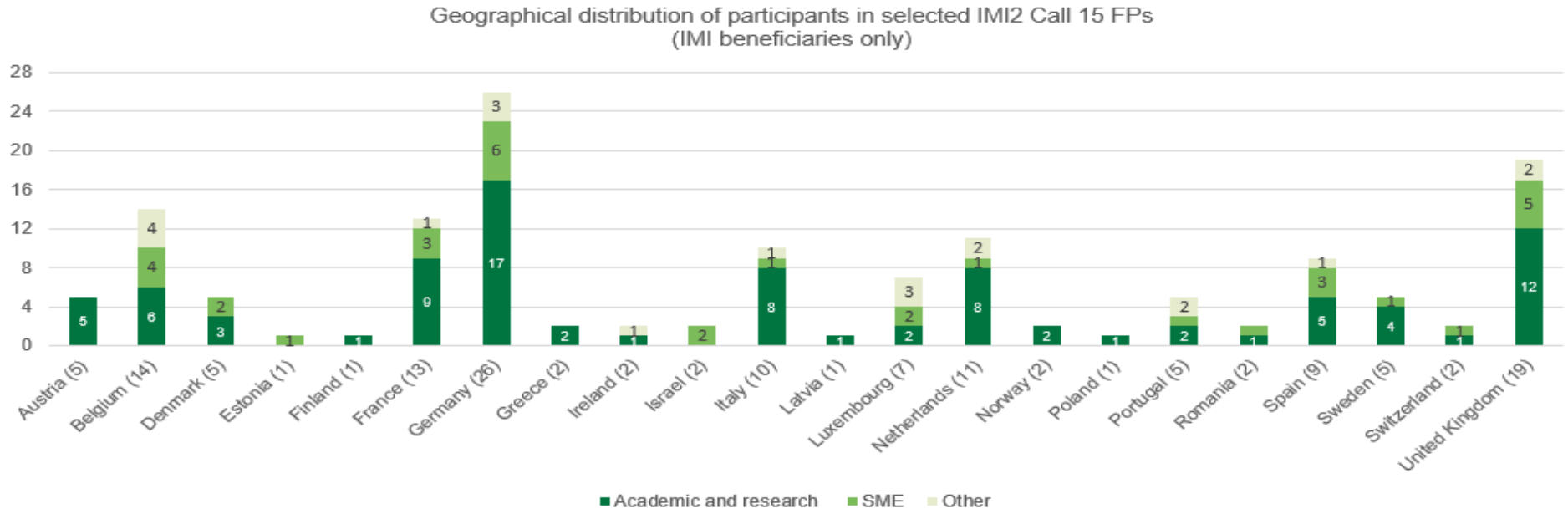
Participant details

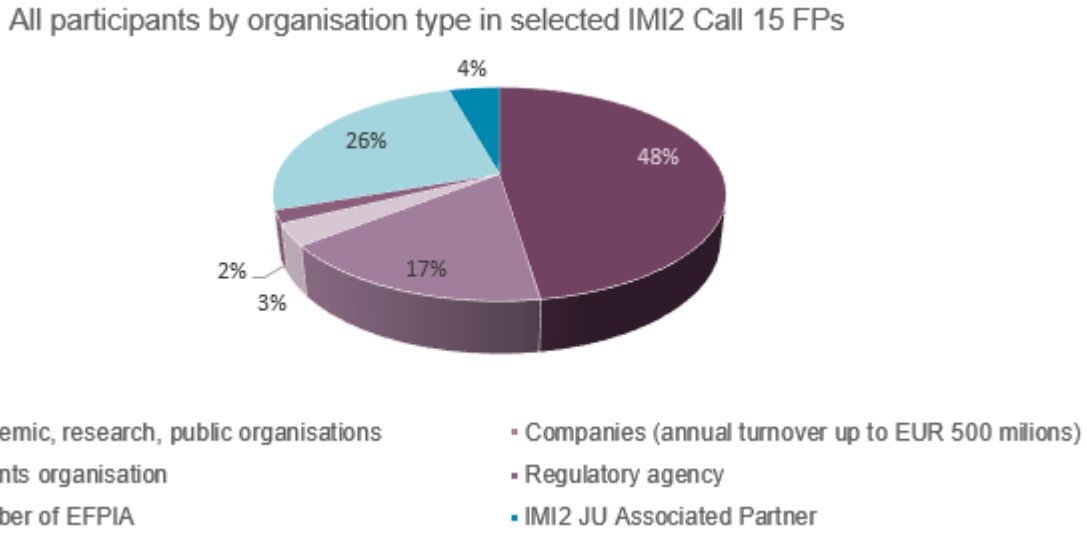
IMI2 – Call 14: Full proposal participant details



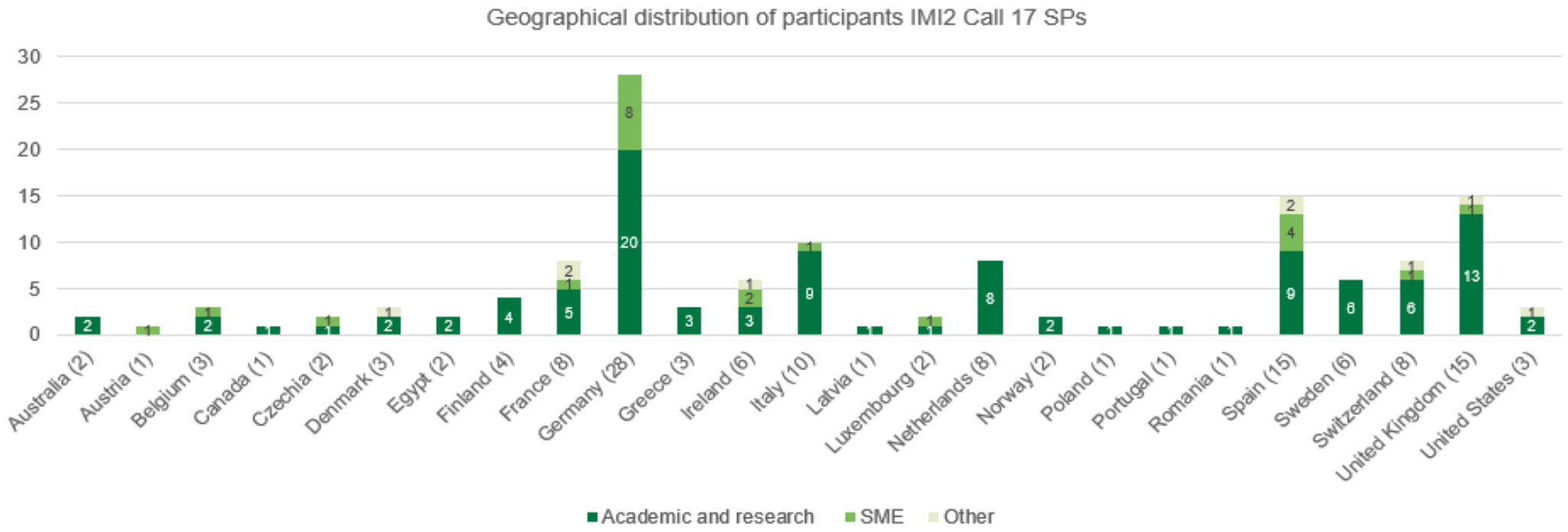


IMI2 – Call 15: Full proposal participant details

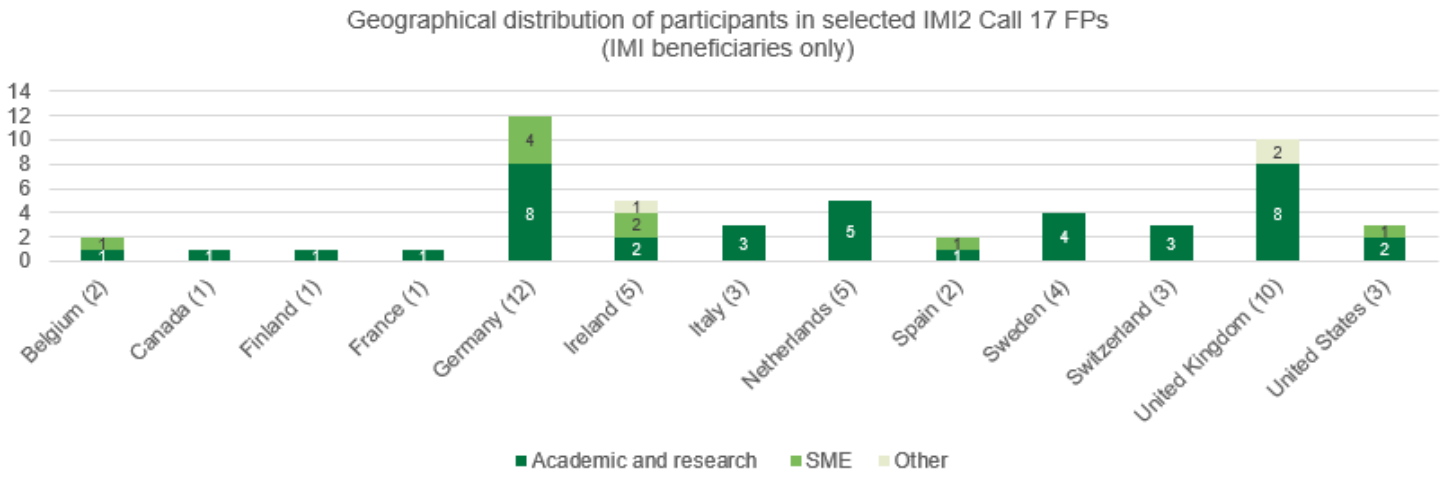


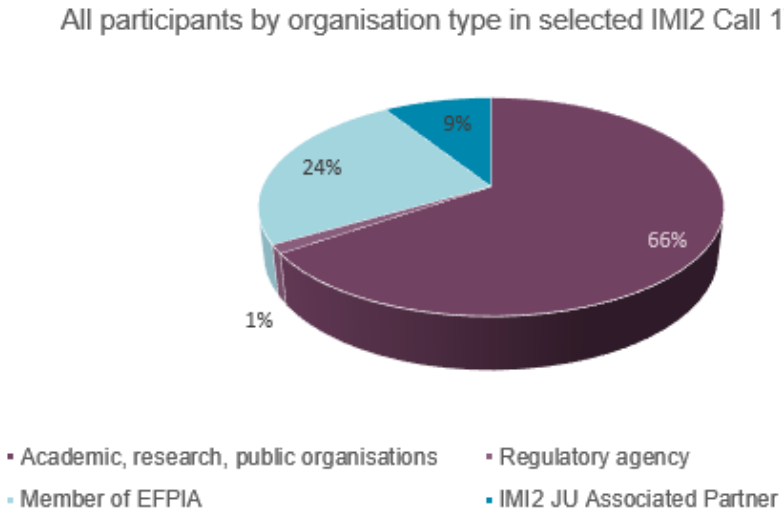


IMI2 – Call 17: Short proposal participant details

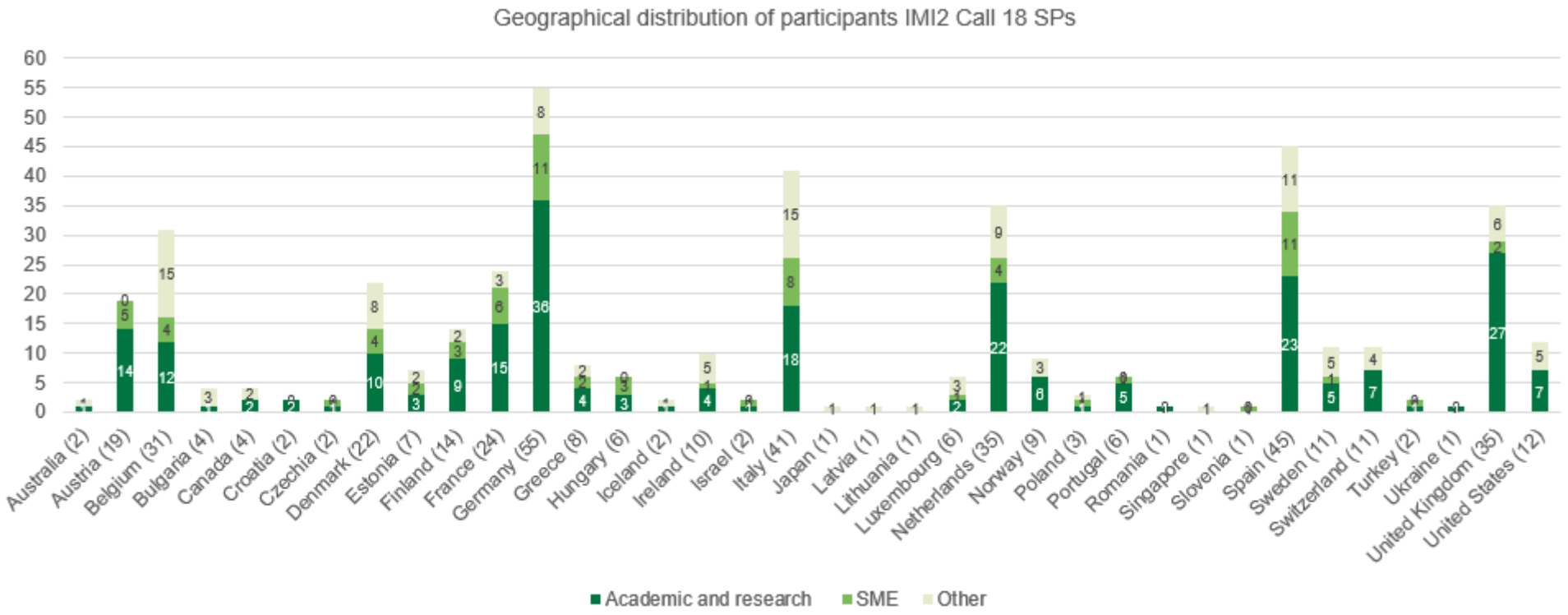


IMI2 – Call 17: Full proposal participant details

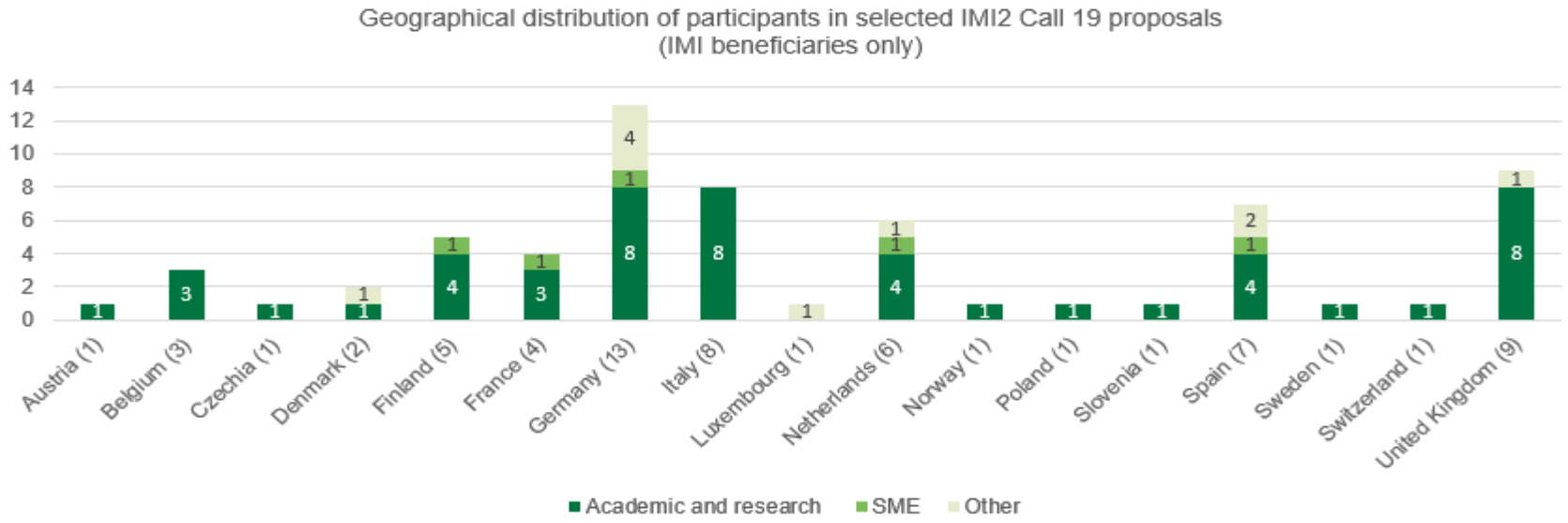




IMI2 – Call 18: Short proposal participant details



IMI2 – Call 19: Proposal participant details



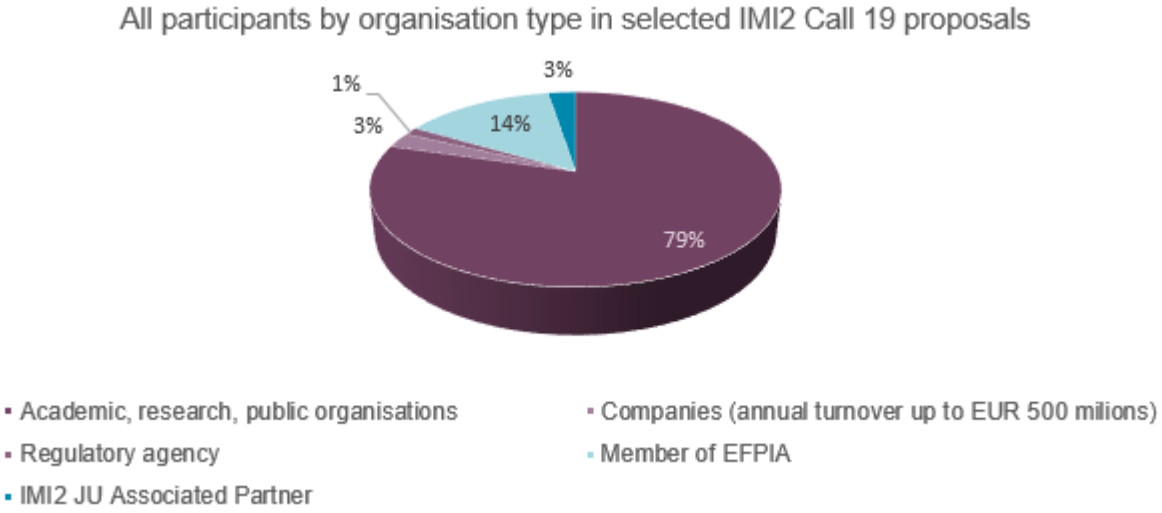


Table summarising the number of beneficiaries and budgets for projects with GAs signed in 2019

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)
13	PD-MitoQUANT	10	3	1	3 960 725.00	537 210.00		0.00	4 497 935.00	2 293 600.00	168 000.00	6 959 535.00
13	BIOMAP	27	5	0	8 857 521.00	1 017 110.00		625 368.75	10 499 999.75	10 384 847.00		20 884 846.75
13	EBiSC2	7	10	0	4 374 648.00	225 000.00		0.00	4 599 648.00	4 272 964.00		8 872 612.00
13	NEURONET	3	5	1		588 250.00	307 625.00	303 250.00	1 199 125.00	1 010 000.00	144 000.00	2 353 125.00
13	NeuroDeRisk	11	7	0	3 999 500.00	748 200.00		583 300.00	5 331 000.00	4 346 500.00		9 677 500.00
13	MOBILISE-D	24	12	0	23 543 297.00	1 852 600.00		0.00	25 395 897.00	23 965 667.00		49 361 564.00
13	VALUE-Dx	20	4	3	6 092 967.00	72 411.00		633 722.00	6 799 100.00	2 782 607.00	4 158 220.20	13 739 927.20
13	TransBioLine	20	7	0	6 700 166.75	6 928 285.00	182 600.00	188 946.00	13 999 997.75	13 906 494.00		27 906 491.75
13	CARDIATEAM	27	3	0	5 766 410.05	420 631.25		512 958.70	6 700 000.00	6 000 000.00		12 700 000.00
13	STOPFOP	5	1	0	529 506.00			470 204.00	999 710.00	1 000 000.00		1 999 710.00
13	IMMUcan	19	9	0	16 119 667.10	0.00	250 000.00	1 460 332.90	17 830 000.00	16 850 000.00		34 680 000.00
13	PD-MIND	8	1	1	882 510.75	100 937.25	16 250.00	0.00	999 698.00	1 000 000.00	117 559.00	2 117 257.00
13	ConcePTION	44	15	0	12 812 015.75	1 054 843.00		1 433 132.25	15 299 991.00	13 387 500.00		28 687 491.00
14	MELLODDY	7	10	0	2 598 303.00	5 401 697.00		0.00	8 000 000.00	10 000 000.00		18 000 000.00
14	Trials@Home	17	14	0	13 166 685.50	2 432 284.50	649 212.50	2 788 815.00	19 036 997.50	19 248 295.00		38 285 292.50
14	3TR	74	8	0	33 635 913.18	2 708 813.49	70 416.25	3 858 048.58	40 273 191.50	40 350 000.00		80 623 191.50
14	Immune-Image	16	7	0	13 400 000.00	1 100 000.00	100 000.00	400 000.00	15 000 000.00	12 154 527.00		27 154 527.00
15	imSAVAR	17	10	1	9 468 010.00	928 750.00		602 556.25	10 999 316.25	11 246 496.00	105 000.00	22 350 812.25
15	COMBINE	8	3	0	4 548 260.00	1 880 625.00		1 571 115.00	8 000 000.00	17 460 100.00		25 460 100.00
15	EU-PEARL	23	10	3	9 272 702.50	1 955 375.00	459 250.00	317 625.00	12 004 952.50	11 957 083.00	2 276 012.00	26 238 047.50
15	ERA4TB	26	3	3	42 634 850.00	3 647 500.00		43 533 250.00	89 815 600.00	48 484 443.00	69 663 848.00	207 963 891.00

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)
15	PharmaLedger	17	11	0	2 736 000.00	4 590 318.75	247 500.00	716 875.00	8 290 693.75	12 630 208.00		20 920 901.75
15	ImmUniverse	22	5	0	14 359 092.50	1 028 563.75	112 343.75	0.00	15 500 000.00	15 500 000.00		31 000 000.00
15	IDEA-FAST	39	11	1	17 410 985.00	3 301 537.50	285 000.00	0.00	20 997 522.50	19 262 286.00	197 250.00	40 457 058.50
16	RespiriNTM	8	1	0	5 363 368.75	324 615.00		0.00	5 687 983.75	2 357 657.00		8 045 640.75
16	RespiriTB	8	1	0	6 529 019.37	310 980.63		0.00	6 840 000.00	3 122 900.00		9 962 900.00
16	TRIC-TB	1	1	0		6 926 375.00		0.00	6 926 375.00	1 417 500.00		8 343 875.00
16	GNA NOW	11	1	0	7 609 813.75	4 690 181.25		0.00	12 299 995.00	19 115 992.00		31 415 987.00
16	AB-DIRECT	6	1	0	3 093 592.00			335 625.00	3 429 217.00	360 500.00		3 789 717.00

Note: The total budgets indicated here do not include additional funds brought in to projects from sources other than IMI, EFPIA or Associated Partners.

1.4.2 Interim reviews for IMI projects

In 2019, IMI conducted 22 reviews of projects from IMI2 – Calls 2, 3, 5, 6, 7, 8, 9 and 10 as shown in the table below:

IMI project acronym	Full project name	IMI2 Call #	Date
NGN-Pet	Modelling neuron-glia networks into a drug discovery platform for pain efficacious treatments	Call 7	21/01/2019
RHAPSODY	Assessing risk and progression of prediabetes and type 2 diabetes to enable disease	Call 3	23/01/2019
COMBACTE-CDI	Combatting Bacterial Resistance in Europe - Clostridium Difficile Infections	Call 9	14/02/2019
BEAT-DKD	Biomarker enterprise to attack DKD	Call 5	01/04/2019
PHAGO	Inflammation and AD: modulating microglia function - focussing on TREM2 and CD33	Call 5	11/04/2019
RADAR-CNS	Remote Assessment of Disease and Relapse in Central Nervous System Disorders	Call 5	10/05/2019
EBOVAC1	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	Call 2	20/05/2019
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: phase II	Call 2	21/05/2019
EBODAC	Communication strategy and tools for optimizing the impact of Ebola vaccination deployment	Call 2	21/05/2019
PREFER	Patient Preferences in benefit risk assessments during the drug life cycle	Call 5	18/06/2019
PERISCOPE	Pertussis correlates of protection Europe	Call 3	18/06/2019
TRISTAN	Imaging biomarkers (IBs) for safer drugs: validation of translational imaging methods in drug	Call 7	24/06/2019
EQIPD	European Quality In Preclinical Data	Call 9	25/06/2019
IMPRIND	Inhibiting misfolded protein propagation in neurodegenerative diseases	Call 7	28/06/2019
DRIVE	Development of Robust and Innovative Vaccine Effectiveness	Call 9	17/09/2019
VSV EBOPLUS	Vaccine safety and immunogenicity signatures of human responses to VSV-ZEBOV	Call 3	24/09/2019
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	Call 10	09/10/2019
ITCC-P4	ITCC pediatric preclinical POC platform	Call 7	13/11/2019
HARMONY	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology	Call 6	19/11/2019
PEVIA	Pan Ebola vaccine innovative approach	Call 8	29/11/2019
BigData@Heart	Big data @ heart	Call 7	03/12/2019
c4c	conect4children - Collaborative network for European clinical trials for children	Call 10	09/12/2019

Each expert reviewer panel consisted of at least three experts, including one from the IMI Scientific Committee and one from the full proposal evaluation panel.

NGN-Pet

The experts found that the project has achieved most of its objectives and milestones for the period with relatively minor deviations and that the project will likely provide results with significant immediate or potential impact in the next reporting period. In particular, the project has developed two models of neuropathic pain that have been established in two laboratories. The pieces are in place to obtain DRGs from the animal models for the next phase of the work. Microdialysis has been set up and preparatory work for high content screening has taken place on a neuroblastoma. In addition, hiPSC-derived neurons have been prepared and specifically a workhorse cell line that shows appropriate viability after freeze-thaw, has been generated. The experts provided a number of recommendations to the project for consideration in their last period.

RHAPSODY

RHAPSODY aims to improve diabetes prevention and treatment by improving our understanding of the factors that drive the progression of pre-diabetes to diabetes, and the deterioration of the condition of people with diabetes. RHAPSODY is working towards development of novel biological markers that will aid in the diagnosis of type 2 diabetes, and the identification of different sub-groups of patients. The reviewers were very positive about the project's progress and achievements so far despite some delays experienced by the project. They emphasised the importance of sustaining the RHAPSODY federated database and analytical tools beyond the project timeframe, as well as making it available to researchers outside of the project. The reviewers also unanimously endorsed the project's plans for a 12 month, no cost extension that would allow it to compensate the delays accumulated due to certain unforeseeable circumstances. Furthermore, the reviewers recommended to maintain interaction with regulatory agencies, and in particular EMA, after the completion of the project in order to secure the final regulation/acceptance of the biomarkers developed by the project.

COMBACTE-CDI

COMBACTE-CDI aims to develop a detailed understanding of the epidemiology and clinical impact of *Clostridium difficile* (CDI) across multiple European countries. The panel noted that despite being a challenging project (ambitious objectives to be achieved within a limited budget and timeline), a number of achievements were made notably with the recruitment of sites from 12 countries for the two sampling days study, the ethical approval obtained from each country/site according to local/national guidelines, the development of a case report form to obtain patient details for cases and controls, and the development questionnaire to obtain country information on CDI diagnosis and treatment.

The panel welcomed the innovative scientific findings obtained so far, e.g. the variation in the *Clostridium difficile* strain types, the difference in testing sensitivity and its potential value for clinical practice, the observation of co-infections. In addition, the panel positively viewed the use of new laboratory testing that may provide opportunities for clinical implementation. The panel was of the opinion nonetheless that the impact of the results would have to be carefully considered in view of the low number of samples from different settings and countries. The panel made some recommendations to the consortium with the view to maximise the impact of the project results.

BEAT-DKD

The BEAt-DKD project aims to deliver tools and knowledge that will facilitate the development of new, personalised treatments for diabetic kidney disease (DKD). The project plans to identify and validate biological markers to help researchers track whether a patient's condition has progressed, and whether a treatment is

working for them. They are also working towards the identification of different sub-groups of patients that respond differently to certain treatments. BEAt-DKD's results are already paving the way for the development of effective personalised treatments for DKD. The reviewers found the project very relevant and on track. The main recommendations focused on ensuring the sustainability of the project results and databases, considering correlation of other complications of diabetes, such as cancer, with kidney disease markers, and considering organising dedicated trainings on the relevant GDPR regulations, addressing protection of research data, secondary use of data and processing of information.

PHAGO

PHAGO aims to improve Alzheimer patient outcomes through a better understanding of the biology of two genes involved in the immune system, TREM2 and CD33, and their biological networks and pathways, and pave the way for the development of therapies aimed at modulating the immune dysfunction in Alzheimer's disease.

The reviewers found that PHAGO is a successful consortium, which has already achieved significant results paving the way for further development of the project according to the original planning. High profile publications have been delivered on some of the attained results.

To maximise the impact of the project results, the panel made some recommendations to the consortium to enhance the dissemination of the new tools, assays and animal strains developed and include the potentially broader roles of TREM2/CD33 in other medical fields and diseases in their exploitation plans.

RADAR-CNS

The experts found that the project has achieved most of its objectives and milestones for the period with relatively minor deviations and that the project will likely provide results with significant immediate or potential impact in the next reporting period. In particular the experts found that the open source platform, RADAR-BASE, released in Q1 2018, had already demonstrated a high impact by being used for many additional studies. The project has also been very active in disseminating and publishing the initial scientific results in conferences, journal and other events. For example, results on acceptance and adherence concerning remote monitoring technologies have been obtained and partly published. The experts made some recommendations including paying particular focus to study recruitment, and suggested a 12-month extension may be necessary to maximise the impact of the data obtained in the studies.

EBOVAC1, EBOVAC2, EBODAC

A panel of experts carried out the interim reviews of EBOVAC1, EBOVAC2 and EBODAC by reviewing all three projects one after another.

All three projects are devoted to supporting the development of the Johnson & Johnson (J&J) candidate vaccine regimen against Ebola virus disease (EVD). In November 2019, J&J submitted marketing authorisation applications to the EMA seeking licensure for this investigational Ebola vaccine regimen for the prevention of EVD.

The panel of reviewers was overall very satisfied by the progress achieved by all three projects and the amount of very important data collected and outputs delivered by the projects so far.

One recommendation that was common to all three projects was that it would be of great benefit if EBOVAC projects together with EBODAC organise a final symposium where overall findings are presented to the international community and where new connections can be made for future investigations and collaboration.

PREFER

PREFER looks at how and when it is best to perform and include patient preferences in decision making during the medical product life cycle. The panel appreciated the excellent work the consortium has done so far in addressing clinical and methodological research questions. This is an ambitious project and the consortium accomplished a number of important research in a high scientific quality manner. While the panel viewed the first results very promising, the real impact will be visible once the results of the ongoing case studies are available. The panel was very positive with the initiation of a joint EMA - HTA qualification procedure, the development of training modules based on the learnings from the project as well as of the sustainability plan. The panel made a number of recommendations to the consortium with the view to further maximise the impact of the project results.

PERISCOPE

The PERISCOPE project is working to better understand how the currently available vaccines work, and to aid the development and licensing of the next generation of improved *Bordetella pertussis* vaccines. The reviewers deemed that PERISCOPE has so far produced important scientific and technological outputs such as study protocols and the necessary analytical tools in order to understand better the immunological response to both *Bordetella pertussis* (Bp) infection and vaccination. The results delivered so far by PERISCOPE are likely to have a major impact in the field of pertussis vaccination. Indeed, the development of study protocols, proof of concept and production of analytical standards for understanding the complex immune response to both Bp infection and vaccination will allow the development of new vaccine development and vaccination strategies.

TRISTAN

The aim of TRISTAN is to validate the use of imaging biomarkers to assess and predict the toxicity of potential medicines on the liver and lungs. It also aims to improve the use of imaging to avoid side effects which arise when certain types of drugs, such as therapeutic antibodies, go to the wrong part of the body. The imaging biomarkers will help translate pre-clinical (animal) findings to healthy volunteers and patients, and clinical trial findings to real-world patients, improving the success of drug development.

The reviewers found that the project has in general achieved the objectives for the reported period and made some technical recommendations on the implementation. They did not identify a major breakthrough in the results obtained so far. However, the future plans, if successful, should lead to very significant impact in predicting toxicity linked to new pharmaceuticals.

EQIPD

Translation of new drugs from preclinical studies to clinical use has failed especially in neurodegenerative diseases (e.g., psychiatric diseases and Alzheimer's disease). There is therefore an urgent need for developing new guides and tools for predicting/monitoring efficacy of new drugs and for searching new sustainable solutions to improve data quality from experimental to clinical practice. Combining the experience of academic and private industry, EQIPD aims to deliver simple, user-friendly recommendations for preclinical data quality.

The project has achieved most of its objectives and milestones for the reviewed period. The consortium has made significant progress, and, apart from some minor delays, is completely on track to finish the agreed-upon work in the allotted timeframe. Much preparatory work has been done for activities planned at a later stage. Collaboration between all the partners for the period was demonstrated and excellent.

Few recommendations were made by the reviewers, especially for the results' dissemination and building adherence of the scientific community to the new guide developed to strengthen the robustness, rigor, and validity of preclinical research data.

IMPRIND

The IMPRiND project aims to understand how aggregated proteins tau and α-synuclein (misfolded proteins which clump together leading to a progressive spreading of neurodegeneration) are handled once inside brain cells and how they are moved from cell to cell. To do this, the project team works collaboratively to develop standardised tools and tests to establish disease-relevant mechanisms that could be targeted by drugs in the future.

The reviewers found that the project has significantly progressed in all of its objectives. A remarkable amount of work has been conducted toward identification of the structural biophysical nature and functional pathological hallmarks of the assemblies and optimization of existing and new in vitro and in vivo models. Results have been published, which contribute to the knowledge and understanding of brain diseases. The reviewers also noted several delays due to technical difficulties that have affected some deliverables but do not impact strongly on the possibility to achieve the final goals of the project. The reviewers asked the consortium to put in place a robust strategy to make models and tools available to the wider community and made some specific technical recommendations to improve the implementation of the project.

DRIVE

The goal of the DRIVE project is to set up a platform, bringing together all stakeholders, to study brand-specific flu vaccine effectiveness in the EU over a five-year period. At the heart of the platform will be a governance framework that allows transparent and efficient collaboration between public and private stakeholders. An early review of DRIVE was requested by the panel of experts following the stage 2 evaluation of the full proposal. At the early review in September 2019, the panel of reviewers deemed DRIVE as a complex and very challenging project, and its development and results will potentially have significant implications for the EU. On the one hand, the results could help support public health authorities by providing yearly influenza vaccine effectiveness (IVE) to evaluate the impact of their influenza vaccination programmes. On the other hand, it would also contribute to fulfil the EMA requirement on the knowledge of vaccine effectiveness per specific vaccine brand. Following the early review, the panel of reviewers considered that DRIVE has achieved most of its objectives and milestones for the period with relatively minor deviations and the project will likely provide results with significant immediate or potential impact in the next reporting periods. However, given that the project is still in the early phase, the dissemination of significant results is not expected yet.

VSV EBOPLUS

The VSV-EBOPLUS project ensures the follow-up of very important developments in an earlier project focused on early clinical development of a vaccine against Ebola. It aims to decipher immune and molecular signatures of the host response to a single intramuscular administration of different doses of VSV-ZEBOV vaccine (developed by MSD) using a systems biology approach. Important samples had been collected to evaluate immunogenicity of the vaccine and potentially find biomarkers for safety issues and immunogenicity.

The panel of reviewers was impressed by the progress achieved and the amount of work delivered by the consortium partners. One recommendation from the panel was to increase the visibility of the project via regular update on project achievements in the project website.

PARADIGM

The overarching mission of PARADIGM is to develop a framework that allows structured, meaningful, sustainable and ethical patient engagement throughout three key decision-making points of the development of medicinal products:

- research priority setting,
- design of clinical trials, and

- early dialogue.

In addition, the PARADIGM will also produce a set of metrics to measure the impact of patient engagement.

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 expected project's results, the panel made some recommendations to the consortium on the methodology and including stakeholders' point of view.

ITCC-P4

ITCC-P4 aims to address the significant preclinical gap in identifying promising molecules to fight paediatric cancer by enabling thorough molecular characterisation of high-risk paediatric malignancies coupled with standardised preclinical testing procedures. The panel was extremely positive with the progress and achievements made so far, notably with the establishment of patient derived xenografts (PDX) models as well as genetically engineered mouse models (GEMMs) and organoids for some indications, the conduct in a systematic and impressive way of reviewing actionable targets, the development of the business model for use of the models and platform to document paediatric oncology indications. The panel congratulated the consortium for the exemplary highly collaborative spirit between academia and industry and for the whole platform approach that goes well beyond delivering models for non-clinical testing and has the potential to transform the field. The panel made a couple of recommendations to the consortium with the view to further maximise the impact of the project results.

HARMONY

Harmony is an ambitious project to use big data from public and private sources to resolve key questions about haematological malignancies. The panel of reviewers was overall very satisfied by the progress achieved and the amount of work delivered by the consortium partners. Among other recommendations, the panel recommended to update the project risk management and dissemination plan.

PEVIA

The project aims to develop a pan-filovirus vaccine covering the different Ebola subtypes and Marburg, based on an innovative and very challenging approach. Despite encouraging results provided by the academic partners of the consortium, overall the panel identified significant concerns that require appropriate follow up.

BigData@Heart

The aim of BigData@Heart is to apply big data approaches to common cardiovascular diseases (CVDs), namely, acute coronary syndrome, atrial fibrillation, and heart failure in the hope to improve patient outcomes. The project's ultimate goal is to develop a big data-driven translational research platform of unparalleled scale and phenotypic resolution. The research platform is expected to deliver clinically relevant disease phenotypes, scalable insights from real-world evidence driving drug development and personalized medicine through advanced analytics.

The panel of reviewers concluded that the project has achieved in general the objectives for the reported period and made some recommendations on the implementation. The panel highlighted the necessity of identifying a concrete plan to address the accumulated delays and to ensure the on time completion of deliverables. In addition, the importance of using further dissemination platforms to reach a broader audience was also recommended.

c4c

c4c aims to address current gaps in paediatric clinical trial research through the establishment of the structure and processes to be used by this pan-European clinical trial network. This was an early review and the panel considered that major progress was made in this important, ambitious and challenging project notably towards organising a productive network (infrastructure, processes and integration), producing a core set of metrics necessary to further enable high quality trials, and identifying the proof of viability (PoV) studies to be done. The panel viewed the development of some new national hubs as an important impact. The panel noted that the consortium despite being very large is composed of highly experienced and enthusiastic partners that work very well together and are very well aware of the challenges. The panel highlighted that it was too early to judge the impact of the project as the actual successful conduct of the trials by the network has yet to be demonstrated. The panel made a number of recommendations to the consortium with the view to maximising the impact of the project results and support the need for an additional review at mid-term of the project.

1.4.3 Progress against key performance indicators (KPIs) and statistics

IMI's performance framework sets out 10 key performance indicators (KPIs) that track IMI's progress towards meeting the ambitious objectives set out in the IMI2 legislation. The KPIs focus on the following elements:

(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 programmes 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.

The 10 KPIs were tracked and reported on for the first time in the AAR 2018. In 2019, IMI continued to track these performance indicators and moved from an online, survey-based methodology to a permanent online, platform-based methodology. This platform offers project coordinators a user-friendly KPI reporting environment. For IMI, as well as ensuring faster, more accurate reporting, the system facilitates data collection, aggregation, and analysis and provides the opportunity to build a history of project achievements that will be accessible over time.

Although the KPIs are officially aligned with the IMI2 programme, IMI also collects data on IMI1 projects where relevant. This shows that IMI projects continue to deliver results and impacts long after the IMI funding period has finished, and also tells the long-term story about the partnership between the EU and the pharmaceutical industry.

The analysis of the data collected up to 31 December 2019 shows that the following priority areas in the IMI2 Strategic Research Agenda (SRA) are addressed by IMI2 projects: antimicrobial resistance; cardiovascular diseases; diabetes; neurodegenerative diseases; psychiatric diseases; respiratory diseases; immune-mediated diseases; ageing-associated diseases; cancer; rare/orphan diseases; and vaccines.

An examination of the data shows that IMI2 projects have generated 54 assets that completed a significant milestone during the project lifecycle (versus a target of 50). If we look at both IMI1 and IMI2 programmes together, the analysis shows that IMI projects have reached 131 assets that completed a significant milestone so far. The terms 'projects' asset and achievements' 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 10 completed procedures (versus a target of 10) and if we look at both IMI1 and IMI2 programmes together, there are 28 complete procedures.

Several new tools and processes generated by IMI2 projects have been implemented by the industry participants (examples of implementations are animal models, standards, biomarkers, standard operating procedures (SOPs), use of screening platforms, clinical trial networks, etc.). The data shows 44 implementation results in IMI2 (versus a target of 50) and 228 implementation results if we consider both IMI1 and IMI2 programmes together.

Additionally, more than half of the projects involve patient organisations and associations of healthcare professionals as consortium partners, members of advisory boards, members of stakeholder groups etc. (63.79 %).

Globally, an analysis of the KPIs reveals a dynamic in which IMI2 projects are getting on track compared to the established targets now that we are in the middle of the IMI2 programme's cycle. It is clear that the projects need time to generate innovations and impacts that can be detected and reported; many project 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 driven by the complex and long-term 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, the longer-term outputs and impacts of the IMI1 and IMI2 programmes (starting from the finished projects that have had some time to generate more longer terms results) for the ultimate benefit of patients, as well as European competitiveness, economic growth, and the advancement of science and innovation.

With this purpose, in 2019 IMI carried out a significant assessment of the socio-economic impact of the 44 IMI1 projects that had finished. This was accomplished using the previously developed methodology that entails reviewing the projects' final reports as well as conducting surveys and interviews with project coordinators and participants, with the support of an external consultant. The final report will be published in early 2020.

In addition, the Programme Office also collects data to report against the relevant standard H2020 key performance indicators, with the goal of tracking IMI's contribution to achieving the objectives of H2020, 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 projects results

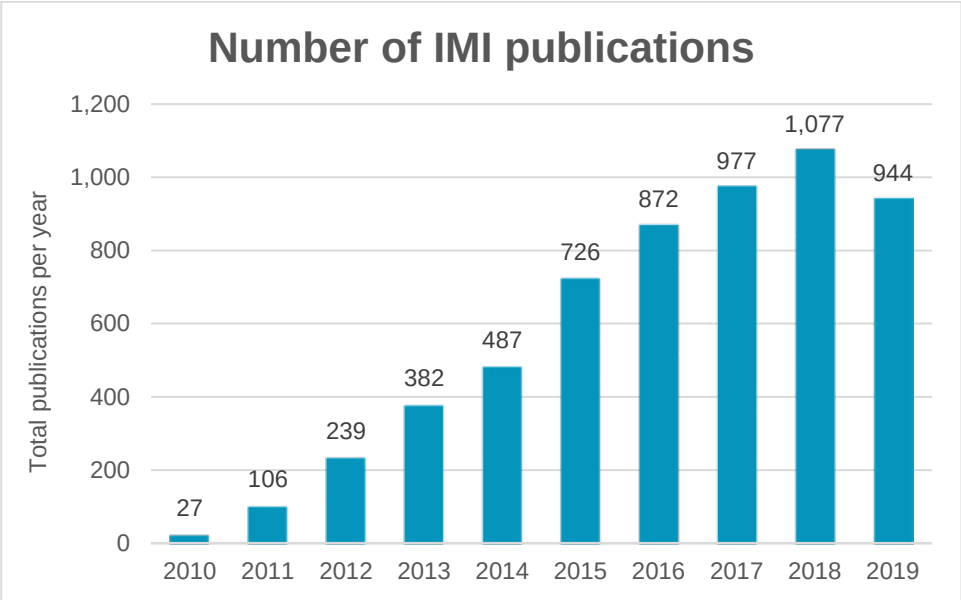
IMI projects are delivering diverse tools, resources and methodologies that are helping to change and improve the way new medicines are discovered and developed. This section describes how these resources, and information on them, are disseminated by the project partners. Scientific publications are 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

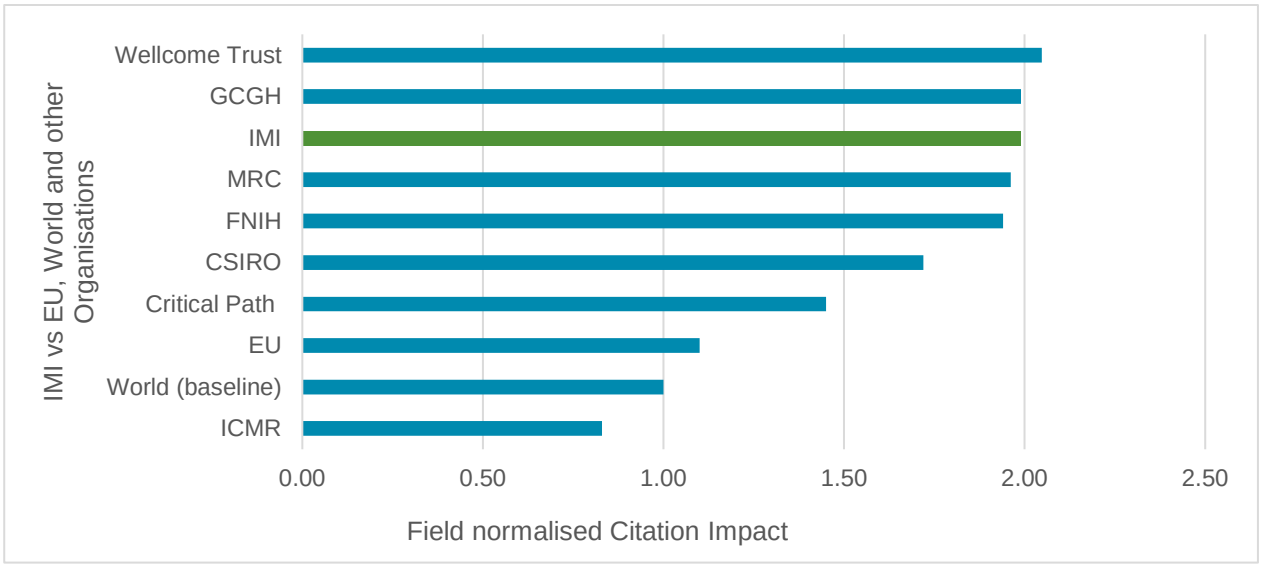
IMI has been monitoring and analysing the papers coming out of its projects since 2012. The analyses, carried out by Clarivate Analytics (formerly Thomson Reuters) have consistently demonstrated both the sheer volume and high quality of research taking place in IMI projects.

As the graph below shows, the number of publications is increasing year-on year. In 2019 alone, IMI projects produced nearly **1 000** publications (944), bringing the total number of publications produced by IMI projects between 2010 and 2019 to **5 837**. With the number of IMI projects on the rise, this trend is set to continue for the coming years.



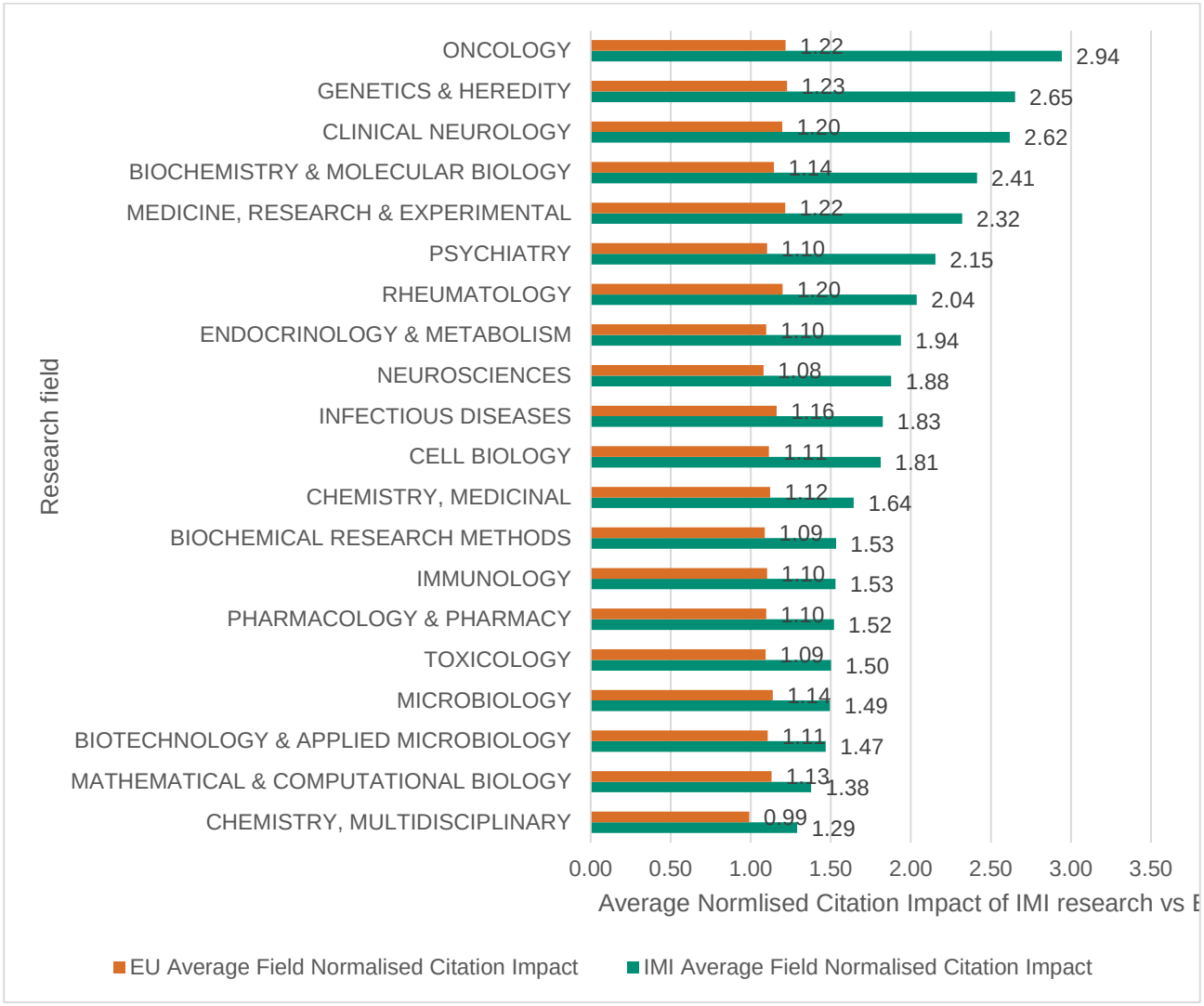
The citation impact of IMI research is higher than EU and world averages

The field-normalised citation impact for all IMI papers is **1.99** (compared to 1.10 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 below shows, IMI research is published in a range of fields within the biomedical sector. In all fields, IMI research has a higher citation impact than the EU average. This is most notable in oncology, genetics and heredity, clinical neurology, biochemistry & molecular biology, where the IMI citation impact is between 2.4 and 3.



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

- 25.33 % 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 1 150 journals to date, and the average journal impact factor for IMI research is 6.50;
- journals with a particularly high impact factor that have published IMI research include 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 (62 %) 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, the citation impacts range between 1.41 and 3.72.

Top 10 IMI projects producing the highest number of publications

Project	Total publications	Mean field normalised citation impact
BTCure	667	1.95
EU-AIMS	431	2.12
ULTRA-DD	279	1.83
EMIF	263	2.51
NEWMEDS	196	2.17
EUROPAIN	171	2.38
CANCER-ID	151	3.72
ORBITO	149	1.76
IMIDIA	143	1.65
TRANSLOCATION	136	1.41

Top 10 journals by number of IMI publications

Between 2010 and 2019, IMI published papers in **1 150 different journals**. The 10 journals in which IMI projects most frequently published are listed in the table below, along with the journal impact factor (JIF).

Rank	Title	JIF	IMI papers
1	PLoS ONE	2.78	169
2	Scientific Reports	4.01	131
3	Annals of the Rheumatic Diseases	14.30	115
4	Nature Communications	11.88	68
5	Diabetologia	7.11	62
6	Arthritis Research & Therapy	4.15	56
7	Journal of Alzheimer's Disease	3.52	50

8	Pain	6.03	49
9	Arthritis & Rheumatology	9.00	48
10	Journal of Medicinal Chemistry	3.48	42

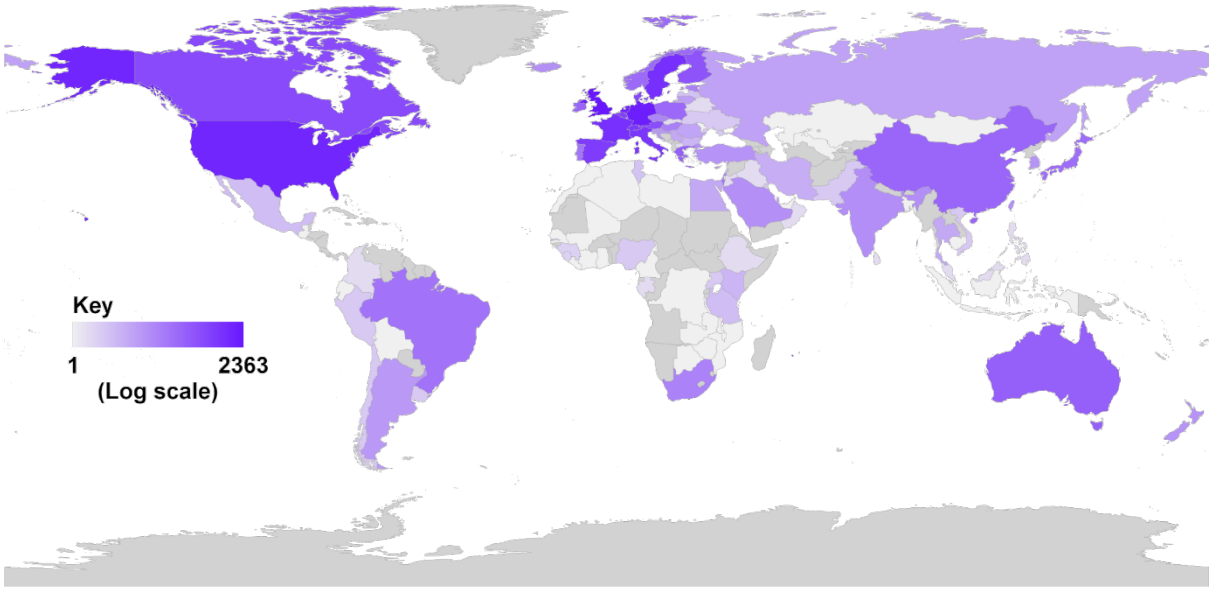
Top 10 journals by JIF

These are the 10 journals, in which IMI projects have published, that have the highest JIF.

Rank	Title	JIF	IMI papers
1	New England Journal Of Medicine	70.67	1
2	Lancet	59.10	2
3	Nature Reviews Drug Discovery	57.62	4
4	Chemical Reviews	54.30	2
5	Nature Reviews Cancer	51.85	2
6	JAMA - Journal Of The American Medical Association	51.27	6
7	Nature Reviews Immunology	44.02	2
8	Nature Reviews Genetics	43.70	3
9	Nature Reviews Molecular Cell Biology	43.35	1
10	Nature	43.07	15

Countries with at least one paper funded by IMI

The analysis also reveals the global reach of IMI's research activities. In total, **113 countries** have at least one paper funded by IMI.



Log scale: It is a scale that shows countries having from 1 publication to 2 363 publications (UK being the top end with 2 363 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[3]. 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 2019

The total operational budget approved for 2019 was EUR 250.3 million in commitment appropriations (CA) and EUR 219.1 million in payment appropriations (PA). In 2019, the operational commitment and payment appropriations reached a level of 99.84 % and 97.93 % respectively.

The commitment appropriations related to H2020 were consumed by Grant Agreements implementing IMI2 – Calls for proposals 13, 14, 15 and 16, and by launching IMI2 - Calls for proposals 17, 18 and 19.

The payment appropriations related to H2020 were mainly used by pre-financing for projects of IMI2 - Calls 13, 14, 15 and 16 and by intermediate payments for projects of IMI2 – Calls 1-11.

The payment appropriations related to FP7 were mainly used by payments for periodic or final reports for projects of IMI1 – Calls 3-11.

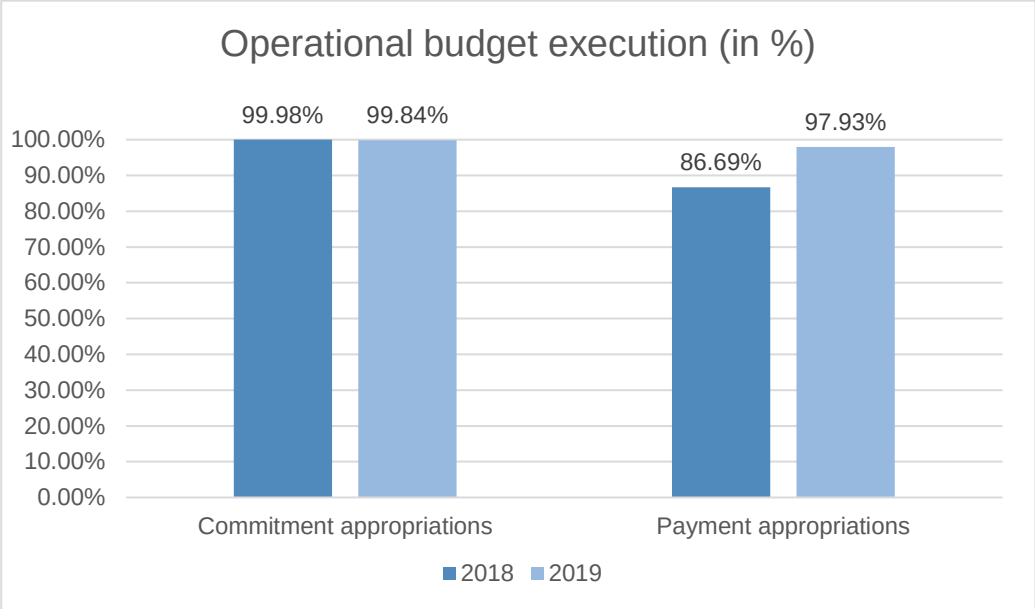
On operational commitment appropriations, IMI achieved an execution rate of 99.84 %, meaning the annual budget has effectively been fully executed.

As regards operational payment appropriations, execution reached 97.93 %. This is a significant increase and a rising trend in the absorption of operational payment appropriations in comparison to the previous years (86.69% in 2018, 71.96 % in 2017 and 69.39 % in 2016). This result is due to continuous actions taken in the budgetary planning and monitoring process:

- A fixed schedule of two fixed Call launch dates per year has been set out so as to ensure better operational planning of tasks and related financial transactions.
- IMI prepared a very detailed forecast and the claim for new payment appropriations (C1 credits) was aligned up front in order to integrate into the total budget envelope the carryover estimates between 2018 and 2019.

3 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 2019 operational budget execution compared with 2018.



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

Execution of commitment appropriations in EUR

	Totals		%
	Appropriations	Execution	
*IMI1 (FP7) **	*128 102*	*101 114*	*78.93%*
IMI2 (H2020)	*250 173 552*	*249 804 102*	*99.85%*
Title 3 implementing the research agenda of IMI	250 301 654	249 905 215	99.84%

*IMI1 (FP7) appropriations - amount recovered during 2019 from projects (assigned revenue)

Execution of payment appropriations in EUR

	Total		%
	Appropriations	Execution	
IMI1 (FP7)	42 459 735	41 182 547	96.99%
IMI2 (H2020)	176 673 446	173 413 228	98.15%
Title 3 implementing the research agenda of IMI	**219 133 181**	**214 595 775**	**97.93%**

In the table below, the commitments carried forward from 2018 to 2019 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. Based on the N+3 rule set out in the IMI2 Financial Rules, the unused commitment appropriations in 2019 were carried over to the 2020 budget.

The table below shows the summary of commitments outstanding for operational expenditure per programme at the end of 2019.

Commitments carried forward from previous year 2018	Commitment appropriations in EUR				
	Carry forward	Commitments made during 2019	De-commitments	Payments	Commitments outstanding at end 2019
IMI1 (FP7)	187 350 906	101 114		41 182 547	146 269 472
IMI2 (H2020)	664 306 892	249 804 102	-18 031 017	173 413 228	722 666 748
Total Title 3	851 657 798	249 905 215	-18 031 017	214 595 775	868 936 220

EU funds committed under IMI1 and IMI2

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

EUR '000

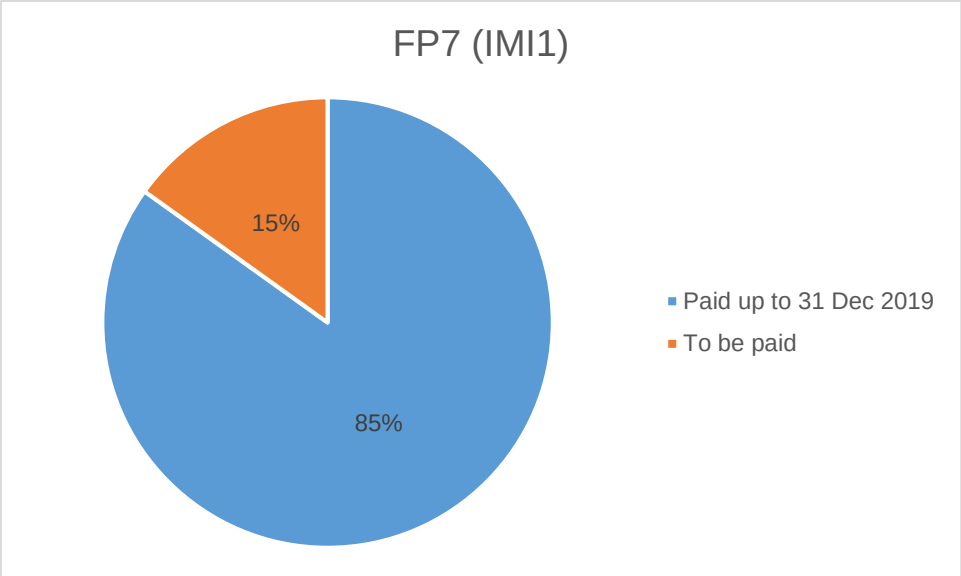
FP7 (IMI1)	Committed	Paid up to 31/12/2019	To be paid
Call 1	116 082	114 607	1 475
Call 2	85 765	85 216	549
Call 3	112 840	110 395	2 445
Call 4	97 944	97 168	776
Call 5	79 999	79 355	644
Call 6	125 417	86 568	38 849
Call 7	13 000	11 700	1 300
Call 8	98 733	72 722	26 011
Call 9	56 441	43 012	13 429
Call 10	6 100	5 418	682
Call 11	173 410	113 702	59 708
Total FP7 (IMI1)	**965 731**	**819 863**	**145 868**

The difference between total to be paid (EUR 145.868 million) and RAL (Rest a liquider) in ABAC (EUR 146.269 million) is EUR 401 675. This amount represents the RAL of the ENSO[4] Call.

At the end of 2019, 8 5 % of the commitment appropriations had been paid out. The outstanding operational payments will be made by the end of 2024 when the last IMI1 (FP7) projects conclude their activities.

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

4 IMI1 Call 'Exploring New Scientific Opportunities'



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

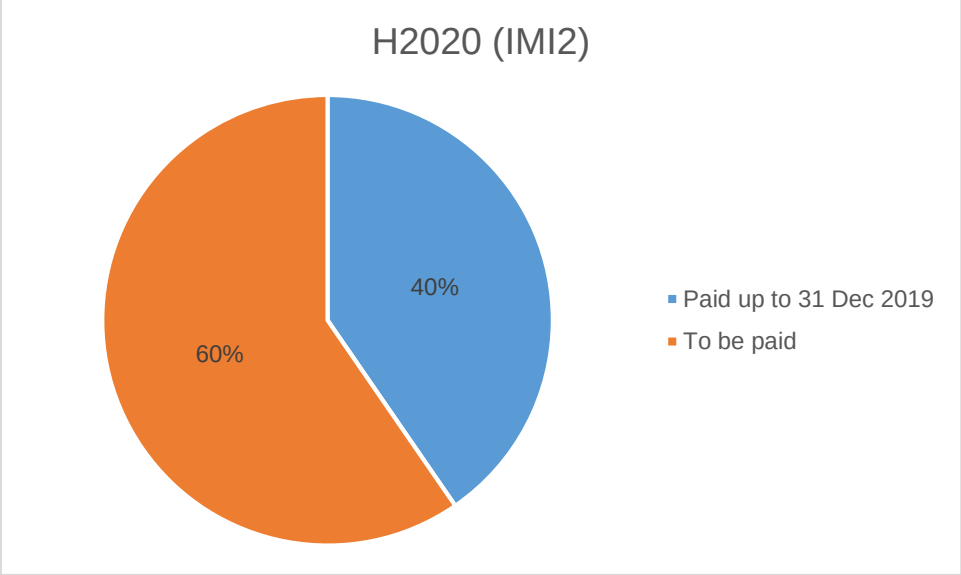
EUR '000

H2020 (IMI2)	Committed	Paid up to 31/12/2019	To be paid
Call 1	17 630	11 578	6 052
Call 2	114 090	101 834	12 256
Call 3 *	56 060	47 565	8 495
Call 4	1 130	1 078	52
Call 5	47 477	28 109	19 368
Call 6 *	46 696	28 466	18 230
Call 7	46 795	28 721	18 074
Call 8	47 462	18 282	29 180
Call 9 *	57 606	28 888	28 718
Call 10	173 874	67 132	106 742
Call 11	3 284	2 839	445
Call 12	64 052	21 953	42 099
Call 13	114 152	33 177	80 975
Call 14	82 310	24 521	57 789
Call 15	165 608	33 582	132 026
Call 16	35 184	10 772	24 412
Call 17	40 786		40 786
Call 18	74 866		74 866
Call 19	20 000		20 000
Total H2020 (IMI2)	**1 209 062**	**488 496**	**720 566**

* 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 difference between total to be paid (EUR 720.566 million) and RAL (Rest a liquider) in ABAC (EUR 722.667 million) is EUR 2.1 million. This amount is linked to the PERISCOPE project.

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



The EU has committed to contribute EUR 1.638 billion from H2020 to the IMI2 programme.

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

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

At the end of 2019, 75.8 % of the operational IMI2 JU budget in commitments had been committed (EUR 1.209 billion out of EUR 1.595 billion).

1.7 EFPIA and IMI2 Associated Partner contributions

IMI2 JU 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[5].

On the one hand, in IMI projects, legal entities eligible for JU funding (beneficiaries receiving JU funding) receive financial support from IMI to fund their activities[6].

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

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 that they incur in IMI projects. IMI controls the eligibility and regularity of the contributions and carefully monitors the development of the total contributions to both programmes (IMI1 and IMI2).

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

- IMI1: EC funding up to EUR 966 million, to match the equivalent contributions from EFPIA.
- IMI2: EC funding up to EUR 1.425 billion, to match the equivalent contributions from EFPIA companies. An additional EUR 213 million in EC funding may be provided to match additional contributions from other Members, Associated Partners, or from their constituent entities or their affiliated entities, bringing the maximum EC funding to EUR 1.638 million, of which EUR 1.596 for operational activities.

5 IMI's legal and financial framework is described in more detail in section 2.2.
6 The management of these funds is described in more detail in section 1.7 and section 4.
7 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 programme

This section highlights the commitments pledged by EFPIA companies. EFPIA's commitment to the IMI1 programme totalled EUR 977.1 million as of 31 December 2019, representing an increase of EUR 12.1 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.

IMI1 In million EUR	EU commitment	EFPIA commitment
Number of signed projects	59	
Up to 31.12.2018	965.7	965.0
2019	0	12.1
TOTAL at 31.12.2019	965.7	977.1

IMI1 EU and EFPIA validated contributions - comparison by year

As of 31 December 2019, EFPIA contributions of EUR 688.6 million had been formally validated (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.

Year	Validated cost claims from beneficiaries (*)	EFPIA in-kind validated 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
2019	62.4	55.2
TOTAL	715.5	688.6

(*) excluding pre-financing

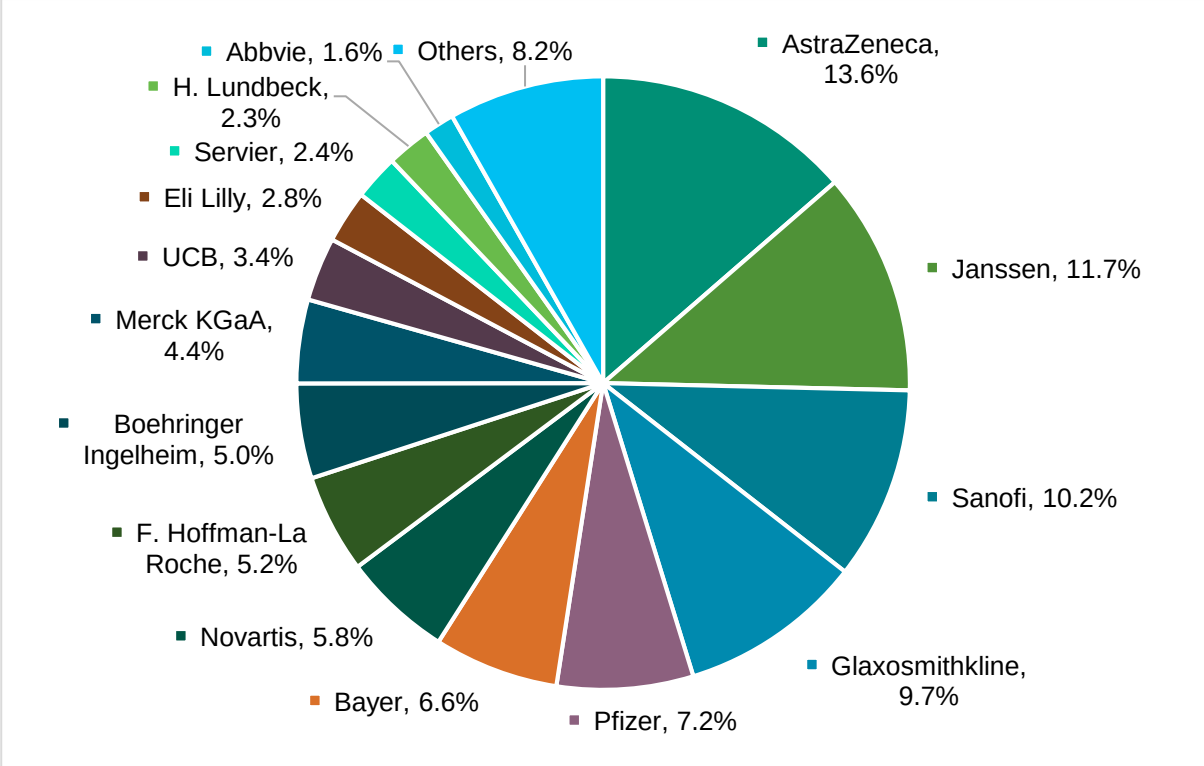
In terms of actual reporting however there is a difference between EU and EFPIA funding which results from the fact that in some projects, tasks for the different consortium partners are not parallel, but sequential.

In 2019, the amount of cost claims validated as well as EFPIA in kind is significantly lower compared to 2018. This stems from the fact that the number of IMI1 projects decreases as projects are finishing (in 2019, there were 16 running projects, of which 5 ended during 2019).

In 2019, the IMI Programme Office continued to closely monitor the overall commitments of industry participants. At the end of 2019, 11 projects were still ongoing. The outstanding contributions will be made by the end of 2024 as the last IMI1 (FP7) projects are due to conclude their activities before then.

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.



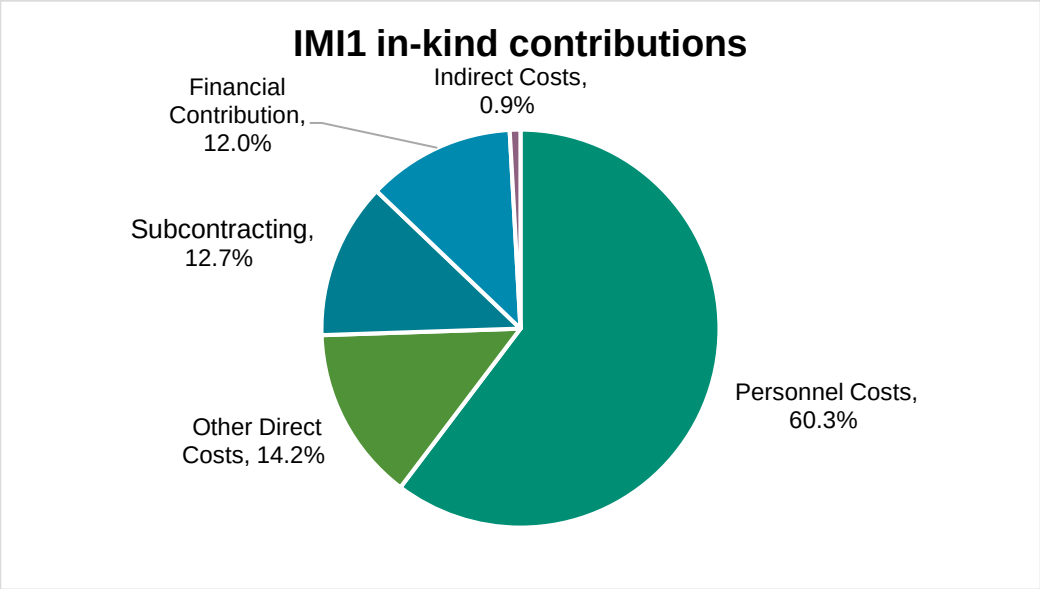
Companies listed under 'Others' are: Abbott, AC Immune, AiCuris, Almirall, Amgen (including Islensk Erfdagreining), Astellas, Basilea, Biogen, BMS Bristol Myers Squibb, Chiesi Farmaceutici, Da Volterra**,** Eisai, Esteve, Farmaindustria, Grünenthal, INFARMA, Ipsen, MSD Merck Sharp & Dohme, Novo Nordisk, Orion, Polyphor, Seqirus, Sigma-Tau, Silicon Biosystems, Takeda, Teva, The Medicines Company, VFA, Vifor.

IMI1 EFPIA contributions - by cost category

The EFPIA contributions at project level can be broken down into the following cost categories:

- Personnel: staff employed by EFPIA companies directly working on IMI projects.
- Other direct costs: consumables, equipment depreciation, samples, compounds.
- Subcontracting: clinical trials, subcontracting to clinical research organisations, subcontracting to data management companies, lab services, communication, project management support, etc.
- Financial Contribution: 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 can be 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.
- Indirect costs: Overheads

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



IMI2 programme

During 2019, 29 grant agreements were signed, bringing the total number of IM2 projects to 89.

At the end of 2019, the total commitments to IMI2 were:

- EUR 1 062.2 million in EU funding;
- EUR 1 097.3 million commitments from EFPIA companies (EUR 939.6 million) and Associated Partners (EUR 157.7 million).

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

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

IMI2 million EUR	EFPIA commitment	AP commitment	Total EFPIA + AP commitment	EU commitment
Up to 31.12.2018	579.9	75.7	655.6	664.9
2019	359.7	81.9	441.6	397.3
TOTAL at 31.12.2019	939.6	157.7	1 097.3	1 062.2

Both EFPIA companies' and Associated Partners' commitments include in-kind contributions, as well as financial contributions directly to the IMI2 JU operational costs[8], or at project level to beneficiaries receiving IMI funding.

The increase of commitment in 2019 of EUR 397.3 million (EU funding) and EUR 441.6 million (EFPIA and Associated Partner commitment), results from the conclusions of 29 new signed Grant Agreements for IMI2 - Calls 13, 14, 15, 16.

Of the EUR 1 097.3 million committed by EFPIA and Associated Partners as of 31 December 2019, 34 % comes from outside the EU and H2020 associated countries. The IMI2 regulation 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. A mitigation strategy is being implemented to reduce non-EU commitments in new IMI2 projects and therefore reduce the level of non-EU commitments to maximum 30 % by the end of the programme.

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

On 31/12/2019, EFPIA companies and Associated Partners had contributed EUR 219.7 million to the IMI2 programme (amount certified by external auditors and validated by IMI).

For comparison, accepted cost claims for JU funding from beneficiaries stood at EUR 170.4 million.

The following table shows the validated EFPIA and Associated Partner contributions as well as cost claims from beneficiaries receiving EU funding.

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

	EFPIA contributions	Associated Partner contributions	Total validated EFPIA and Associated Partner contributions	Validated cost claims from beneficiaries receiving EU funding *
2016	47.3	2.9	50.2	13.0
2017	35.3	1.0	36.3	26.3
2018	47.7	1.3	49.0	50.4
2019	75.5	8.7	84.2	80.7
TOTAL	**205.8**	**13.9**	**219.7**	**170.4**

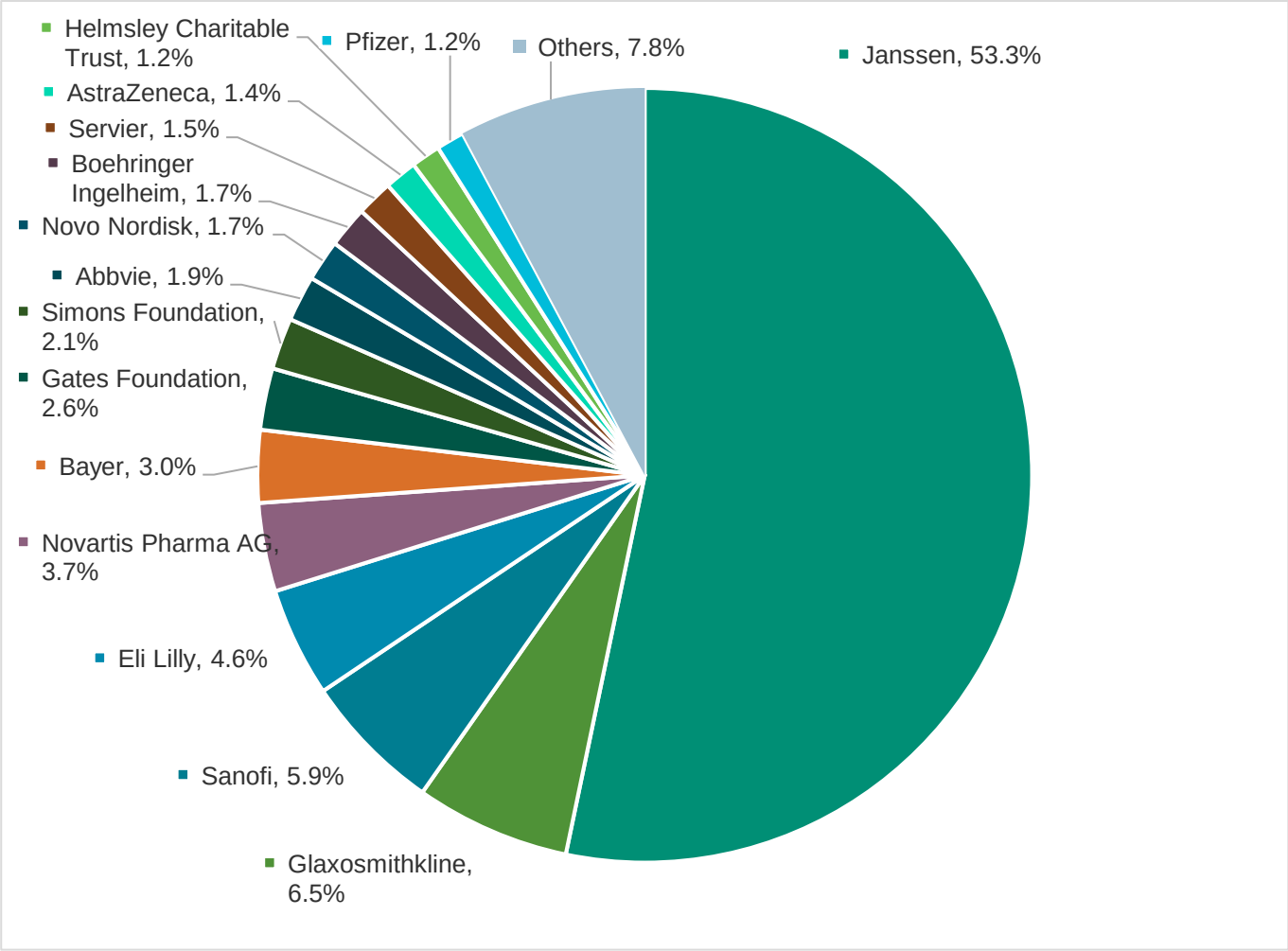
(*) excluding pre-financing

The substantial increase of in kind contribution and costs claim in 2019 is due to the fact that the number of IMI2 running projects has significantly increased from 54 at the end of 2018 to 79 at the end of 2019.

IMI2 validated EFPIA and Associated Partner contributions by organisation up to the end of 2019

There are now more than 40 EFPIA companies and Associated Partners contributing to IMI2 projects. As the organisational breakdown below shows, 53 % of the total validated IMI2 contribution is provided by Janssen. This is mainly due to the fact that Janssen was the main contributor to the first IMI2 projects, launched as part of the emergency response to the 2014 Ebola virus outbreak in western Africa. The remaining 47 % contribution comes from other EFPIA companies and Associated Partners (the Gates Foundation, JDRF - the Juvenile Diabetes Research Funding and Advocacy, The Leona M. and Harry B. Helmsley Charitable Trust, the Simons Foundation).

The chart below includes both in-kind contributions and financial contributions at the level of the action to beneficiaries receiving IMI funding; this totals EUR 219.7 million.



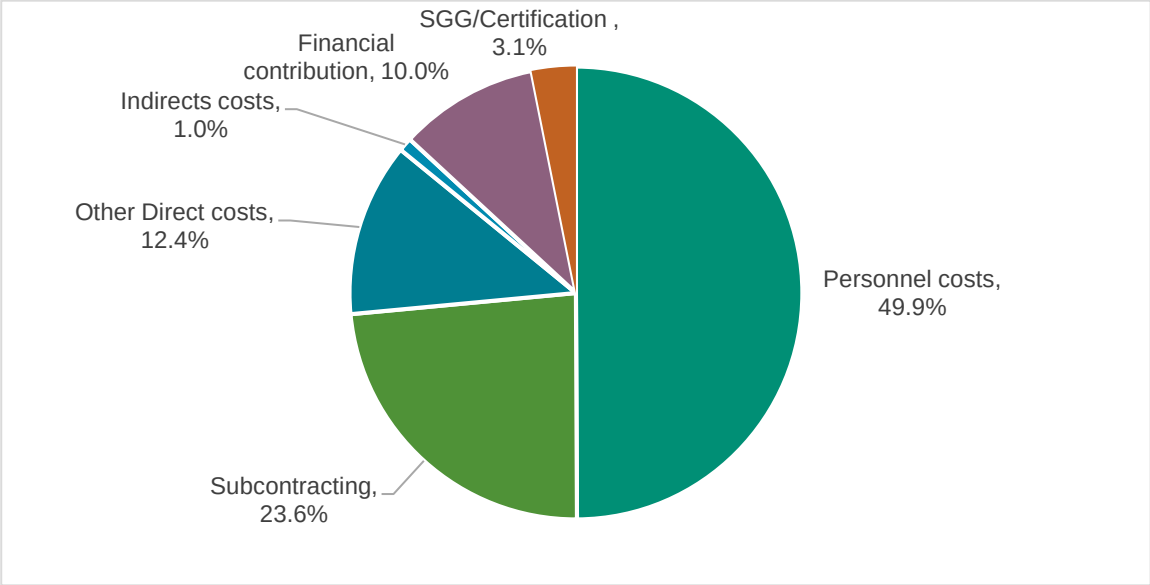
Organisations under 'other' include Actelion, Amgen, Biogen, bioMérieux, Bms, British, Celgene, Charles River, Da Volterra, EFPIA, Egg, Esteve, Farmaceutica Grunenthal, Intervet, JDRF, Lundbeck, Menarini, Merck, Merial, MSD, Orion, Psychogenics, Rentschler, Takeda, Teva, UCB, VFA, Zoetis.

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.

- 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
- Financial Contribution: EFPIA companies can also make a financial contribution (FC), i.e. a transfer of funds from an EFPIA company to beneficiaries receiving IMI2 JU 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.
- SGG/Certification: In addition to costs incurred on projects, in-kind contributions also include costs (contributions) related to Strategic Governing Group (SGGs) and are reporting the costs of having their in kind contribution certified by external auditors..

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



The high percentage of subcontracting costs and other direct costs in IMI2 projects compared to IMI1 projects is due to the particularities of the IMI2 projects with significant clinical trials (among others AIMS-2-Trials project and Ebola projects), where significant tasks are subcontracted.

Ex-post control 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 20 EFPIA companies, covering a total of EUR 617.9 millions of accepted contributions to IMI1 projects or 90 % 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 31/12/2019 (EUR million)
Total finalised audits	617.9
Total all EFPIA companies	688.6
Audit coverage	**90 %**

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 4 493 979, corresponding to 0.73 % of the total audited amounts.

Validated IKC (EUR million)	IKC of audited companies (EUR)	Cover-age	Negative adjustments (EUR)	Positive adjustments (EUR)	Total absolute adjustments (EUR)	% of absolute adjust-ments
688.6	617.9	90 %	-2 293 847	2 200 131	4 493 979	0.73 %

A further three audits were launched at the end of 2018, one has been finalised in 2019 and two will be finalised in 2020.

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[9]. 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.

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

2 Support to operations

2.1 Communication activities

Keeping a high level of engagement throughout the year

Traffic to IMI's social communication channels has been influenced by key IMI events, notably the Stakeholder Forum, Call launches and vacancy openings, with high peaks of activity during these key moments. The communications team goal in 2019 was to maintain traffic at the same peak levels throughout the rest of the year. We did this by:

- publishing shorter news items with a more informal style, and doing so more frequently;
- producing short, dynamic videos, with clear text and simple visual effects as teasers and explainers;
- creating an editorial monthly calendar that links today´s biggest health challenges to IMI's research portfolio.

Figures show that this new approach has reverted the previous trend of peak activity and has kept a high level of engagement throughout the months of October, November and December.

Focus on results

Building on last year's IMI tenth anniversary campaign, IMI has continued to put the focus on communicating project results, evolving, however, in its approach by adapting the communication style to the general trend of fast, frequent and active content consumption.

A special mention should be made of the fact that five new success stories featuring IMI projects were added to the EC catalogue of research success stories:

- PHAGO https://ec.europa.eu/research/infocentre/article_en.cfm?artid=50725
- RADAR AD https://ec.europa.eu/research/infocentre/article_en.cfm?artid=50705
- RTCure https://ec.europa.eu/research/infocentre/article_en.cfm?artid=49896
- PROACTIVE https://ec.europa.eu/research/infocentre/article_en.cfm?artid=49943
- PRECICEADS https://ec.europa.eu/research/infocentre/article_en.cfm?artid=49706

In addition, IMI coordinated the CORDIS Results Pack, 'How the digital revolution is transforming EU-funded brain research', in collaboration with the ERC, DG RTD and DG CNECT. The brochure was published to coincide with IMI's Stakeholder Forum on the same subject and features the IMI projects AETIONOMY, EU-AIMS and PRISM.

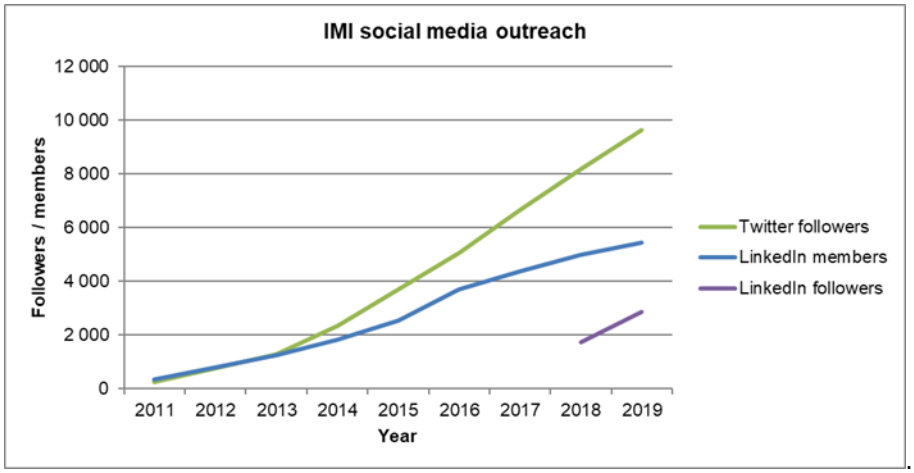
Social media

Although the IMI Twitter community is made up of a loyal nucleus of relevant stakeholders, the account is also one of the main tools for distributing content to a wider audience.

@IMI_JU tweeted 352 original messages in addition to regular retweets, particularly from IMI projects, which resulted in 1 065.9K impressions and 1 954 link clicks. IMI Twitter account followers retweeted @IMI_JU messages 1 925 times and liked them 2 860 times. By the end of 2019, the IMI Twitter account had 9 640 followers.

IMI uses LinkedIn to specifically target members of the professional community who are interested in both scientific and corporate information such as Call promotion, open vacancies and project stories. In 2019, IMI continued to promote its activities via the LinkedIn group, which now has 5 450 members, and the LinkedIn profile, which has 2 862 followers. Engagement rates for the LinkedIn profile are particularly strong. An analysis of IMI's followers reveals that 13 % are based in Brussels; other clusters are in Paris, Antwerp,

London, Barcelona, Lisbon, and Basel. Just under a quarter are in the pharmaceuticals industry, with other followers coming from the research sector (15 %), biotechnology (10 %), hospitals and healthcare (9 %), and higher education (6 %).



As the graph shows, IMI's social media channels continue to show a steady growth curve with the number of new members subscribing to both channels year on year increasing at a regular pace.

Website

The IMI website continued to be the key reference for IMI's stakeholders for the retrieval of information regarding its activities. The most visited page, besides the IMI home page, was the Future Topics page followed by About IMI and the Call 17 topic page.

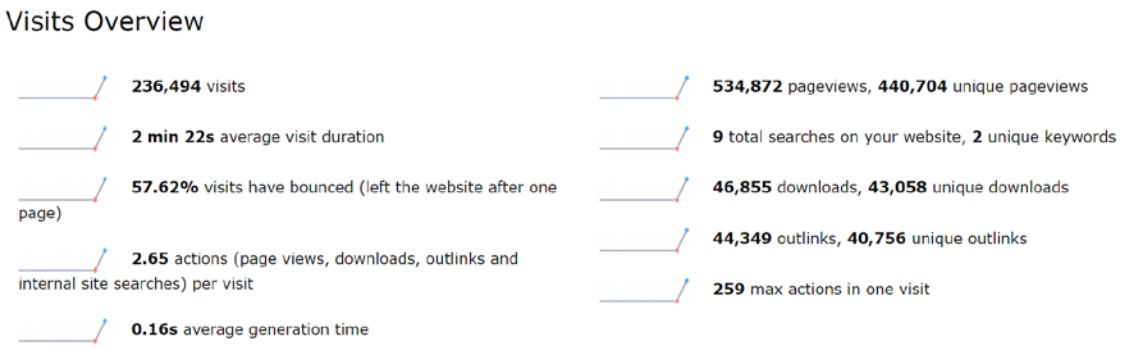
In order to enhance GDPR compliance, IMI changed from Google Analytics to Europe Analytics in January 2019. Since each analytics platform uses its own methodology, the Communications team decided to run both systems in parallel during the first two full implementation months. The goal was to monitor the impact of this factor on the figures provided. During these two months, it became apparent that the numbers provided by Europe Analytics were significantly lower than those provided by Google; this is due to the GDPR 'do not track' policy.

The following table shows the difference in results between the two web analytics platforms for the numbers of unique visitors:

Month	Google Analytics	Europe Analytics
February	17 395	13 009
March	14 420	10 742

According to Europe Analytics, in 2019 the average number of visitors per month was 14 751, and while this appears to be very similar to the 2018 figure, it does not reflect the real increase in visitors we would have seen had we continued with the Google Analytics.

The figures below provide a snapshot of 2019 website visits-related indicators:



Source: Europe Analytics

Geographically speaking, Belgium, the United States, the UK, Germany and Spain were the countries from which most visitors originated.

Press

During 2019, IMI was mentioned in 3 234 articles in a range of magazines, industry press and online media worldwide (1 230 of them in the EU), which clearly indicates the international relevance of the PPP. A selection of the most significant articles can be found in Annex 11. Highlights for IMI include a segment on CNN on IMI's work in the artificial intelligence field; coverage in the mainstream press in Ireland and the UK of the PERISCOPE project's work on whooping cough (pertussis); and coverage across Europe of the CONCEPTION project.

IMI was mentioned in the title or opening lines of some 15 % of these articles. The tonality of the media coverage was predominantly neutral (97 %), with the remaining 3 % of articles registering a positive tone.

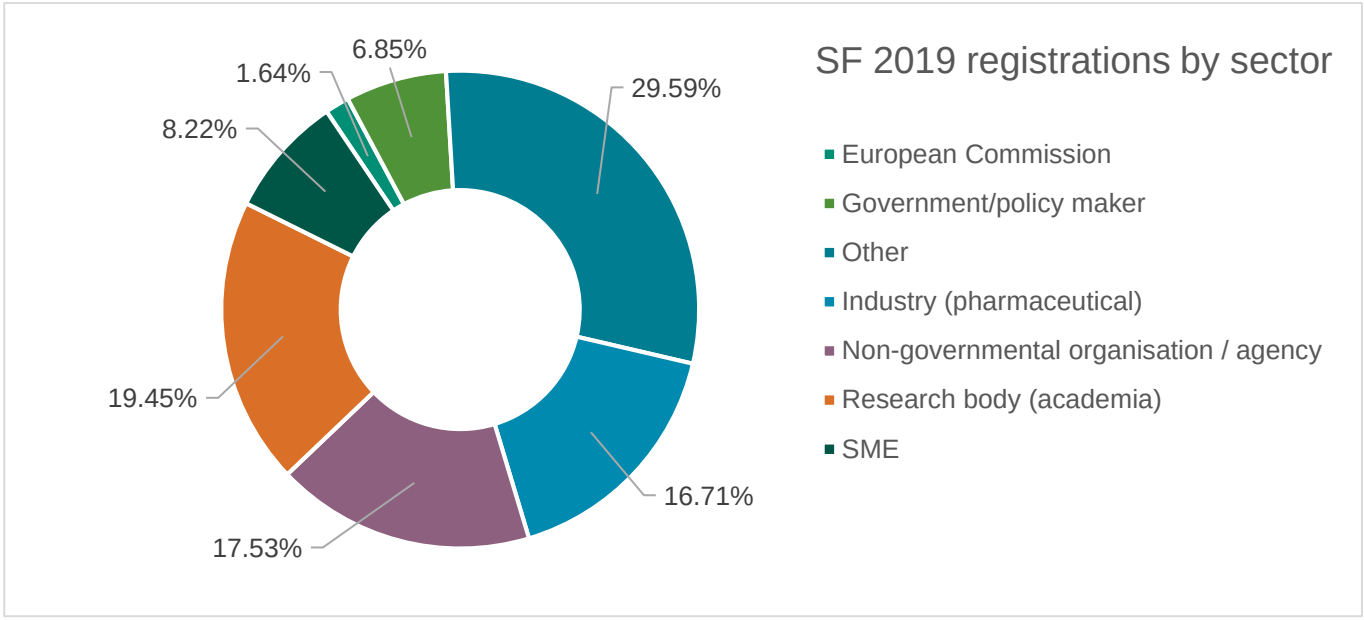
Newsletter

IMI publishes a monthly newsletter with corporate news and highlights from its projects. By the end of 2019, there were 3 211 subscribers (compared 2 398 in 2018). The breakdown of subscribers' organisations is as follows: 64 % research organisations, universities and hospitals; 13.5 % SMEs; 13.2 % large industry (354 pharma industry subscribers and 70 other large industry subscribers) and 2.8 % non-profit organisations, largely comprised of patient organisations. It is worth noting that almost 20 % of subscribers come from organisations that act as amplifiers of IMI such as EU, national and regional authorities (7 %), consultancies (7.7 %) and press/PR agencies (1.2 %).

Stakeholder Forum

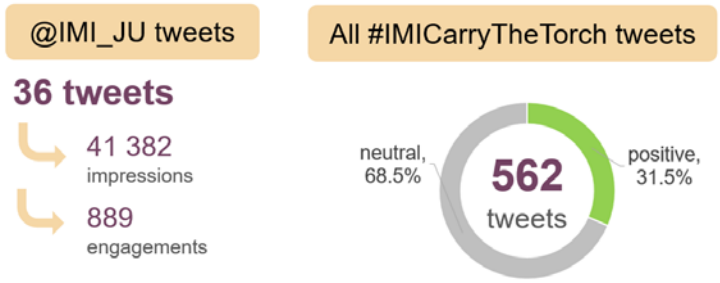
The theme of the IMI Stakeholder Forum 2019, held on 12 June 2019 in Brussels, was 'Brain health and disease in the digital era - 2020 & beyond'. Throughout the day, experts from different fields offered their perspectives on how digital technologies could advance prevention, diagnosis, treatment and care, with the explicit goal of exploring ways of building IMI Call topics that converge around this relatively new space.

The event was attended by 382 participants. As the graph shows, the breakdown of participants was well balanced. Moreover, the main actors from each sector were present in the room, making the event a true Stakeholder Forum.



The full list of speakers, presentations, recordings and summary of the outputs of all the sessions can be found on the event web page.

As shown below, the impact of the event in social media was remarkable, creating a true stakeholder dialogue online.



It is noteworthy that *CORDIS News* published an article on the Stakeholder Forum, with interviews of PRISM and AETIONOMY's coordinators, linking the event to the Digital Brain Result Pack.

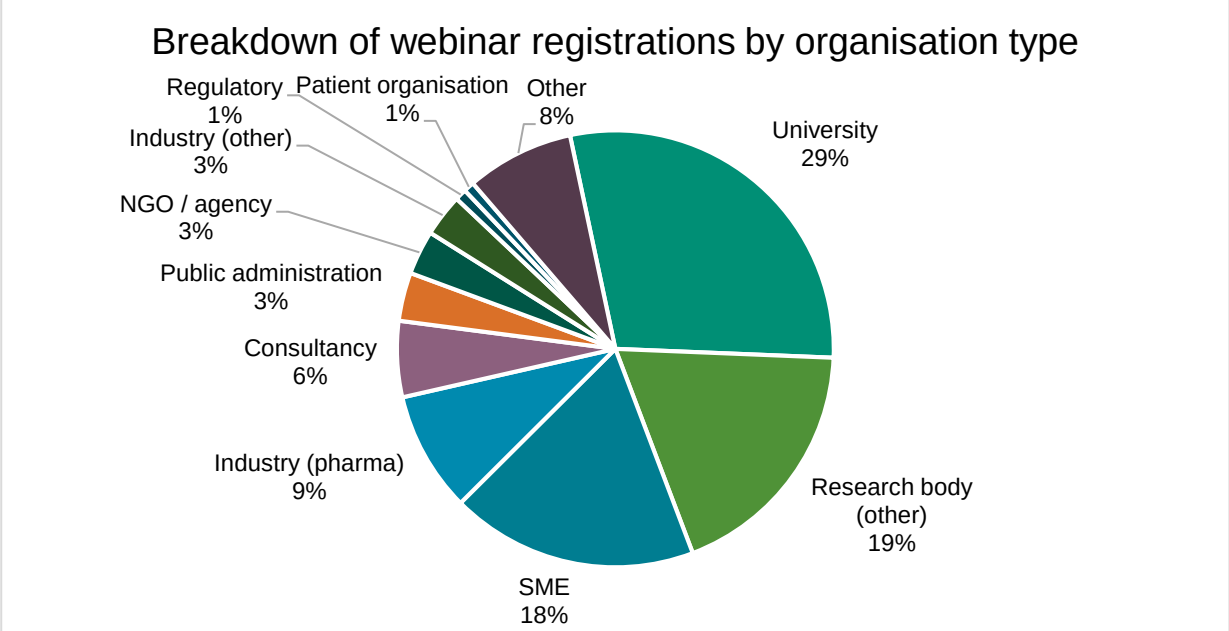
The Stakeholder Forum continues to have a positive influence on stakeholders' understanding of IMI. Asked through a survey if the event had improved their understanding of what IMI is doing, participants' response was largely positive: from the 130 responses collected, 94 % of the participants either totally agreed or tended to agree with the statement.

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 - 96.92% - answered affirmatively.

Call outreach activities

IMI launched three Calls for proposals in 2019 (IMI2 – Call 17 on 22/01/2019, and IMI2 – Calls 18 and 19 on 26/06/2019). 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 13 webinars covering the Call topics, IMI's rules and procedures, and opportunities for SMEs in the Call. In total, these webinars attracted 831 participants. The graph below shows the breakdown of registrations for the Call 17, 18 and 19 webinars by organisation type.



All webinars on the Call topics featured a presentation by the EFPIA topic coordinator and time for questions and answers. The webinars represented an excellent opportunity to learn more about the Call topics, interact directly with the topic coordinators, and get in touch with potential project partners. To help applicants to prepare, IMI publishes draft Call topic texts around two months ahead of the Call launch. Proof of the interest among the research community is the fact that the *Future Topics* page was the second most visited IMI website page, with 24 462 views.

Close-out meetings 2019

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.

- **BTCURE** summary of project achievements |success story
- **ABIRISK** summary of project achievements
- **PRECISEADS** summary of project achievements | success story
- **ORBITO** summary of project achievements
- **CHEM21** summary of project achievements | success story
- **ELF** summary of project achievements | success story
- **FILODIAG** summary of project achievements | interview with project coordinator

- **EBOLAMODRAD** summary of project achievements | interview with project coordinator
- **VSV-EBOVAC** summary of project achievements | video
- **DRIVE-AB** summary of project achievements | success story
- **TRANSLOCATION** summary of project achievements |video
- **QUIC-CONCEPT** summary of project achievements | success story
- **ETRIKS** summary of project achievements
- **DIRECT** summary of project achievements | video
- **AETIONOMY** summary of project achievements | video and interview with project coordinator
- **EU-AIMS** summary of project achievements | editorial in the journal Cyberpsychology, behaviour and social networking

Target audiences

IMI participation at the European R&I Days

The first European Research and Innovation Days (Brussels, 24-26 September) were conceived as an important part of the strategic planning process, bringing together stakeholders to debate and shape the strategic priorities for the future Horizon Europe programme. In this context, IMI's Executive Director set the scene at the session 'Ensuring an innovative, sustainable and globally competitive health-related industry'.

The event also aimed to mobilise EU citizens and increase awareness of how important research and innovation are in addressing the challenges that society faces. This was done by showcasing the very best EU-funded research in the 'Science is Wonderful' exhibition, including IMI's RADAR-AD and RADAR-CNS projects.

Researchers

BIO International Convention (US, 3-6 June) is the world's largest biotechnology partnering event, attracting 16,000+ biotechnology and pharma leaders. As such, it provides an excellent opportunity to raise awareness of IMI and present project results in a cutting-edge context. This year, IMI organised two sessions in the education programme. Speakers in the first session, entitled 'Getting to grips with data quality issues through international neuroscience initiatives' discussed the work of IMI's EQIPD project. The second session, 'Building a brighter future for children: How will large paediatric trial networks help to deliver safe, effective medicines?' focused in part on IMI's C4C project. Presentations from both sessions can be found on the BIO 2019 web page. In addition, IMI was an active partner on the European Commission's stand at the BIO exhibition.

IMI projects

On Tuesday 2 April, 73 IMI project representatives who are responsible for communications gathered in Brussels, Belgium, for the IMI Projects Communication Event. The goal of the event was to provide projects with information and networking opportunities to help them improve the way they communicate about their projects to diverse audiences throughout the project life cycle. Presentations addressed topics such as (i) IMI communication channels available to IMI projects, (ii) European Commission and Publications Office channels available to projects, (iii) current and future trends in communications, and (iv) case studies from projects on how to build a communications strategy, and how content and channels evolve as the project progresses. There were also brainstorming workshops on shared challenges such as how to encourage large consortia to engage in communications activities.

SMEs

Besides the two SME-targeted webinars linked to Call 17 and 18, IMI reached out to SMEs at the following events.

- BIO-Europe 2019 (Hamburg, 11-13 November): IMI teamed up with the European Commission to take part in Europe's largest partnering conference serving the global biotechnology industry. The European Commission, EMA and IMI jointly organised a session on support schemes for SMEs. In addition, IMI had a joint booth with DG RTD at the exhibition. This year, BIO-Europe attracted 4 335 participants, including

senior executives of leading biotech companies, business development teams from large and mid-size pharmaceutical companies, investors and other industry experts.
- ELIXIR SME and Innovation Forum, Milano, 27-28 November: IMI presented its digital health portfolio and provided SME-targeted information on the benefits to participate in IMI projects.

Patients

In 2019, IMI set up its pool of patient experts, and the communication team played a key role in promoting the Call for expressions of interest to the patient community. The pool is described in detail in section 1.3.2.

European Parliament

26 February	Alzheimer Europe organised a lunch debate focusing on dementia as a European research priority. IMI´s Executive Director presented IMI's Alzheimer's disease portfolio. Hosted by MEP Anneli Jäätteenmäki (FI, ALDE), the debate was attended by 64 delegates from across Europe, including the Chair of the European Working Group of People with Dementia, national Alzheimer's Associations, research partners, pharmaceutical representatives and Members of the European Parliament.
20 March	The European Parliament Interest Group on Allergy and Asthma held a policy meeting on championing a renewed EU agenda on Allergy and Airways diseases for a healthier Europe. The event was co-hosted by MEPs Sirpa Pietikäinen (FI, EPP) and Pavel Poc (CZ, S&D).
10 July	IMI Executive Director participated in the debate 'A new deal for EU industrial research: how to reach EU policy objectives', hosted by MEP Michel Gahler as part of the Kangaroo Group's series of debates on the 'Future of EU research'.

In addition to the events listed above, IMI staff members ensured the presence of IMI in a large number of high-level events in Europe and elsewhere.

- 8 January: Informal Group of R&I Liaison Offices (IGLO) Health meeting | Brussels, Belgium
- 9 January: IMI Info day | Israel
- 16 January: Meeting University of Copenhagen Faculty of Health and Medical Services | Denmark
- 17 January: IMI Info day organised by BAPEMED | Bulgaria and Romania
- 22 January: Science Business Roundtable on Innovation engines: A roadmap towards a healthier Europe | Belgium
- 29 January: InfoDay IMI-INSERM at Clora | Brussels
- 31 January: InfoDay | Budapest
- 1 February: bioMérieux | Lyon, France
- 5 February: DIA Europe 2019 – Executive Director a panellist in the Patient session (N Bedlington, chair) | Vienna
- 19 February: EFGCP annual conference, Executive Director a speaker | Brussels
- 21 February: IMI info day | Ankara, Turkey
- 6 March: Brain Research & Tech: How can Horizon Europe improve human brain health and performance? Aix-Marseille University AMU at Committee of the Regions | France
- 11 April: working meeting with CRUE-CRUP | Belgium
- 6-7 April: HEVER Group | New York, USA
- 7-10 April: EFMI STC 2019 ICT for Health Science Research | Germany
- 8-9 April: MIE STC Hanover | Germany
- 14 May: IMI Info day | France
- 8-9 May: Conference Companion Diagnostics for Immuno-Oncology | Lisbon, Portugal
- 15-16 May: HNN2.0 training on legal and financial issues in SC1 | Poland
- 28 May: AMR Hub, Workshop "increasing investments for AMR R&D" | Geneva, Switzerland
- 17 June: Conference on the evaluation of orphan & paediatrics legislations | Brussels, Belgium
- 17-18 June: ECSEL symposium | Bucharest, Romania
- 27 June: EFPIA Conference 2019 | Brussels, Belgium
- June: Health and Industry 4.0 | Spain
- 3 July: The Guild, Science and Innovation for Europe's Future: Towards a Strategic Approach | Brussels, Belgium
- 4 July: Horizon 2020 Health Partnering Day 2019 | Brussels, Belgium
- 15-16 July: Working group, National Academy of Medicine | Washington DC, USA

- 23 July: Roundtable discussion with IMI and interested parts | Vilnius, Lithuania
- 30 July: EFPIA-IMI InfoDay | Bulgaria
- July: HNN2.0 Brokerage event SC1 | Belgium
- July: Roundtable discussion on IMI | Lithuania
- July: IMI Info day | Bulgaria
- 3 September: IMI InfoDay | Helsinki
- 3 September: Health Tuesday | Finland
- 5-6 September: REA, MSCA Cluster on neurodegenerative diseases | Brussels, Belgium
- 7-10 September: 32 ECNP Congress | Denmark
- 11 September: Nordic Life Sciences Day | Malmö, Sweden
- 11-13 September: Int'l Summit on Population Genomics, Hampshire | United Kingdom
- 16 September: DIA/EFGCP “Better Medicines for Children” | Amsterdam, The Netherlands
- 24 September: Science Business “keeping Europe-wide collaboration in healthcare strong” | Belgium
- 27 September: EU Platform in Science for Health (EurSci4Health) | Brussels, Belgium
- 30 Sep-02 Oct: ADITEC, University of Siena on “Advanced Immunization Technologies” | Italy
- 8-9 October: ADA - Advancing Precision Diabetes Medicine | Spain
- 15 October: K4I Forum Working Breakfast, discussing about European Partnerships and Missions under Horizon Europe | Brussels, Belgium
- 15 October: Bio Pole's Partnering Days | Lyon, France
- 17 October: Innovative Medicines Initiative Programme | Ireland
- 18 October: World Dementia Council Summit, Defeating dementia: the int’l collaboration challenge | Tokyo, Japan
- 30 October: AMR Hub, Stakeholder Group | Paris, France
- 31 October: EC’s New HORRIZON project, Social lab 7, Health - “Patient involvement in clinical service design” | Athens, Greece
- 7 November: Societal Impact of Pain | Brussels, Belgium
- 11-12 November: FT Global Pharmaceutical and Biotechnology | London, United Kingdom
- 21 November: Health Innovation annual IPHA conference, ‘Innovate for Life’ | Dublin, Ireland
- 22 November: Delegation University of Oslo at IMI office | Brussels, Belgium
- 26 November: DG RTD Scientific Panel for Health Workshop, in cooperation with the Finnish Ministries Social Affaires & Health and of Education and Culture – the role of health research | Brussels, Belgium
- 27-28 November: ELIXIR SME and Innovation Forum | Milano, Italy
- 3-4 December: IMI-EMA-FDA Regulatory Science Summit | Brussels, Belgium
- 4 December: BioDataEurope | Switzerland

2.2 Legal and financial framework

The legal (Council Regulation 557/2014 of 6 May 2014) and financial framework (Regulation 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, and IMI2 JU Financial Rules of 22nd December 2015, IMI2-GB-DEC-2015-44[10]) of the IMI2 JU have not changed in 2019.

Within this remit, the IMI Executive Director has set up the organisational structure of the JU and the internal control systems suited to the performance of duties. The Programme Office handles and regularly reviews a number of internal policies, guidance and operating procedures intended to carry out the internal operations correctly and always in the same manner. This also allows to document routinely activity operated by the Programme Office and to facilitate the respect of the regulatory framework as well as consistency in the quality of expected results.

In this context, and in order to maintain the operational processes consistent, efficient and effective, the IMI2 JU Programme Office has adopted or reviewed during 2019 a number of procedures such as the:

- vade mecum for the implementation of H2020 programme (Grant Agreement preparation, project management and reporting, ex-post audit, etc.);
- operating procedure and related templates for periodic and final reports of IMI1 projects;
- checklists on financial circuits;
- policy for implementation of the new document management system HAN (Ares).

10 Following the revision of the Financial Regulation 2018/1046 f August 2018, the IMI2 JU has to revise and adopt new Financial Rules, which are still under revision by DG BUDG. The final text of these new Financial Rules is currently under approval and is planned to be adopted within Q1 / 2020.

2.3 Budgetary and financial management

2.3.1 2019 budget approval

The total IMI budget for 2019 was EUR 261 371 750 in commitment appropriations (CA) and EUR 231 316 906 in payment appropriations (PA). The budget execution of the commitment appropriations and the payment appropriations reached 99.17 % and 96.33 % respectively.

The IMI budget is divided into three titles:

- Title 1 covers staff expenditure such as salaries, training, costs associated with recruitment procedures, missions and staff well-being.
- Title 2 covers the costs associated with functioning of IMI such as renting of premises, IT needs, meetings, 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 (i.e. project expenditure)[11].

The IMI Governing Board adopted the 2019 budget on 12 December 2018.

The Governing Board adopted the first budget amendment on 21 June 2019 in order to include the carry over amounts (EUR 12 599 206 commitment appropriations and EUR 30 943 429 payment appropriations) from the previous year. The first budget amendment also included the return of EUR 139 million of commitment appropriation to the EU budget, which originated from EFPIA's request to lower the total industry commitment under IMI2 JU. The limited capacity of EFPIA companies to absorb the funds available in 2019 was caused by a combination of several factors, including major projects launched in 2018 and early 2019 under the Think Big themes that significantly drew on available industry resources. Having evaluated various options available in mid-2019 and the uncertainties about the potential to use remaining 2019 appropriations if moved to 2020, the Governing Board opted to hand back the commitment appropriations to the European Commission with a view to supporting additional collaborative health projects under Horizon 2020, where immediate absorption capacity was available.

The Governing Board adopted the second budget amendment on 13 December 2019 in order to include the increase of financial contribution from Bill and Melinda Gates Foundation, an IMI2 JU Associated Partner, to operational activities, of EUR 2 142 862.

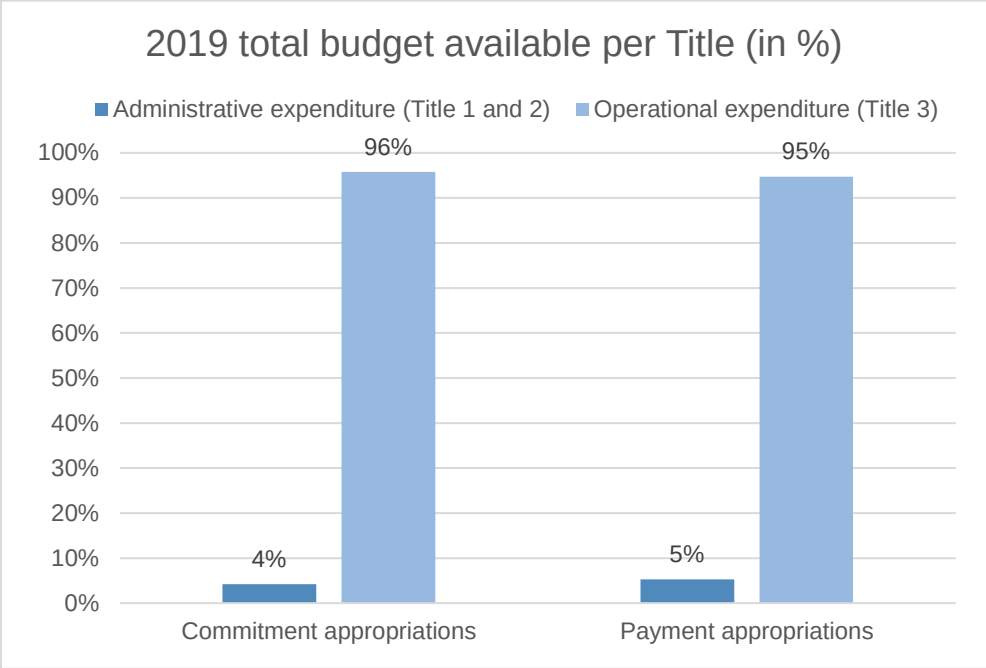
11 See section 1.6.

Budget 2019 in EUR

	Adopted budget		Amending budget no 1		Amending budget no 2		Assigned revenue*		Final budget	
	CA	PA	CA	PA	CA	PA	CA	PA	CA	PA
Revenue										
EC contribution (incl. EFTA contribution) to administrative and operational cost	267 722 662	190 575 842	-139 100 891						128 621 771	190 575 842
Appropriations carried over	114 341 000		12 599 206	30 943 429					126 940 206	30 943 429
EFPIA contribution to administrative costs	5 510 077	5 510 077							5 510 077	5 510 077
EFPIA constituent entities and affiliated entities contribution to operational costs		1 000 000							-	1 000 000
Associated Partners contribution to operational costs		845 000				2 142 862			-	2 987 862
Assigned revenue							299 696	299 696	299 696	299 696
Total revenue	387 573 739	197 930 919	-126 501 685	30 943 429	-	2 142 862	299 696	299 696	261 371 750	231 316 906
Expenditure										
Title 1	6 330 000	6 330 000	-	54 019	-	-	913	913	6 330 913	6 384 932
Title 2	4 690 154	4 690 154	-	1 059 611	-	-	49 029	49 029	4 739 183	5 798 794
Title 3	376 553 585	186 910 765	-126 501 685	29 829 799	-	2 142 862	249 755	249 755	250 301 655	219 133 181
Total expenditure	387 573 739	197 930 919	-126 501 685	30 943 429	-	2 142 862	299 696	299 696	261 371 750	231 316 906

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

The graph below shows the total 2019 budget available per Title in %.



2.3.2 Budget transfers

In 2019, there were no budget transfers between titles. Budget transfers between chapters (activities) were authorised in 2019, which led to the following changes in commitment appropriations:

Chapter		Budget adopted (EUR) Commitment Appropriations	Budget transfer (EUR) Commitment Appropriations	Budget after transfers (EUR) Commitment Appropriations
11	Staff in active employment	5 740 000	-138 200	5 601 800
12	Staff recruitments - miscellaneous expenditure	20 000	7 000	27 000
13	Missions and duty travels	190 000	-	190 000
14	Socio-medical structure	360 000	-21 944	338 056
15	External staff services	-	153 144	153 144
17	Representation	20 000	-	20 000
20	Rent and related expenditures	756 000	-6 425	749 575
21	Information technology (hardware and software)	779 000	250 000	1 029 000
22	Office equipment	153 000	-148 000	5 000
23	Current administrative expenditure	123 000	49 815	172 815
24	Telecommunication and postal expenses	78 000	-20 990	57 010
25	Formal meetings	158 000	27 000	185 000

26	Administrative expenditure in connection with operational activities	388 154	4 000	392 154
27	External communication, information and publicity	625 000	-	625 000
28	Service contracts	730 000	-160 197	569 803
29	Expert contracts and cost of evaluations	900 000	4 797	904 797

2.3.3 Budget execution

The table below shows the execution of the 2019 budget per Title in absolute amounts.

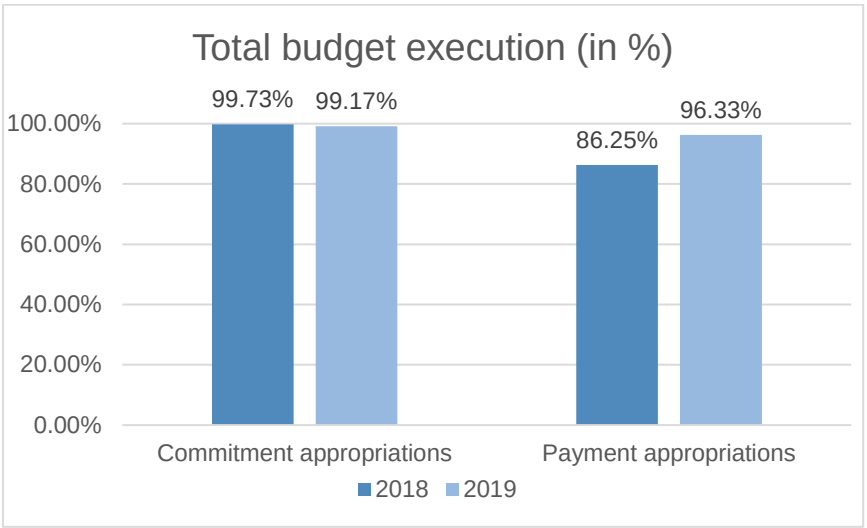
2019 final budget execution per title in EUR

Title	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	6 330 913	5 495 647	86.81%	6 384 932	5 404 478	84.64%
Title 2	4 739 183	3 811 720	80.43%	5 798 794	2 821 004	48.65%
Subtotal administrative expenditure	*11 070 095*	*9 307 367*	*84.08%*	*12 183 725*	*8 225 482*	*67.51%*
Title 3	250 301 655	249 905 215	99.84%	219 133 181	214 595 775	97.93%
Total (Title1, 2 and 3)	**261 371 750**	**259 212 582**	**99.17%**	**231 316 906**	**222 821 258**	**96.33%**

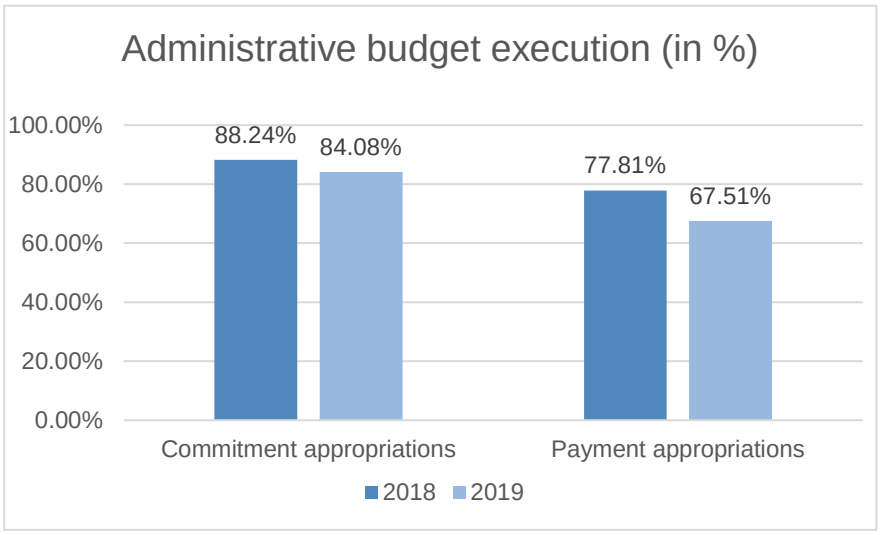
In general, the execution of administrative budget execution in 2019 was in line with the trend, comparable with the previous year, except the payments execution for Title 2.

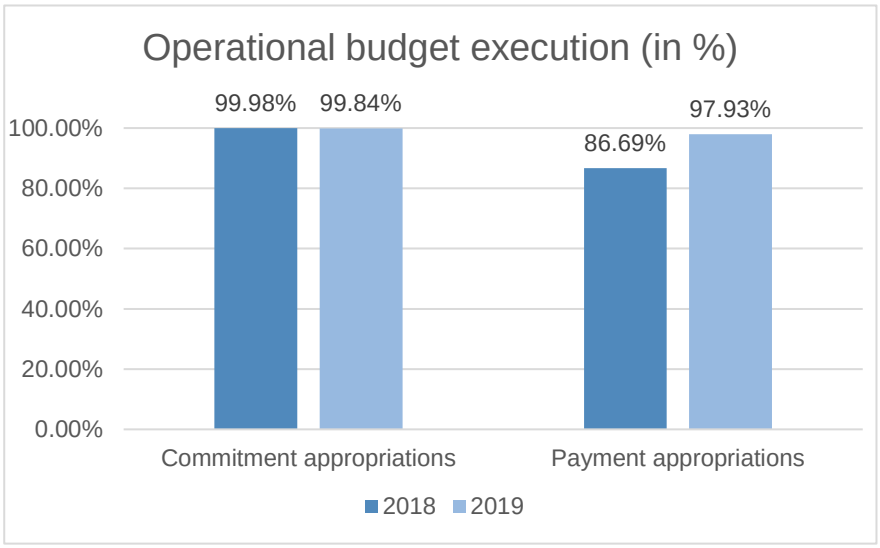
The low payments execution for Title 2 is due to several factors. The planned payment appropriations were not consumed for expert payments, as fewer experts were needed in 2019 compared to the original estimation. Additionally, payment appropriations were envisaged for ex post audits due to ongoing discussions on the cost of additional H2020 audits, but eventually the costs were covered by the EC services. The lower payment execution also relates to the lower volume of audits on FP7 due to phasing out.

The graph below shows the 2019 total budget execution compared with 2018.



The graphs below show the 2019 budget execution for administrative costs (staff and infrastructure) and operational activities (project-related) compared with 2018.





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

Regarding administrative expenditure, the budget execution of the commitment and payment appropriations was 84.08 % and 67.51 % respectively.

The EC part of unused appropriations for administrative costs will be made available for operational activities in the 2020 budget – see section 2.3.4 for details.

In 2019, the time to pay (TTP) for administrative costs was 14 days on average and the number of payments made on time increased from 90.92 % in 2018 to 96 % in 2019.

The following table shows the number and amount of all administrative transactions (including experts).

No. all administrative transactions made in 2019			
	No.	Amount (EUR)	% payments
Total no. payments	1 111	3 557 763.30	100 %
No. payments on time (within 30 days)	1 065	3 190 829.22	96 %
No. late payments	46	366 934.08	4 %

The following table shows the number and amount of all payments made to experts only (evaluations and reviews). In 2019, the TTP for payments made to experts only was 12 days on average and the number of payments made on time have not changed.

	No payments	%
Total experts' payments	249	
Total on time payments	243	98 %
Total late payments	6	2 %
Total amount paid (EUR)	623 264.90	

The table below shows the summary of commitments outstanding at the end of 2019, for administrative and operational expenditure.

	EUR
Commitments carried from previous year	852 771 428
De-commitments (-)	-18 151 634
Payments made during 2019 related to commitments carried forward (-)	-182 090 676
Commitments made during 2019	259 212 582
Payments made during 2019 related to commitments made during 2019 (-)	-40 730 582
Total commitments outstanding at the end of 2019	**871 011 118**

2.3.4 Overview of the carry over appropriations to 2020

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 2020 budget the unused commitment and payment appropriations from 2019.

Administrative expenditure: Payment appropriations of EUR 2 074 898, corresponding to the amount of commitments carried forward from the 2019 to the 2020 budget.

Operational expenditure: Unused commitment and payment appropriations to be carried over to 2020 budget of EUR 1 338 112* corresponding to commitment appropriations, and EUR 4 537 406* corresponding to payment appropriations.

	Commitment appropriation (EUR)	Payment appropriation (EUR)
Unused appropriations (operational and administrative)	* 1 338 112	* 6 612 304

* estimated; subject to Governing Board approval

2.4 Procurement and contracts

The majority of the IMI2 JU's contractual commitments in 2019 were concluded on the basis of existing multiannual 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 interinstitutional, thus minimising the administrative burden and ensuring economies of scale.

The table below shows tender procedures in 2019 outside existing FWCs with a value exceeding EUR 15 000.

Subject	Procedure	Contractor	Value (EUR)	Signature date
Catering services	Negotiated procedure with three candidates	Biorganic Factory	22 000	16/04/2019
Event-related services	Negotiated procedure with three candidates	The Hotel	33 500	06/02/2019
External legal services for litigation support in the operational field	Negotiated procedure with three candidates	ASHURST L.L.P	16 000	16/02/2019

All procedures were administered 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

Common IT infrastructure

IMI shares a common IT infrastructure and facilities with six other joint undertakings co-located in the White Atrium building and participates in formally established common IT governance.

The major common IT project in 2019 was the successful installation of advanced and adaptable audio-visual equipment in Common meeting rooms 3 and 4.

Another important project launched in 2019 was the renewal of the network infrastructure in the White Atrium building. The existing infrastructure (installed in 2010, for a much smaller number of staff) is reaching the end of its life and can no longer be technically supported. Following an extensive site survey and an analysis of several different scenarios, the common IT governance group adopted a decision and scheduled procurement and installation for 2020.

Business support tools provided by European Commission

In line with current trend, the IMI Programme Office continues to implement more and more EC tools to support IMI's core business (eGrants) and administrative and financial workflows.

Following our request and after detailed analysis of existing workflows and security groups, the Common Implementation Centre (CIC) of DG RTD implemented an entirely new IMI2 organigram in SECUNDA+ and granted access to IMI single point of contact (SPOC) allowing us to manage independently all IMI teams' access rights to different Compass workflows and some eGrants applications.

Another major achievement in 2019 was the successful migration to the European Commission corporate document management system HAN - Hermes/Ares/NomCom. HAN is a suite of IT tools which have been developed to allow staff to work in accordance with the 'e-Domec' rules within the Commission's DGs and services, the executive agencies, the EEAS, EU delegations, and decentralised EU agencies, bodies and other EU institutions. The IMI Document Management Officer (DMO), supported by the Deputy DMO and HAN working group, and in coordination with Commission's Secretariat General, performed extensive preparatory work including the drafting and approval of the document management policy, filing plan and the specific retention list. All staff were trained in September before the migration to HAN. After the migration, the previous document management system DORA was frozen.

In the beginning of 2019, IMI also finalised the SYSPER migration project and implemented in production the main SYSPER modules: ORG (organigram), (DOT) job quota management, TIM (time management), PER (personal data), JIS (job information system), (DOC) document management, CAR (Career), and PMO: RIG & FAM (individual rights, flexitime and teleworking). The IMI IT team took the lead on this and supported the migration process for all JUs by establishing a security convention with DG HR, and installing and managing a dedicated Oracle server.

Enhancements of in-house applications

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

- SOFIA (Submission of Information Application)
  - entirely new KPI tracking functionality;
  - key performance indicator (KPI) report submission for all IMI1 and IMI2 projects performed by the project coordinator or other project responsible (e.g. legal entities, project manager(s), managing entity etc.);

- improved dataflow from the data warehouse (DW) to enable regular automatic updates of IMI2 projects' data for the annual reporting of costs by EFPIA companies and Associated Partners; and new KPI functionality;
- improvements in the XML export of IMI2 data for integration with CORDA (Common Research Data warehouse).

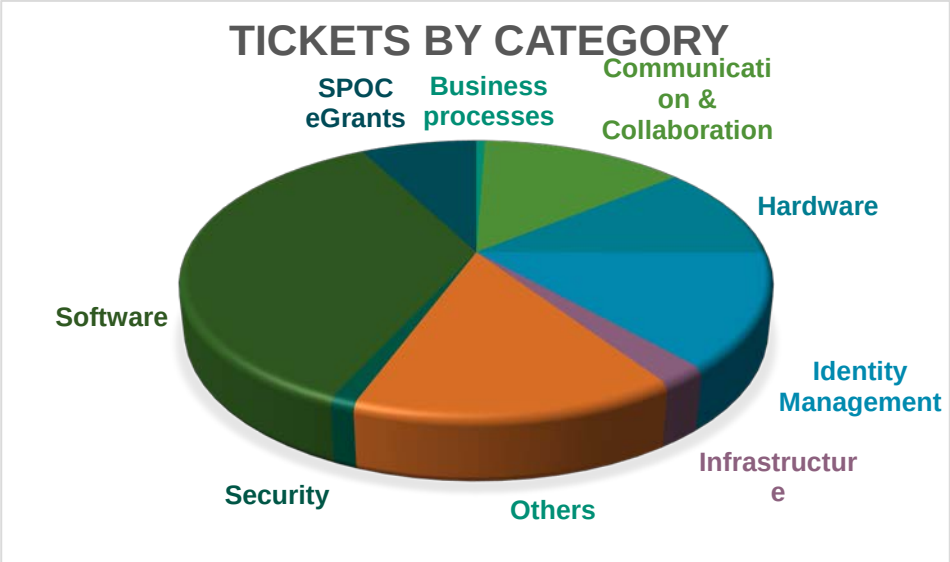
- New intranet

  In 2019, IMI started a major revision of the intranet. The intranet is the main internal communication tool, enabling collaboration, and supporting business activities. The core part of new intranet are service pages by teams/area of activities with the main purpose of informing other colleagues.

- Cloud applications:
  - Redesign of DORA as a collaborative platform and archive document management system after successful ARES implementation in May 2019;
  - Improvements and new features in other existing applications: Vacancy, eMA, and collaboration platforms.

Servicedesk support

In 2019, a total of 1 033 requests for support were handled by the IMI IT Helpdesk. The following graph depicts the various categories assigned to the tickets



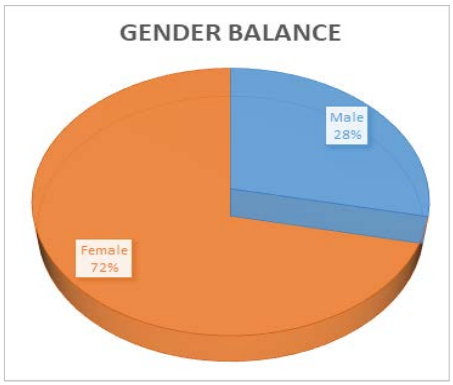
2.6 Human resources

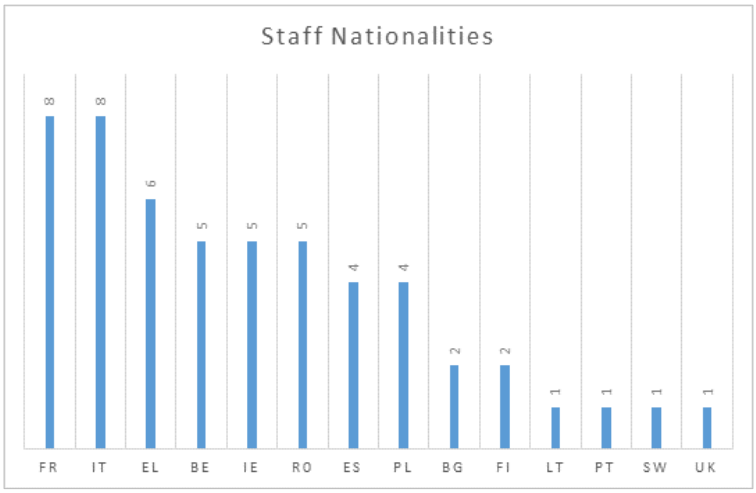
Staff and recruitment

The staff establishment plan (SEP) allows for 39 temporary agents, 15 contract agents and 2 seconded national experts (SNEs), in total 56 staff members. On 31/12/2019 there were 53 positions occupied: 38 out of 39 temporary agents (97.44%), 14 out of 15 contract agents (93.33%) and 1 out of 2 seconded national experts (50%)[12]. The table below provides a summary of the staff planning:

	Positions planned in SEP	Positions filled on 01.01.2019	Resignations / end of service in 2019	Recruitment / appointment in 2019	Positions filled on 31.12.2019
Temporary Agents	39	36	2	3	38
Contract Agents	15	10	1	5	14
SNEs	2	1	N/A	0	1
Total	56	47	3	8	53

The two graphs below show the gender and geographical balance (13 EU nationalities were represented in IMI) within IMI on 31/12/2019.





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 for example on SyGMA, Compass and Audit Implementation Workflow (AURI).
- Financial framework: all actors in the IMI finance workflows were trained and kept up-to-date with new developments and best practices in ABAC.
- 12 in-house training courses were organised and delivered as follows: a well-being training programme composed of 4 lunchtime sessions and a 1-day training on resilience; 2 half-day sessions for all staff on

12 The deadline for the call for expression of interest for Seconded National Experts - Scientific Project Officer- Digital health was extended until 06.01.2020.

protecting the dignity of the person and preventing psychological harassment and sexual harassment; 2 half-day sessions on ethics and integrity; and one 1.5 day course on public speaking.
In addition, specific training courses for managers were organised on subjects such as protecting the dignity of the person and preventing psychological harassment and sexual harassment, giving and receiving feedback, and conflict management. A coaching programme was also launched.

- IMI staff members also attended several 'soft' and 'hard' skills courses as well as language training courses at the European Commission. The European Commission's 'EU Learn' system helped IMI staff in the selection of their training needs, on both hard and soft skills.
- 10 HR info sessions for staff and managers were organised in order to provide IMI staff with a wider understanding of HR procedures and processes and to increase transparency as well as to train IMI staff on the use of the new tool, SYSPER.

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 2019, in accordance with the Staff Regulations. As a result, 6 staff members (5 temporary agents and 1 contract agent) were reclassified to the immediate higher grade.

Staff regulations and implementing rules

During 2019, IMI continued working on the implementing rules in line with the new Staff Regulations and the EC Human Resources and Security Directorate General (DG HR) guidelines. In total 11 implementing rules were adopted, including the rules on protecting the dignity of the person and preventing psychological harassment and sexual harassment, outside activities, and teleworking.

2.7 Data protection

In 2019, the IMI2 JU pursued its efforts to adapt to the new EU data protection regime, in the wake of the entry into force of 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 Joint Undertaking participated in various interinstitutional data protection activities, and provided relevant training to its staff.

2.8 Access to documents

Regulation (EC) No 1049/2001 applies to the IMI2 JU.

In 2019, the IMI2 JU, consulted as a third party, disclosed documents in the context of an access to documents request lodged with the European Commission.

No requests for access to documents were lodged directly with IMI2 JU.

3 Governance

3.1 Governing Board

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

In 2019, the Governing Board held four meetings. The list of decisions taken by the Governing Board in 2019 is available on a dedicated page of the IMI website.

The role of Chair of the Governing Board in 2019 was assumed as follows:

Dates	Chair
1 January - 6 July 2019	Mr Jean-Christophe Tellier (EFPIA)
7 July - 31 December 2019	Mr Wolfgang Burtscher (European Commission)

3.2 Executive Director

Dr Pierre Meulien was Executive Director of IMI throughout 2019.

3.3 States Representatives Group

The SRG is composed of one official delegate from each EU Member State and each country associated to the EU's research programmes. Official delegates might be accompanied by their deputies and/or national experts where needed. 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 programme orientation, progress and achievements. Information on SRG membership, including CVs and links to national websites, can be found on the SRG page of the IMI website.

In 2019, the SRG met in January, April and October in Brussels (Belgium). At the meetings, the IMI Programme Office provided detailed updates on its activities and projects, including on synergies explored with other EU programmes (such as ECSEL JU, the public-private partnership for Electronic Components and Systems). The SRG members also explored how to better support the participation of EU13-based organisations and scientists, and provided an overview of national and regional initiatives and activities that could be of interest for the implementation of the Strategic Research Agenda and the scientific priorities for 2019. During 2019, the SRG was consulted on the Call topics and documents and on the Annual Work Plan (including amendments).

In 2019, the IMI Programme Office organised a third annual joint meeting with the IMI2 JU Scientific Committee (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 Scientific Committee, which is chaired by Professor Isabelle Bekeredjian-Ding, met three times in 2019.

As part of their role, the members provided in 2019 advice on the proposed scientific priorities for 2020 that are part of the Annual Work Plan, as well as on the proposed topics that were included in IMI2 - Calls 18 and 19 (launched in 2019) and Call 20 (launched in 2020).

In 2019, the Scientific Committee's recommendations on 'Public private partnership funding – what makes a topic ultimately suitable for this kind of funding model?' were published on the Scientific Committee page of the IMI website. In addition, the Scientific Committee agreed on a work plan with a view to providing recommendations to the IMI Governing Board on matters important to the IMI objectives. The work plan, which is published on the IMI website, covers both topics related to IMI's governance and structures (i.e. data infrastructure and integration, involvement of regulators and regulatory science, equitable access) as well as topics related to the research programme (research on rare diseases within a public-private partnership, repurposing of drugs). The Scientific Committee progressed on the elaboration of these recommendations and plans to have them finalised, transmitted to the Governing Board and published on the IMI website in early 2020.

At the Governing Board's request, the Scientific Committee also produced on an opinion paper on lessons learnt from IMI in view of a public private partnership continuation in a new EU framework programme. This opinion paper was transmitted to the Governing Board and the European Commission.

The Scientific Committee is also represented in the Strategic Governing Groups (SGGs), with committee members participating in their meetings and contributing to their discussions, and subsequently providing feedback to the Committee on any relevant information. Scientific Committee members also reported on the IMI project reviews carried out in 2019 (see section 1.4.2), as well as on close-out meetings on IMI projects that have ended. Finally, representatives of the Scientific Committee participated actively in the IMI Stakeholder Forum 2019 and the IMI-EMA-FDA 6th Regulatory Science Summit.

Interactions between the States Representatives Group and Scientific Committee

The IMI Programme Office organised a third joint SRG - SC meeting on 24 October 2019. The objective was to continue to benefit fully from these two advisory bodies on topics of mutual interest. This third joint meeting provided notably an opportunity to share thoughts on the proposed scientific priorities for 2020, to get further information on sustainability measures implemented at national or regional levels and that could be of interest for IMI project results, as well as on measures to better engage with healthcare professionals / physicians in research activities, taking lessons learned from national/regional experience. The members of the two IMI advisory bodies agreed that such a joint meeting was very valuable and they looked forward to meeting again in 2020.

3.5 Stakeholder Forum

The IMI Stakeholder Forum 2019 was held on Wednesday 12 June in Brussels, Belgium. The event is described in more detail in the section 'Communication activities'.

3.6 Strategic Governing Groups (SGGs)

Cross-SGG coordination

One cross-SGG coordination meeting was held in April. This meeting was the second joint cross-SGG and EFPIA Partners in Research (PiRs) meeting. It brought a valuable perspective from different types of companies (e.g. contract research organisations, diagnostics, connected technologies, biomedical engineering, etc.). SGGs and PiRs were encouraged to increase the promotion and engagement of industry partners of different types in IMI2 JU idea generation and projects. In 2019, efforts continued to optimise the use of, and benefit from the SGG IT platform, including sharing of agendas, publishable minutes and attendance lists across SGGs and IMI advisory bodies, especially the SRG. In 2019, the EC representation in the SGGs encompassed DG RTD, DG CNECT and DG SANTE.

SGG Immunology

The SGG Immunology met once in 2019 via teleconference. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2019 and developed one Call topic that will be launched under IMI2 - Call 20.

SGG Diabetes / metabolic disorders

The SGG Diabetes Metabolic Disorders (DMD) met once in 2019. The group has not proposed any new topics for future calls and rather focused on monitoring progress of ongoing project in the DMD portfolio, maximising their synergies, as well as discussing the challenges related to sustainability of the value generated by the projects and possible strategies to address them.

SGG Neurodegeneration

The SGG Neurodegeneration met twice in plenary session during the year, once face-to-face and once via teleconference. The SGG Neurodegeneration provided input to the IMI Governing Board regarding the scientific priorities for 2019.

SGG Translational safety

The SGG Translational Safety met twice in 2019. 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 under the IMI2 - Call 18.

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 three times during 2019: two face-to-face meetings and one teleconference. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2019, and developed three topics that were launched in IMI2 - Call 18.

SGG Infections control

The SGG Infections control met four times in plenary session during the year, twice face-to-face and twice via teleconference. The SGG Infections Control was very active in providing input to the IMI Governing Board regarding the scientific priorities for 2019. Moreover, the SGG Infections control also contributed to the development of topics with a budget of almost EUR 200 million and which were published through IMI2 – Calls 20.

SGG Oncology

The SGG Oncology met twice face to face in 2019 and had several teleconferences. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2019 and developed two call topics that were launched under IMI2 - Call 18 and one call topic that is launched under IMI2 - Call 20.

3.7 Associated Partners

IMI has continued to develop Associated Partner methodologies that includes the refinement of Associated Partner application documentation and processes. The IMI website was continually updated as new Associated Partners or new participations of existing Partners were approved and now shows a total of 32 Associated Partners, many of whom are participating in multiple topics. There are also a further four new Associated Partners whose applications are in the process of finalisation and two expansions of scope of existing Associated Partners anticipated.

As of the end of 2019, the following organisations had become IMI2 JU Associated Partners. As detailed in section 1.7, at the end of 2019 the total Associated Partner commitment to IMI projects stood at EUR 170 million. It is anticipated that the IMI2 JU target of EUR 213 million committed from Associated Partners will be attained in 2020.

- Accelerate Diagnostics contributes to the VALUE-Dx project on diagnostics for antimicrobial resistance.
- 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 contributes to the VALUE-Dx project on diagnostics for antimicrobial resistance.
- Bill and Melinda Gates Foundation contributes to the PERISCOPE project on pertussis (whooping cough) vaccines and to the 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 contributes to the VALUE-Dx project on diagnostics for antimicrobial resistance.
- Cepheid Europe contributes to the VHFMoDRAD project on diagnostics for Ebola and related diseases.
- CEPI (Coalition for Epidemic Preparedness Innovations) contributes to the Ebola vaccine project EBOVAC-3.
- CHDI Foundation contributes to IMI2 - Call 15, topic 6 (Digital endpoints in neurodegenerative and immune-mediated diseases).
- Children's Tumor Foundation contributes under IMI2 - Call 15, topic 1 (Integrated research platforms enabling patient-centric drug development).
- Datapharm contributes to IMI2 – Call 18, topic 3 (Improving patient access, understanding and adherence to healthcare information: an integrated digital health information project).
- Diamond Light Source contributes to IMI2 – Call 17, topic 2 (open access chemogenomics library and chemical probes for the druggable genome).
- European Hematology Association (EHA) contributes to IMI2 – Call 18, topic 6 (Supporting the development of engineered T cells).
- International Diabetes Federation contributes to the Hypo-RESOLVE project on diabetes.
- Invicro will contribute to IMI2 – Call 15, topic 5 (Development and validation of translational platforms in support of synaptopathy drug discovery).
- JDRF contributes to the diabetes projects INNODIA, BEAT-DKD and Hypo-RESOLVE. JDRF will also contribute to IMI2 - Call 15, topic 4; (Emerging translational safety technologies and tools for interrogating human immunobiology); IMI2 - Call 17, topic 1 (Optimising future obesity treatment); and IMI2 - Call 18, topic 2 (Health Outcomes Observatories – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes).
- KTH Royal Institute of Technology contributes to IMI2 – Call 17, topic 2 (open access chemogenomics Library and chemical probes for the druggable genome).
- Leona M. and Harry B. Helmsley Charitable Trust contributes to the diabetes projects INNODIA and Hypo-RESOLVE.
- McGill University contributes to IMI-2 Call 17, topic 2 (open access chemogenomics Library and chemical probes for the druggable genome).
- Medicines for Europe contributes to IMI2 - Call 18, topic 3 (Improving patient access, understanding and adherence to healthcare information: an integrated digital health information project).
- Medicines for Malaria Venture (MMV) contributes to the ESCULAB project on a European Screening Centre as a unique library for attractive biology.
- Obesity Action Coalition (OAC) contributes to IMI2 - Call 17, topic 1 (Optimising future obesity treatment).
- Ontario Institute of Cancer Research will contribute to IMI2 - Call 17, topic 2 (Open access chemogenomics library and chemical probes for the druggable genome).
- Parkinson's UK contributes to the PD-MitoQUANT project on mitochondrial dysfunction in neurodegeneration; the NEURONET coordination and support action for IMI projects in the neurodegeneration area; and the PD-MIND project on Parkinson's disease. It will also contribute 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 contributes to the RADAR-AD project on digital technologies and Alzheimer's disease.
- SpringWorks Therapeutics contributes 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 contributes 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).
- Trial Nation contributes to IMI2 - Call 18, topic 2 (Health Outcomes Observatories – empower patients with tools to measure their outcomes in a standardised manner creating transparency of health outcomes).

- University of Dundee contributes 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 contributes to the VALUE-Dx project on diagnostics for antimicrobial resistance.

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[13] and operating procedures. In particular, in 2019 IMI applied/followed the Manual of Financial Circuits (and related checklists and workflows) adopted by Executive Director Decision No 55/2018 of 18.12.2018.

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 implements two different framework programmes - IMI1/FP7 and IMI2/H2020[14] - with different obligations and modus operandi. In 2019, IMI continued the implementation of its programme in accordance with the two above-mentioned financial frameworks. In this context, the activities in 2019 included the following:

- An update of the internal procedure for review and assessment of FP7 periodic and final reports (including updated templates for Coordinators);
- Effective implementation of the Commission IT operational tool for H2020 management (for Grant management, Project monitoring, reporting and payment, Audit implementation and Recovery order);
- Active communication and cooperation with the CSC, through participation in various working groups (e.g. the Common Legal Support Service, etc.) with the aim of enhancing a common understanding and interpretation of the requirements of newly developed workflows for H2020 in the context of the IMI2 JU environment.

13 See above Section 2.2 "Legal and financial framework".
14 See above Section 1.6 "Operational budget execution".

4.2 Ex ante control 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)[15].

Overview of the control system for operational budget implementation

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 as summarised in the following table. A key element of this system is the implementation of the 'Guidance Horizon 2020 ex-ante controls on interim & final payments'[16], which allow a simplified and trust-based approach to beneficiary controls. In any case, based on a lesson learned, the finance and the operational team perform ad hoc controls to ensure sound financial management and perform a proper risk assessment at the grant preparation phase.

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

Overview of the operational expenditure

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 31/12/2019.

15 See above Section 2.3 'Budget and financial management'.
16 Adopted by the CSC Steering Board on 15 December 2016.

IMI1 (FP7) project portfolio on 31/12/2019

				Pre-financing payments	Interim & final payments[17]	Total paid
Total projects funded	59	Running on 01/01/2019	16	0	41 182 547	41 182 547
		Ended[18] during 2019	(5)			
Total IMI1 projects running on 31/12/2019			**11**	**0**	**41 182 547**	**41 182 547**

IMI2 (H2020) projects portfolio on 31/12/2019

				Pre-financing payments	Interim & final payments[19]	Total paid
Total projects funded	89	Running on 01/01/2019	54	102 051 882	71 361 346	173 413 228
		Ended during 2019[20]	(4)			
		Signed in 2019	29			
Total IMI2 running on 31/12/2019			**79**	**102 051 882**	**71 361 346**	**173 413 228**

I

MI1 and IMI2 full project portfolio on 31/12/2019

				Pre-financing payments	Interim & final payments[21]	Total paid
Projects	90	Total running projects	90	102 051 882	112 543 893	214 595 775
		Total ended projects[22]	(9)	/	/	/

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 IMI1 projects which have ended their activities and presented, or are being to present the final report.
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 IMI2 projects which have ended their activities and presented, or are being to present the final report.
21 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).
22 Of which 5 IMI1 projects and 4 IMI2 projects.

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 'Funding and Tenders Portal'.

The goal of controls performed at this stage is to make sure that the best proposals are selected; that they match the conditions set out in the Call for proposals; and that the beneficiaries are capable of completing the projects successfully and on time. To this end, the following checks are performed:

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

Indicator	Results 2019	Result 2019	Result 2018	Result 2017
% of annual coverage of Call topics identified in AWP 2019	Topics planned in AWP 2019: 10 Topics launched in 2019: 10 ▪ Call 17: 3 topics ▪ Call 18: 6 topics ▪ Call 19: 1 topic	100 %	100 %	100 %
No. redress procedures on the result of the evaluation		2	1	0

The Programme Office addressed two redress applications in the period of 2019. The first application related to Call 15, Stage 1 and the second application concerned Call 15, stage 2. In response to both applications, the Programme Office assembled dedicated teams to analyse the redress request and take appropriate action. The main task of the teams was to establish whether the IMI2 JU staff had complied with the mandated procedures while conducting IM2 evaluations.

On both matters, the dedicated teams found that there was no shortfall in performance from IMI2 JU staff or the retained independent evaluators and that established IMI2 JU procedures were followed at all times. This was confirmed in both Independent Observer Reports for Call 15 (stages 1 and 2) which noted the IMI2 JU staff's professionalism; the latter report particularly praised the staff for 'always being visible, approachable, and highly knowledgeable'.

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 2019, IMI2 JU confirmed and consolidated the efficiency and robustness of its granting process as reflected by the three performance indicators described in the following table. This is the result of the efficient management of the H2020 IT management tools, the quality control ensured by the grant coordinator, and the enhanced management supervision and regular monitoring.

- **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 2019, the average TTI was 73 days against a legal target of 153 days, and 2 days fewer than in 2018.
- **Time to Grant (TTG)** represents the maximum eight months between the Call deadline and grant signature. In 2019, the average TTG improved again and is at 210 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 2019, pre-financing payments confirmed the previous positive result of 9 days on average, against a target of 30 days.

Indicators	Target	Result 2019	Result 2018	Results 2017
Total average Time to Inform (TTI)	153 days	**73 days**	75 days	81 days
Total average Time to Grant (TTG)	245 days	**210 days**	232 days	270 days
Total average Time to Pay (TTP) for pre-financing	30 days	**9 days**	9 days	11 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[23].

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.

23 More information can be found in Section 1.4.2 above.

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.

Within IMI, the verification process of each transaction is particularly complex due to the nature of the projects implemented, the amounts at stake per project (average EUR 30.6 million with projects having a budget higher than EUR 250 million) and the high number of participants per project (average 26). In addition, a portion of the processed operational transactions involves final payments to the projects (11 out of 91 transactions in 2019). As a rule, the payment of the final balance needs a more in depth and extensive analysis and assurance elements in comparison to interim payments.

The tables below provides a multiannual overview of operational transactions, namely:

- Pre-financing payments made to new projects selected within the H2020 programme (which increased compared to 2018) and
- Interim and final transactions[24] made to ongoing projects funded within FP7 and H2020 programmes.

The trend shows that in 2019 the total volume of financial transactions related to IMI projects (91 in total) remains substantially the same compared to the previous year.

Number of operational transactions

	2012	2013	2014	2015	2016	2017	2018	2019
Pre-financing payments	12	14	18	16	16	16	20	**29**
Interim & final payments [25]	26	33	32	30	59	66	70	**62**[26]
Total	38	47	50	46	75	82	90	**91**

However, the attribution for the transactions made during the year have changed considerably in 2019:

- Transactions related to IMI1 (FP7 Programme) projects are progressively decreasing (18 compared to 37 in 2018), while
- Transactions related to IMI2 (H2020 Programme) are increasing (73 compared to 53).

The reduction of the number of cost claims received, as indicated in the table below, is actually due to the decrease of transactions related to final payments of IMI1 projects. This figure is correspondingly balanced by the increasing number of pre-financing payments for new IMI2 projects that will generate an increasing number of interim payments in the upcoming years.

The table below also explains the modalities of the reporting process, where the number of payments made during the year may not match with number of reports received. That is because the reports received during the last quarter - and to be handled within the legal deadline of 90 days – have to be carried over to the following year.

24 The wording “transaction” is used here to indicate both, direct payments and “clearings”. In some cases, payments for the interim or final periods are fully or partially compensated (“cleared”) 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.
25 Including the clearings of pre-financing.
26 Of which, 18 on IMI1 projects and 44 on IMI2 projects.

Cost claims received with project reports against payments made

		2019	2018	2017
1.	Cost claims received before year 'N'	17	7	15
2.	Cost claims received within the year 'N'	57	80	58
3.	Cost claims not validated at the end of the year (to be paid the following year)	12	17	7
4.	Cost claims processed during the year (1 + 2 - 3)	62	70	66
5.	Pre-financing new projects	29	20	16
6.	**Total transactions (4 + 5)**	**91**	**90**	**82**

b) Value of operational transactions

The breakdown of the costs accepted and paid in 2019 by IMI based on the operational transactions described above is presented in the table below.

The total value of the processed transactions amounted to EUR 245 195 352, of which EUR 214 595 775 was actually paid to beneficiaries as pre-financing or interim/final payments, while EUR 30 599 577 are the result of full and partial clearing made against pre-financing paid at the beginning of the project.

Although the value of the transactions processed decreased slightly in 2019 (from 254 to 245 million), the value of actual payments (excluding clearings) increased from 194 to 214 million.

Overall, it is worth noting that the continuous improvements in the project management workflow and the coordinated effort made by the staff resulted in a considerable increase of the annual operational budget execution rate, which reached 98 % in 2019.

This demonstrates that cautious planning and enhanced monitoring of payment appropriation absorption yielded a positive result.

		No of transactions		Value of payments	Value of clearings[27]	Value of all transactions
IMI1 (FP7)	Pre-financing payments	0	**18**	0		
	Interim payments	9		41 182 547	21 294 875	62 477 422
	Final payments	8				
	Full clearing	1				
IMI2 (H2020)	Pre-financing payments	29	**73**	102 051 882	N/A	102 051 882
	Interim payments	41		71 361 346	9 304 702	80 666 048
	Final payments	3				
	Full clearing	0				
TOTAL		**91**		**214 595 775**	**30 599 577**	245 195 352
Annual approved budget				**219 133 181**		
		Budget execution		**97.93 %**		

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 2019, the financial impact of the systematic ex-ante controls on the cost claims was the following.

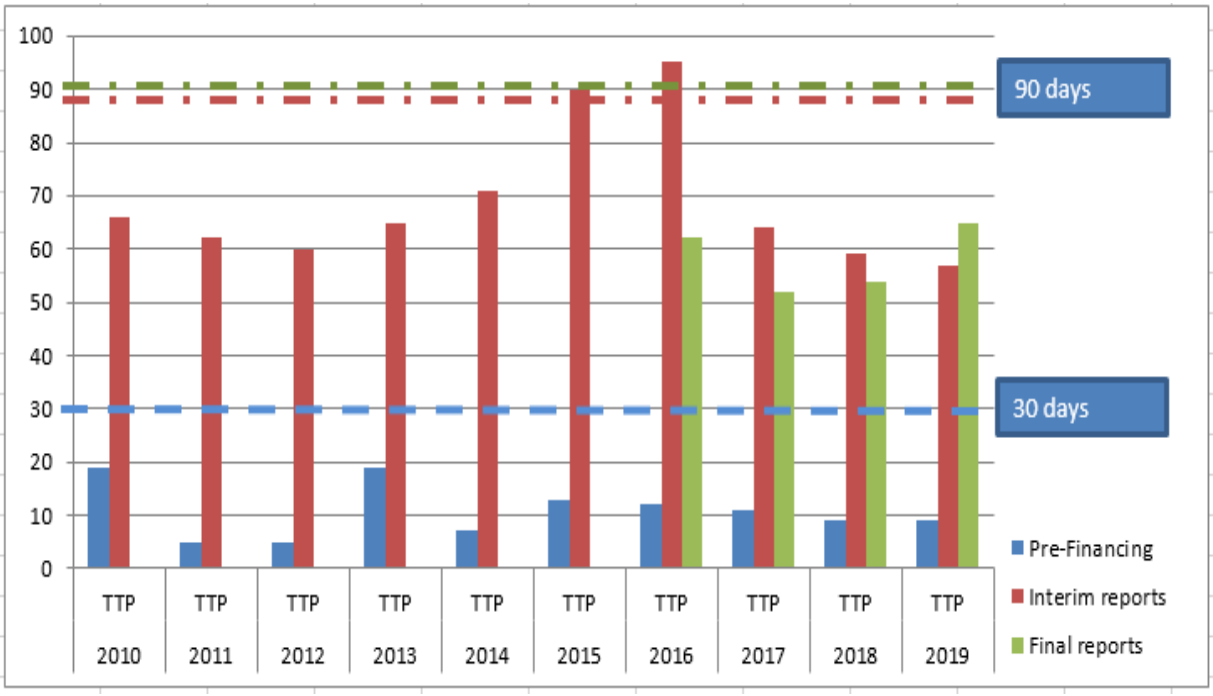
Total reported costs	IMI1	64 040 023	144 936 867
	IMI2	80 896 844	
of which covered by CFS			46 029 509
Accepted costs	IMI1	62 477 422	143 143 470
	IMI2	80 666 048	
Rejection	**IMI1**	**1 562 601**	**2.44 %**
	IMI2	**230 796**	**0.29 %**

d) Time to Pay (TTP)

Figures of 2019 confirm the positive trend undertaken by IMI. TTP for pre-financing payments remained at 9 days average per project, while interim payment time further improved. The IMI office managed to further bring down the average time to pay for interim payments from 59 to 57 days average for IMI1 and IMI2. The time taken for final payments was on average 65 days well below the target of 90 days.

27 Which includes both full and partial clearing.

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



Control efficiency and cost-effectiveness

This section presents an analysis of the costs and benefits of controls. 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. The two sections below describe respectively the cost-effectiveness of IMI controls related to the ex-ante phase, and as a whole (including call management and evaluation, and ex-post controls).

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

In terms of human resources allocated to ex-ante controls (i.e. scientific, financial and other support officers), there are 17.5 FTEs 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 56.5 % of the FTEs allocated to the management of the operational programme and around 33 % of the staff currently employed.

While total IMI administrative costs in 2019 represent 3.6 % of the total IMI payments, the costs for ex-ante controls have been estimated at EUR 2 648 700/year of which:

- EUR 745 000 for controls related to evaluation, selection and grant preparation phase; and
- EUR 1 903 700 for controls related to grant management and reporting including the costs of externalised interim reviews (see table below Section b).

The cost for ex-ante controls represent 1.19 % of the IMI operational expenditure in 2019 as described in the first table below, and can be quantified as EUR 29 430 per Grant Agreement, which corresponds to 0.01 % of the total operational expenditure.

IMI budget 2019 (Payments in EUR)		% in total budget	Total estimated costs of ex-ante control	Cost of ex-ante control as % of annual expenditure
Administrative expenditure	8 225 482	3.6 %	2 648 700	32.20 %
Operational expenditure	214 595 775	96.4 %		1.23 %
Total	**222 316 906**	**100 %**	***/***	**1.19 %**

Benefits of ex-ante controls (in EUR)	**1 793 397**
Total cost of ex-ante controls (in EUR)	**2 648 700**
Average cost (in EUR) of ex-ante control for one running Grant Agreement (Total costs / no. 90 projects running as at 31.12.2019, including projects that concluded their activities in 2019)	**29 430**

b) Cost-effectiveness of all controls applied to 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 FTEs allocated to controls	FTEs costs[28]	Other costs related to controls	Total
Call management, selection and evaluation phase	2.0	268 000	40 000*	
Grant award	3.5	437 000	/	
Grant management	14	1 643 700	260 000*	
Total cost of ex-ante controls		**2 348 700**	**300 000**	**2 648 700**
Ex-post control	1.5	169 000	168 000	
Total	**21**	**2 517 700**	**468 000**	**2 985 700**
Cost-effectiveness ratio	Cost of controls / Total expenditure 2019 (Administrative and operational)			**1.34 %**
	Cost of controls / Operational expenditure 2019			**1.39 %**
	Cost of controls / Total accepted cost 2019 (only beneficiaries' cost claims)			**2.1 %**
	Cost of controls / Total accepted cost 2019 (both beneficiaries' cost claims and validated EFPIA contribution)			**0.9 %**

* Estimates

In conclusion, the established control framework ensures 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.

28 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 in section 4.2.

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 2019 for the total value of EUR 143 143 470[29], 56 % of the costs are paid under H2020 Grant Agreements, EUR 80 666 048, compared to EUR 62 477 422 under FP7 Grant Agreements.

Ex-post control: 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 is presented 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 is presented in Annex 10 – Materiality Criteria.

Given the multi-annual nature of both programmes and 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 programmes advance, 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.

29 This amount includes the costs accepted against pre-financing (clearing) but excludes pre-financings which remain IMI assets.

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

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 under IMI1 (FP7), namely:

- selection of audits;
- coordination with the EC;
- preparation of the audit input files;
- contract management;
- monitoring of the external audit firms' progress and deliverables. In particular, regular follow up of the audit status and quality checks of audit reports;
- endorsement of the audit firm opinion and recommendations;
- analysis of errors detected and implementation of audit results.

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	242	35.5 %
Projects	59	55	93.2 %
Contributions accepted by IMI (EUR, cumulative)	**581 308 088.62**[30]	**93 391 719.53**	**16.07 %**

The following table gives an overview of the status of individual audit assignments as of 31 December 2019.

	Total audits	Audits finalised[31]	Audits ongoing
Representative	252	244	8
Risk-Based	17	14	3
Total	**269**	**258**	**11**

In 2019, 22 audits were finalised in total. One sample of representative audits was drawn in June 2019.

30 Figure as of the cut-off date of 23 May 2019, 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 of 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.

Representative and residual error rates as of 31 December 2019

At this point, the **cumulative Representative Error Rate** (RepER) resulting from all representative audits finalised by 31 December 2019 is 2.05 % in terms of IMI contribution.

The **cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.66 % 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 2019.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
195	192	98 %	2 599 149

Extension of audit findings

When an audit detects 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	259
Pre-information letters / letters of conclusion sent	259
Of which affected by systematic errors[32]	66
Extrapolation feedback received from beneficiary	63
Of which implemented	53

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 Implementation 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 in the implementation of the common audit strategy, contributes to the relevant working groups, provides inputs during the entire audit cycle from selection of audits to implementation of audit findings and provides opinions on draft audit reports and extensions of audit findings.

32 This does not include positive systematic errors and systematic errors below the materiality threshold.
33 Horizon 2020 Ex-post Audit Strategy (2016 – 2025).

As part of the H2020 programme with a harmonised legal framework, IMI2 cost claims are included in the programme level sampling, notably the H2020 common representative sample (CRS). Accordingly, IMI reports on the error rates drawn from these programme level controls. 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 control of the H2020 programme globally in 2019

The Horizon 2020 audit campaign started in 2016. At this stage, three Common Representative Samples (CRS)[35] with a total of 467 expected results have been selected. By the end of 2019, cost claims amounting to EUR 16.2 billion have been submitted by the beneficiaries to the services. The error rates on the H2020 programme level at 31 December 2019 are:

- Representative detected error rate**:** 2.78 %[36], expected to rise to 3.30 % taking into account the results of draft audit reports.
- Cumulative residual error rate for the R&I family of DGs: 2.15 % (2.24 % for DG R&I), expected to rise to around 2.31 % (2.40 % for DG R&I) when taking into account the results of the draft audit reports.

Due to its multi-annual nature, the effectiveness of the control strategy of the Research and Innovation Directorates-General can only be fully measured and assessed in the final stages of the H2020 programme, once the ex-post control strategy has been fully implemented and systematic errors have been detected and corrected.

The error rates presented above should be treated with caution. Since not all the results of the three CRS are yet available, the error rate is not fully representative of the expenditure under control. Moreover, the nature of expenditure in the first years of the programme may not be totally representative of the expenditure across the whole period. As H2020 is a multi-annual programme, the error rates, and especially the residual error rate, should be considered in a time perspective. Specifically, the cleaning effect of audits will tend to increase the difference between the representative detected error rate and the cumulative residual error rate, with the latter finishing at a lower value.

Ex-post control specific to IMI's population in 2019

By 31 December 2019, IMI had launched five individual representative samples (one sample of representative audits was drawn in June 2019). Audits were finalised from the first four of these samples. A total of 26 representative audits sampled by IMI were finalised. In addition, three risk-based audits were finalised by the end of 2019.

The total IMI accepted contribution in the finalised audits is EUR 21 043 179 including both representative and risk-based audits. This represents 15.5 % of the total population of accepted contributions paid out, EUR 135 915 091[37].

The following table gives an overview of the status of individual audit assignments as of 31 December 2019.

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

35 In addition to the Common Representative Samples, Common Risk Samples and Additional Samples have also been selected. The total of all samples represents 3245 participations. The audits of 2115 participations were finalised by 31/12/2019 (out of which 962 in 2019). 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 Based on the 298 representative results out of the 467 expected in the three CRS.

37 Figure as of the cut-off date of 15 June 2019, corresponding to the last audit sample drawn in 2019.

	Total audits	Audits finalised	Audits ongoing
Representative	59	26	33
Risk-Based	6	3	3
Total	**65**	**29**	**36**

Representative and residual error rates specific to IMI's population as of 31 December 2019

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

- **Cumulative representative error rate** (RepER) resulting from the 26 finalised audits considered representative is 0.85 % in terms of IMI contribution.
- **Cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.52 % in terms of IMI contribution.

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 2019.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
12	8	67 %	466 336

Extension of audit findings

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	29
Pre-information letters / letters of conclusion sent	29
Of which affected by systematic errors[38]	4
Extrapolation feedback received from beneficiary	3
Of which implemented	1

Under H2020, the extension of audit findings on IMI actions may also be triggered by audits performed by other EU services on IMI beneficiaries. For these cases, IMI provides its opinion to the coordinating unit, the Common Audit Service, and implements the correction. As of 31/12/2019, IMI has implemented six extension of audit findings triggered by audits performed by other EU services on IMI beneficiaries.

38 This does not include positive systematic errors and systematic errors below the materiality threshold.

4.4 Audit of the European Court of Auditors

Audit on IMI annual accounts for the financial year 2018

On 14 November 2019, the European Court of Auditors (ECA) published specific *Annual report on the EU research Joint Undertakings for the financial year 2018* as well as a report on *2018 audit of EU Joint Undertakings in brief*[39].

This was the first consolidated report on JUs, following the European Parliament request to align with the reporting approach used for EU agencies. While the audit work for financial year 2018 was performed by a dedicated ECA IMI team, no individual report was issued on IMI. IMI is presented in the dedicated paragraphs of the joint report.

ECA gave a clean bill of health for the IMI2 Joint Undertaking, issuing 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 observations on the following subjects:

- Implementation *of the 2018 budget* – the auditors noted that whilst compared to the previous year the situation with payment appropriations improved following IMI's implementation of several corrective measures and reached 87% (72% in 2017), some weaknesses regarding the planning and monitoring of the need for new payment appropriations remained.
- *Other issues* – the auditors noted that in 2018, the JU's staff turnover rate was high and particularly high for contract agents. The situation worsened due to long-term sick leaves. To overcome the staff situation in 2018, the JU made use of interim staff.

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

In order to break the cycle of over budgeting, the continuous corrective measures have been implemented in the budgetary planning and monitoring process (see also section 1.6 of the report). In particular:

- A fixed schedule of two fixed Call launch dates per year has been set out so as to ensure better operational planning of tasks and related financial transactions.
- IMI also prepared a very detailed forecast and the claim for new payment appropriations (C1 credits) was aligned up front in order to integrate into the total budget envelope the carryover estimates between 2018 and 2019.

The measures put in place have yielded results. A clear positive trend has emerged in the implementation rate of IMI operational budget (2016: 69.6 %, 2017: 72 %, 2018: 87 %, 2019: 98 % in payment appropriations).

IMI took measures to reverse a negative trend and stabilise staff situation, as further specified in section 2.6 of this report.

IMI has invested resources to retain its talents by organising training activities and by implementing a wellbeing programme. A continuous effort to reach full staffing brought results. By 31 December 2019 there were 53 positions occupied out of 56 post in the current Staff Establishment Plan: (38 out of 39 temporary agents (97.44%), 14 out of 15 contract agents (93.33%) and 1 out of 2 seconded national experts (50) %), with a 6% turnover (3 staff members left the organisation in 2019).

39 https://www.eca.europa.eu/en/Pages/DocItem.aspx?did=51982

Audit on IMI annual accounts for the financial year 2019

In accordance with the IMI2 Financial Rules, IMI's 2019 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 2019.

The Court of Auditors will draw the final audit opinion on the 2019 accounts, revenue and transactions on the basis of the work by independent external auditors as well the substantial audit work performed by the ECA dedicated team. They will report on it in autumn 2020.

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.

In line with the International Standards for the Professional Practice of Internal Auditing, the Internal Auditor confirms the organisational independence of the internal audit activity to the Board[40] on annual basis.

On 26 June 2019, IAS issued the 2019-2021 Strategic Internal Audit Plan for IMI2 JU. The plan is based on the results of IAS risk assessment conducted in December 2018, which consisted of fieldwork, including meetings and interviews with IMI staff, and a subsequent desk review of information and documents provided by IMI. IMI comments on the draft plan were provided on 20 June 2019.

The IMI Governing Board took note of the plan on 13 December 2019 as duly recorded in the minutes. In this regard, IAS has a mandate to perform internal audit engagements within IMI.

Follow up of open recommendations

IMI continued implementing the action plan[41] stemming from the audit report on the 'Coordination with the Common Support Centre and implementation of CSC tools and services in the IMI2 JU' issued on 9 March 2018. As recommended by auditors, IMI further investigated with the common implementation centre (former CSC) IT development team on how to accommodate the reporting in the common H2020 IT system of in-kind contributions by members of EFPIA and Associated Partners.

IMI collaborated closely with the common IT services and industry partners, and consulted legal experts and business process owners. Eventually, due to legal and operational constraints, it was decided to follow that recommendation as a lesson learned while designing reporting modalities for the upcoming research framework programme. IMI informed IAS about the outcome of the extensive consultations and analysis of business processes on 27 August 2019.

The IAS acknowledged the conclusions of the exploratory work conducted by IMI2 and CSC IT development team. On 21 January 2020 IAS closed this recommendation[42] and earmarked the related risks expected from the introduction of Horizon Europe IT tools for the next full risk assessment, scheduled to take place in 2022.

40 IAS note on Organisational Independence of the Internal Auditor Ares(2020)356476 of 20/01/2020
41 The action plan was approved by the IAS on 4 May 2018
42 Ares(2020)378476

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)[43] 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 2019, the Programme Office systematically monitored the evolution of the risks identified at operational and corporate level in the annual risk assessment exercise towards the AWP 2019[44]. The regular follow up ensures that risk management is a dynamic and proactive process in view of evolving corporate priorities. Throughout the year, 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 the:

- Strategic Risk Register (SRR), which brings together the most critical risks at corporate level;
- Operating Risk Register (ORR), which is the operational tool managed at department level.

Both these 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 2019 focused on the following areas.

1. Optimising resources available for the implementation of the programme

Programme Office actions:

- Extensive preparatory consultations with the Members.
- Development of a fixed plan of Call stages shared in advance with all stakeholders.
- Assistance to the SGGs to ensure coordination in certain strategic areas and making the development of new topics more transparent and effective.
- Advanced collaboration between IMI Scientific Officers and Call topic writers through targeted briefings and training courses.
- Developing collaborations and connections with other EU initiatives and with other JUs (e.g. ECSEL JU) in the health cluster.
- Particular attention paid to human resources management, especially as regards project related activities, the efficiency of which is dependent upon a sound interaction between science and finance. In addition, a particular effort was given to ensure business continuity in the absence of the Head of Administration and Finance and to recruit a new manager. To that purpose, the temporary revision of the organisational structure put in place in autumn 2018 continued until the recruitment of the new manager in October 2019. Collectively applied those measures ensured adequately the efficiency of operations and the robustness of controls on the financial transactions.

43 The annual risk assessment is performed in accordance with the methodology defined in the Guideline for risk management approved by the Executive Director.
44 RAE Report 2018/2019 of 3 October 2018 (IMI2/INT/2018-01652).

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.
- Carrying on with the new SME strategy, and exploring and drafting potential call topics adapted to SME needs and activities to address the low rate of SME participation (further details on this action can be found in Section 1.3.1 “SME involvement”).
- Improving interactions and involvement with regulatory authorities and with patients through involvement in IMI projects of patient organisations and their participation in advisory bodies or consulted for topics of relevance (further details on this action can be found in Sections 1.3.2 and 1.33 above).

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 2019 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.
- Communicated on IMI’s added value and further increased the awareness of IMI stakeholders at events organised by the EC, EFPIA and the Programme Office.

6. Impact of the external environment on programme implementation

- Under the supervision and the direction of the European Commission, the IMI Programme Office monitored with the members and project participants the development and potential impact of Brexit on the project management.

4.7 Fraud prevention and detection

IMI has developed and implements its own antifraud strategy aligned with the Common Anti-Fraud Strategy in the Research Family (RAFS)[45]. 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[46].

This common strategy is implemented at JU level and in coordination with DG RTD and other members of the research family through a multiannual action plan coordinated by the Fraud and Irregularity in Research (FAIR) Committee. In 2019, IMI's activities focused on:

- participation in the assessment of the outcome of the implementation of the action plan made by the FAIR Committee, and
- drawing a new strategy and action plan[47] aligned with the new Commission's Anti-Fraud Strategy (CAFS) of 29 April 2019, and in particular with the Common Research Family Anti-fraud Strategy (RAFS) set up by the Common Audit Service (Unit RTD B2-CAS).

The IMI2 JU Strategy implements the overall RAFS and addresses the specificities of its programme and the complexity of the public-private partnership. In this context, the IMI internal action plan offers a proactive approach to managing the risk of fraud, which is analysed at two levels:

- as part of the annual risk assessment exercise of JU activities, and
- 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 2019 IMI did not identify any new cases of irregularities or suspected fraud while managing its project portfolio and did not receive any OLAF enquiries or requests for information.

45 This strategy, which is the preceding one, was adopted for all the Research family (DG RTD, CNECT, ENER, MOVE, GROW, HOME, AGRI, EAC, REA, ERCA, EASME, INEA, Clean Sky, IMI, ECSEL, FCH, BBI, SHIFT2RAIL, SESAR and GSA) by the Executive Committee of the Common Support Centre of DG RTD on 7 February 2015. The current Common Anti-Fraud Strategy in the Research Family was endorsed by the Executive Committee of the Common Implementation Centre on 21 March 2019.
46 Office européen de lutte antifraude (European Anti-Fraud Office).
47 Adopted by the IMI2 JU Governing Board decision No 2020-12 on 27 April 2020

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[48] and was adopted by the Governing Board in December 2017[49]. 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 Head of Administration and Finance - as Risk Management and Internal Control manager (RMIC) - the Management team and the Audit Manager. IMI personnel at all levels ensure the implementation of the internal control framework.

Management's key internal control responsibilities during 2019 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 2019, IMI's internal control action plan continued to improve its effectiveness and robustness focusing on the following objectives:

- Objective 1: Effective and reliable internal control system giving the necessary guarantees concerning the legality and the regularity of the underlying transactions;
- Objective 2: Effective and reliable internal control system in line with sound financial management;
- Objective 3: Maintain an effective risk management process, which allow to identify, assess, and managing risks, i.e. potential problems (or changes) that could affect the achievement of the IMI2 JU objectives;
- Objective 4: Minimisation of the risk of fraud through application of effective anti-fraud measures, integrated in all activities of the JU and revision of the anti-fraud strategy (AFS).

Management assessment of the effectiveness of the internal control system

The self-assessment of the effectiveness of the internal control framework in 2019 was based on the criteria set out in the implementation guidance applied by IMI, 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 2019;
- 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.

In order to assure that all aspects of IMI operations and control (financial management, governance, administration and horizontal support, procurement and contracts, HR, IT, communication) were covered by

48 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.
49 GB Decision of 20 December 2017 (IMI2-GB-DEC-2017-28).

the assessment, the 17 control principles were analysed both individually and as part of the corresponding control component[50]. The ranking of each principle, in terms of compliance, effectiveness and consistency is then summarised in an operational dashboard.

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; reports are entered into the register through a dedicated procedure and using pre-defined templates. The central register is reviewed regularly by the Risk Management and Internal Control (RMIC) manager, the Internal Audit Service (IAS) and, in the course of the Declaration of Assurance (DAS) procedure, by the European Court of Auditors (ECA).

The reasons of the events reported in 2019 have been analysed by IMI management 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

The annual evaluation 2019 of the IMI local financial systems was performed by DG BUDG (Note to IMI of 16.12.2019 - Ares(2019)7714999) according to Article 49 (e) of the Financial Rules.

DG Budget has reviewed the available information as regards changes in the local systems and/or in the control environment and assessed the risks underlying any internal control deficiencies identified by audits and supervisory controls. DG Budget has also verified a sample of the operations authorised during the 2018 financial year and reviewed key performance indicators.

The evaluation has not identified any internal control weakness, 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. Based on the available evidence, DG Budget concluded that the internal control systems were working as intended. The accounting systems implemented in IMI JU are therefore validated.

Assessment of the functioning of the internal control system

In conclusion, the results of the 2019 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 2019, the IMI internal control system was strengthened by implementing the action plan addressing IAS audit recommendations, addressing ECA remarks as well as IMI's Accounting Officer's observations.

50 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[51];
  - 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;
  - Stakeholder Forum feedback.
- Findings and opinions from internal and external audits:
  - reports and follow up notes 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 European 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 2019, 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.

51 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.

5.4 Statement on management reporting

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 the present Annual Activity Report and in its annexes is, to the best of my knowledge, accurate and complete.

Brussels, 29 February 2020

Elise Oukka, Head of Administration and Finance

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 the present Annual Activity Report and in its annexes is, to the best of my knowledge, accurate and complete.

Brussels, 29 February 2020

Hugh Laverty, Head of Scientific Operations

6 Declaration of assurance

I, the undersigned,

Executive Director of the Innovative Medicines Initiative 2 Joint Undertaking

In my capacity as authorising officer

Declare that the information contained in this report gives a true and fair view[52].

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, 29 February 2020

Pierre Meulien

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

Annexes

Annex 1 - Organisational chart

Annex 2 - Establishment plan

Annex 3 – Project outputs

Annex 4 - Publications from projects

Annex 5 - Patents from projects

Annex 6 - Scoreboard of Horizon 2020 common KPIs

Annex 7 - Indicators for monitoring cross-cutting issues

Annex 8 - Scoreboard of KPIs specific to IMI

Annex 9 – Provisional annual accounts

Annex 10 - Materiality criteria

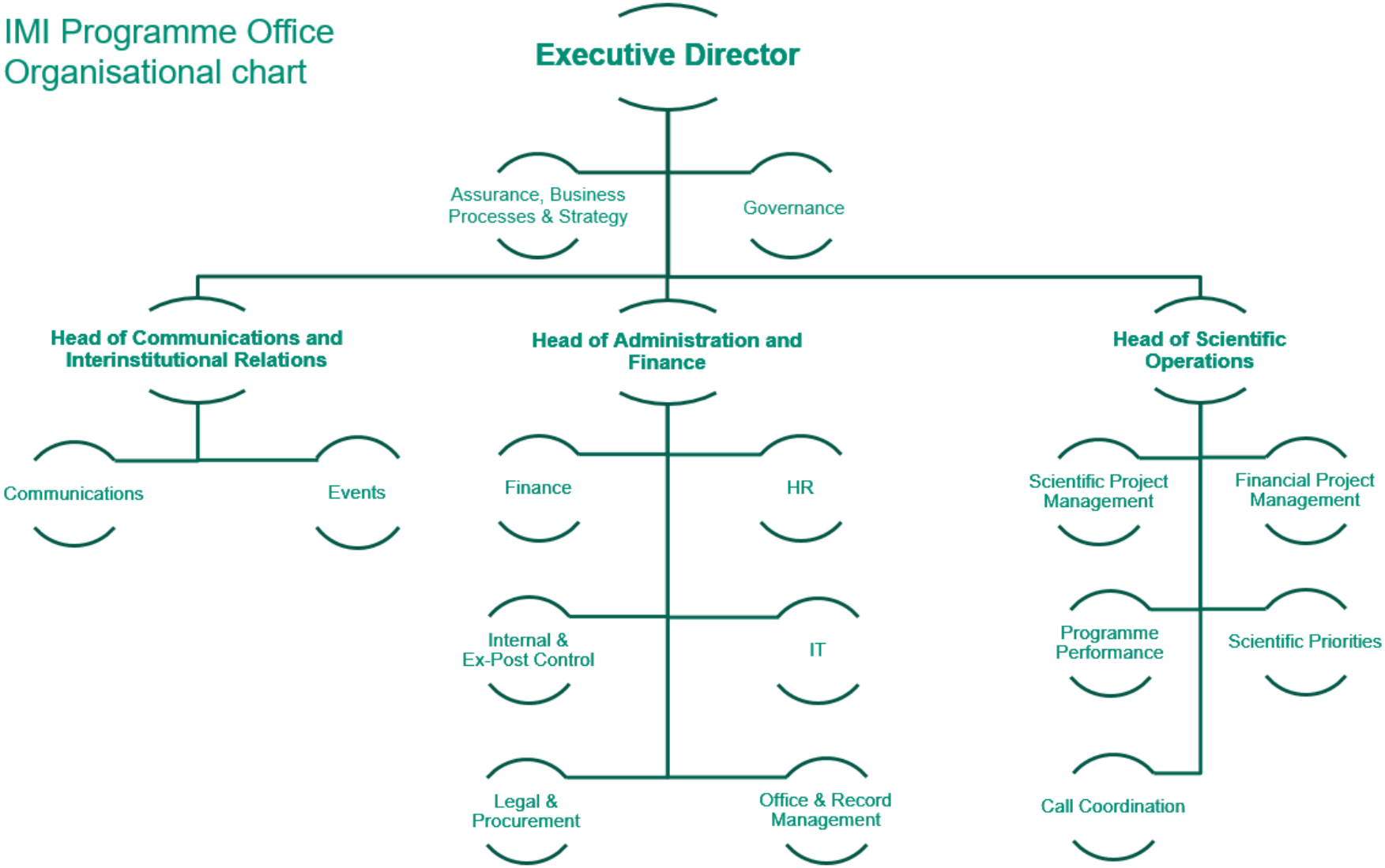
Annex 11 – Media highlights

Annex 12 - List of acronyms

Annex 13 – Table of IMI projects

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

Annex 1 - Organisational chart



Annex 2 - Establishment plan

Grade	Year 2018			Year 2019												
	Establishment plan 2018			Evolution in posts						Organisational evolution			Establishment plan 2019			Posts filled on 31/12/19
				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		5	5		**+ 1**									**6**	**6**	5
AD8		7	7		**- 1 + 1**									**7**	**7**	4
AD7		4	4		**- 1**									**3**	**3**	6
AD6		2	2		**+ 2**									**4**	**4**	4
AD5		10	10		**- 2**									**8**	**8**	9
Total AD		**33**	**33**											**33**	**33**	**32**
AST11																
AST10																
AST9																
AST8		1	1											**1**	**1**	1
AST7																

AST6															
AST5															
AST4		2	2										**4**	**4**	2
AST3		2	2										**0**	**0**	2
AST2															
AST1		1	1										1	1	1
Total AST		**6**	**6**										**6**	**6**	**6**
SC6															
SC5															
SC4															
SC3															
SC2															
SC1															
Total SC		**0**	**0**										**0**	**0**	**0**
Overall total		**39**	**39**										**39**	**39**	**38**

Notes

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

Contract agents

Grade	2018	2019	Posts filled on 31/12/19
CA FG IV	2	2	2
CA FG III	12	12	11
CA FG II	1	1	1
CA FG I	0	0	0
Total CA	**15**	**15**	**14**

Notes:

- CA = contract agent
- FG = function group

Seconded national experts (SNEs)

SNEs	2018	2019	Posts filled on 31/12/19
Total	**2**	**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(s)
CANCER-ID cancer	Developed circulating tumour cells, circulating tumour DNA and microRNA technology benchmarking protocols for clinical implementation have been. The benchmarking protocols can be used by different stakeholders for the following purposes: ▪ technology developers for optimising their technologies and protocols; ▪ pharmaceutical companies for decision making on which technology is fit for the intended context of use; ▪ analytical laboratories to implement technologies in their facilities and determine whether staff operating the technologies are appropriately trained and the internal processes are adequate; ▪ regulators to understand benefits and limitations of technologies used in clinical studies.
CANCER-ID cancer	Developed best practice documents for pre-analytical sample handling (with CEN/TC 140 (European Committee for Standardisation): Standardisation in the field of *in vitro* diagnostic medical devices). The best practice documents facilitate the implementation of new technologies at analytical sites and the respective collaboration with CEN/TC 140 helps to establish and publish them as technical documents at the international level with the aim to make the results of CANCER-ID part of emerging ISO (International Organization for Standardization) standards.
DIRECT diabetes	Developed several prediction models for non-alcoholic fatty liver disease (NAFLD) using clinical and omics data by machine learning tools and released a publicly available tool for liver fat prediction www.predictliverfat.org.
DIRECT diabetes	Performed clustering of type 2 diabetes patients based on baseline characteristics and investigated the molecular signature of diabetes progression. This has led to the identification of aetiological processes for diabetes development and how these associate with the progression of diabetes.
ELF drug discovery	The European Lead Factory and the German Cancer Research Center teams developed highly effective chemical leads against Kallikrein-related peptidase 6 (KLK6), the protein that was initially identified as potentially playing a role in the development of some types of cancer, including colon cancer and melanomas. Subsequent profiling showed that one of the KLK6 compounds reduced the invasion of human colorectal carcinoma cells (HCT116) in a dose-dependent manner. These findings could contribute to the development of potential new cancer treatments and have been published in ChemMedChem (https://doi.org/10.1002/cmdc.201900536).
ENABLE antimicrobial resistance	The project has selected a new antibiotic candidate, a Mutabilis oral combination, for the treatment of complicated urinary tract infections and acute pyelonephritis caused by bacteria (i.e. *E. coli, Klebsiella spp.* and *P. mirabilis*) resistant to antibiotics such as fluoroquinolones and cephalosporins. The Mutabilis candidate combines an oral prodrug of a known beta-lactam of the cephalosporin class with MUT485, an oral prodrug of a novel highly potent beta-lactamase inhibitor that restores the activity of the cephalosporin partner against resistant bacteria and reduces the risk of resistance development. Administration of the oral combination is expected to reduce the use of last-line agents, such as carbapenems, and result in fewer hospital admissions or reduce the length of stay in the hospital.
ENABLE antimicrobial resistance	The project has advanced one compound, apramycin, from preclinical into a Phase I clinical study. ENABLE selected Juvabis's apramycin as a new antibiotic candidate in October 2018, and it is currently being evaluated in a Phase I randomised, double-blind, placebo-controlled single ascending dose study in healthy volunteers. This is a first-in-human study to evaluate the safety, tolerability, and pharmacokinetics of

Project title	Description of result(s)
	apramycin, an aminoglycoside antibiotic that has demonstrated encouraging efficacy against a variety of WHO priority pathogens.
ORBITO drug delivery	The project has developed a best practice guidance for physiologically-based pharmacokinetic (PBPK) *in silico* modelling to help the achievement of consistent outputs. This provides extensive guidance on the selection of input parameters and modelling assumptions for different molecular classes and formulation types. This is useful guidance for the industry and can provide a basis for a more standardised application of models and facilitate their use in future regulatory applications.

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

Project title	Description of result(s)
APPROACH osteoarthritis	A list of 18 biochemical biomarkers to be assessed in the APPROACH clinical study has been collected according to technical performance data. The list includes biomarkers validated in previous well-described cohorts as well as new biomarkers developed and tested within APPROACH. The majority of them have been derived from joint tissue. These biomarkers will be used to identify osteoarthritis phenotypes and stratify patients into specific subsets that correlate with disease progression.
CANCER-ID cancer	Assessing the correlation between the number of circulating tumour cells, the number of tumour mutations and their frequency in circulating tumour tDNA by next generation sequencing with response to immuno-oncology drugs in NSCLC (non-small cell lung cancer). Preliminary analysis implies an inverse correlation of the aforementioned markers with therapy response – i.e. an increase in the number of CTCs suggests a less effective response to treatment (manuscript in preparation).
DIRECT diabetes	Identified 25 omics features (potential biomarkers) from transcriptomics, metabolomics and proteomics data linked to early diabetes remission after obesity surgery.
DIRECT diabetes	Glycaemic response to GLP-1RA treatment varies markedly among patients with T2D yet the mechanism for this variation is uncertain and it has not been possible to predict who will respond well and who will respond poorly. The DIRECT project has identified a gene variant in the GLP-1R region associated with response to GLP-1R agonist treatment in T2D patients, which may help predict the patients' response to those treatments.
DIRECT diabetes	In a meta-GWAS (genome-wide association study) that included ~5 500 subjects of European ancestry from six different cohorts treated with sulphonylureas, a gene variant with glycaemic response to sulphonylureas at a genome-wide scale was identified. This gene has strong biological evidence of involvement in the pharmacokinetics of sulphonylureas and may pave the way for more informed clinical decisions for diabetes patients.
EU-AIMS autism spectrum disorders	In a sample (n = 47) of 23 adolescents with autism and 24 controls, the project found that in adolescents with autism there is an altered pupil dilation while watching scenes of human interactions which predict social cognitive performance. The new method will complement the use of brain scans to measure brain differences between autistic and non-autistic people when processing social or sensory information.
EU-AIMS autism spectrum disorders	In a sample of 417 children, adolescents, and adults with autism spectrum disorder (ASD), older age, lower intelligence quotient and more severe social-communicative symptoms, but not sensory or repetitive symptoms or co-occurring psychiatric symptoms, are associated with lower adaptive functioning and greater ability-adaptive function discrepancies. Thus, interventions targeting adaptive skills acquisition should be adapted in their timing and intensity across developmental periods, levels of cognitive ability and take account of social-communicative ASD symptom severity.

Project title	Description of result(s)
FLUCOP vaccines	Dynamic mathematical models for evaluating and predicting vaccine efficacy of influenza virus infection have been built. These are based on humoral and cellular immune-mediated mechanisms of protection against influenza and demonstrated the added value of cellular immunity at both individual and population levels for reducing disease and epidemic burdens, even in the case of vaccine mismatch (low degree of similarity between the circulating viruses and the viruses in the vaccines).
PRECISESADS autoimmune diseases	Biomarker discovery at tissue level: the project finalised the proteomic and transcriptomic analyses of skin samples in systemic sclerosis (SSc) patients and kidney biopsies in lupus nephritis patients, resulting in the identification of tissue markers of disease severity and progression. Analysis of disease tissue matched to blood and urine samples led to the identification of novel biomarkers of diagnostic and prognostic utility to patients and physicians.
PRECISESADS autoimmune diseases	Specific protein biomarkers were identified that reflect activation of immune effectors and tubular damage in lupus nephritis.
PRECISESADS autoimmune diseases	Patterns of miRNA enrichment were found in urinary extracellular vesicles from patients with systemic autoimmune diseases (SADs) and kidney involvement.
PRECISESADS autoimmune diseases	Innovative technology: Unique standardisation of flow cytometry analyses across 11 different instruments – enabling high quality and reproducible scientific multi-centre collaboration in SADs research
SPRINTT geriatrics	Completion of the SPRINTT randomised clinical trial in October 2019: 1 519 participants (70 years and older) were randomised among a panel of 6 759 screened people into either the healthy aging lifestyle education (HALE) group or the multicomponent intervention (MCI) group in 11 European countries; 75 % of the trial population has completed the expected 2-year follow-up. The data are now being analysed to see whether the MCI programme (physical activity [PA], nutritional counselling/dietary intervention, and information & communication technology [ICT] intervention) is more effective than the HALE programme on the hazard rate of mobility disability assessed by the inability to complete a 400 metre walk test in less than 15 minutes, in nondisabled older people with physical frailty and sarcopenia (PF&S).

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
AETIONOMY Alzheimer's disease and Parkinson's disease	Developed and validated a new machine learning method for grouping time series data even when there are many data missing. The method is called ‘variational deep embedding with recurrence’ (VaDER). VaDER can accurately recover clusters from simulated and benchmark data and successfully stratified patients with Alzheimer’s disease and patients with Parkinson’s disease into subgroups characterised by clinically divergent disease progression profiles.
AETIONOMY Alzheimer's disease and Parkinson's disease	Developed a new machine learning approach, ‘variational autoencoder modular bayesian networks’ (VAMBN) that allows simulating virtual patients in a sufficiently realistic manner without issues of data privacy. In addition, VAMBN allows for simulating artificial scenarios (e.g. an age shift) and captures expected causal relationships in the data. Hence, VAMBN could facilitate data sharing as well as design of clinical trials unblocking current ‘data silos’.
COMBACTE-NET	First patient recruited in the EXPECT-1 study, a prospective observational pilot study to assess success factors and barriers for a future Phase 3 randomised controlled trial, where the efficacy of a new vaccine to prevent invasive extra-intestinal pathogenic

Project title	Description of result(s)
antimicrobial resistance	*Escherichia coli* (ExPEC) disease will be tested in community-dwelling adults. This is the first study in the project in which participants are enrolled in primary healthcare through close collaboration of the local research teams with general practice networks. https://clinicaltrials.gov/ct2/show/NCT04087681?term=expect-1&draw=2&rank=1
COMBACTE-NET antimicrobial resistance	Active recruitment in the ARTHR-IS ('Arthroplasty infections due to *Staphylococcus aureus*') case-control study whose main objective is to determine the risk factors for joint prosthetic infection due to *Staphylococcus aureus* (SA-PJI) in 20 European hospitals. The results obtained from this study will help identify the patients most at risk of developing a SA-PJI and who would benefit more from a prophylactic intervention. https://clinicaltrials.gov/ct2/show/NCT03826108?term=ARTHR-IS&draw=2&rank=1
COMBACTE-NET antimicrobial resistance	Completed enrolment for the ASPIRE-SSI study. After an enrolment period of nearly 3 years, 5 000 subjects were enrolled in 33 hospitals across 10 countries in the EU. ASPIRE-SSI ('Advanced understanding of *Staphylococcus aureus* infections in Europe – surgical site infections') is a prospective, observational, multicentre cohort study that aims to engender advanced understanding of *Staphylococcus aureus* infections in Europe incurred in surgical site infections. https://clinicaltrials.gov/ct2/show/NCT02935244?term=ASPIRE-SSI&draw=2&rank=1
COMBACTE-NET antimicrobial resistance	Database lock of all data in the ASPIRE-ICU study, a prospective, observational, multicentre, epidemiological cohort study aiming to advance understanding of *Staphylococcus aureus* and *Pseudomonas aeruginosa* infections in Europe in intensive care units (ICU). 11 countries in Europe; 30 hospitals; 10 526 patients screened; 2 031 patients enrolled; 8 297 queries closed; 31 372 samples taken and almost 10 000 documents filed. https://clinicaltrials.gov/ct2/show/NCT02413242?term=ASPIRE-ICU&draw=2&rank=1 Descriptive data on the numbers of *S. aureus* ICU pneumonias that occur, divided per region and per *S. aureus* colonisation status, based on local culture results were presented at ECCMID 2019.
COMBACTE-NET antimicrobial resistance	Completion of the SAATELLITE study, a phase II trial of suvratoxumab, a novel monoclonal antibody (mAb) targeting *Staphylococcus aureus* (SA). The trial is the first of its kind and assessed the novel mAb's ability to prevent *Staphylococcus aureus* ventilator-associated pneumonia (VAP) in mechanically ventilated intensive care unit (ICU) patients. The results are promising, showing that suvratoxumab provided a 31.9 % relative risk reduction (90 % confidence interval, -7.5 % to 56.8 %) in incidence of SA pneumonia (26 [26%] in placebo versus 17 [17.7%] in suvratoxumab recipients. P = 0.166). Results posted in https://clinicaltrials.gov/ct2/show/results/NCT02296320?term=SAATELLITE&draw=2&rank=1 and EUDRACT https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-001097-34/results
COMBACTE-CARE antimicrobial resistance	Final steps of data analysis of the EURECA study, an observational study that enrolled more than 2 000 patients, with over 1 000 carbapenem-resistant strains already processed from 50 sites and 9 European countries. The results will provide critical new insight on the risk factors, clinical management and outcomes of patients with multidrug resistant Gram-negative bacteria infections and inform the development programmes for new antibiotics.
COMBACTE-CARE antimicrobial resistance	Publication of the results of REJUVENATE study, a Phase 2 open-label study of the pharmacokinetics and safety of aztreonam-avibactam plus metronidazole in hospitalised adults with complicated intra-abdominal infections. The results supported the selection of the aztreonam/avibactam 500/167 mg (30 min infusion) loading dose and 1 500/500 mg (3 h infusions) maintenance dose q6h regimen, in patients with creatinine clearance >50 mL/min, for starting the phase 3 trial (REVISIT) initiated in collaboration with the Biomedical Advanced Research and Development Authority

Project title	Description of result(s)
	(BARDA) (protocol, sites selected). J Antimicrob Chemother. 2019 Dec 12. pii: dkz497. doi: 10.1093/jac/dkz497. [Epub ahead of print]
COMBACTE-MAGNET antimicrobial resistance	Completion of enrolment in the EVADE trial. Of the 1 023 subjects screened into the study, 188 have been randomised in 48 sites. EVADE ('Effort to prevent nosocomial pneumonia caused by *Pseudomonas aeruginosa* in mechanically ventilated subjects') is a Phase II, randomised, controlled safety and efficacy trial of MEDI3902, a bispecific monoclonal antibody against two *P. aeruginosa* proteins, for the prevention of ventilator-associated pneumonia in adult ICU patients. https://clinicaltrials.gov/ct2/show/NCT02696902?term=EVADE&draw=2&rank=5
iABC antimicrobial resistance	The Novartis sponsored iBEST-1 Phase II clinical study of inhaled tobramycin inhalation powder) in bronchiectasis patients was completed. The recruitment was curtailed: 107 patients enrolled at 34 sites (6 countries) instead of the 180 planned for administrative reasons unrelated to safety findings. Database lock was achieved in May 2019. Initial analysis of the results is very positive and the final clinical study report will be published soon. The design of the study has been published (Pulm Pharmacol Ther. 2019 Oct; 58:101834. doi: 10.1016/j.pupt.2019.101834. Epub 2019 Aug 18.)
iABC antimicrobial resistance	The Polyphor POL7080 programme continued to progress well towards clinical trial with substantial preclinical testing completed. Testing of different nebulised and dry powder formulations of POL7080 completed and stability testing completed. A protocol for the POL7080 Phase 1 clinical study has been finalised, a key milestone before initiating the study.
iABC antimicrobial resistance	The consortium started clinical trials to support the clinical development of two new compounds added to the project: a Novartis sponsored Phase II study testing the compound CFTR Potentiator QBW251 in bronchoectiasis patients that will start recruiting in 2020, and an Alexia sponsored Phase I and Phase studies testing their compound ALX-009. The Phase 1 study has started recruitment (https://clinicaltrials.gov/ct2/show/NCT02598999).
iABC antimicrobial resistance	The EU Bronchiectasis registry (EMBARC) has to date recruited over 17 200 patients in 33 countries, which makes this registry the largest such data resource in the world. Each patient record has 8 pages of information, totalling 20-30 data points. There are now 11 000+ patients with more than 1 year of data.
iABC antimicrobial resistance	Whole genome sequencing of the 1 000 CF (cystic fibrosis) and BE (bronchiectasis) pathogens collected has been completed. The availability of whole genome sequence data makes it a possibility to assess the breadth of activity of a compound within a species and informs about potential resistance mechanisms.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s) (400 characters max. including spaces)
ZAPI infectious diseases	The project developed a set of human monoclonal antibodies targeting functionally distinct domains of the MERS-CoV spike protein that showed protection when provided either before infection or after lethal MERS-CoV challenge in animal models (mice). These antibodies are good candidates towards the development of antibody-based therapies against MERS-CoV.
ZAPI infectious diseases	The project demonstrated the efficacy of a recombinant spike S1-protein vaccine in blocking MERS-CoV virus transmission in llamas: in contrast to naïve animals, in-contact vaccinated llamas did not shed infectious virus upon exposure to directly inoculated llamas, consistent with the induction of strong virus neutralizing antibody responses. This data provide evidence that vaccination of the reservoir host may impede MERS-CoV zoonotic transmission to humans.

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

Project title	Description of result(s) (400 characters max. including spaces)
AETIONOMY Alzheimer's disease and Parkinson's disease	The analysis of 21 selected inflammatory markers in cerebrospinal fluid (CSF) of a multicentre cohort of 227 subjects (non-demented/ND, mild cognitive impairment/MCI, Alzheimer's disease/AD and Parkinson's disease/PD) demonstrated striking differences in age-dependent trajectories of immune markers between tau-positive or -negative individuals, independent of clinical diagnosis of MCI, AD, or PD. This paves the way to a molecular-based patient stratification independent from clinical diagnosis.
AETIONOMY Alzheimer's disease and Parkinson's disease	Devised the candidate mechanism perturbation amplitude (CMPA) algorithm that is able to calculate the magnitude of regulation of a biological network using gene expression datasets. CMPA successfully showed that molecular mechanisms specific to Alzheimer (AD) and Parkinson Disease (PD) regulate with different intensities across spatial and temporal resolutions. This work paves the way to score complex biological networks that explain disease aetiology for a precision medicine based stratification of patient populations for clinical trial design.
PRECISESADS autoimmune diseases	Systemic autoimmune disease (SAD) patient blood biomarker profiles including auto-antibodies, cytokines, chemokines, inflammatory markers and metabolites were established and compared with the four new molecular SAD patient clusters identified by gene expression and methylation. The genome-wide DNA blood methylation profile was analysed in a total of 1 721 samples including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren's Syndrome (SjS), mixed connective tissue disease (MCTD), undifferentiated connective tissue disease (UCTD) and antiphospholipid syndrome (APS) patients, in addition to controls. To summarise, PRECISESADS performed an in-depth molecular study in over 2 500 patients with autoimmune diseases – unprecedented in immunology research. This identified molecular pathways that may be common to SADs (until now classified as different based only on a clinical phenotype). Therefore, it paved a way towards a molecular taxonomy of autoimmune rheumatic diseases: https://www.ncbi.nlm.nih.gov/pubmed/29463931

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

Project title	Description of result(s) (400 characters max. including spaces)
APPROACH osteoarthritis	The two-stage recruitment procedure for the clinical study, based on selection and screening through a machine learning algorithm, was completed with a final sample of 297 patients with osteoarthritis. The clinical study aims to identify different robust osteoarthritis phenotypes through innovative stratification techniques, thus allowing the development of guidelines for diagnosing the right patient for the right treatment. The focus is now placed on data collection and data analysis of baseline MRI images, blood and urine samples.
COMBACTE-MAGNET antimicrobial resistance	Study as part of EPI-NET: The performance and feasibility of an easily implementable framework to develop algorithms for semi-automated surveillance of deep incisional and organ-space surgical site infections (SSIs) after orthopaedic, cardiac, and colon surgeries was assessed. Results showed that algorithms for semi-automated surveillance of SSIs could be successfully developed and has promise for broader implementation. Infection Control & Hospital Epidemiology. 2019 Dec 30:1-8. https://doi.org/10.1017/ice.2019.321
COMBACTE-MAGNET antimicrobial resistance	Study as part of EPI-NET: A review was conducted to identify and assess publicly accessible mandatory surveillance systems and outbreak reporting for 12 high and critical WHO priority pathogens in the 28 EU and 4 European Free Trade Association Member States.

Project title	Description of result(s) (400 characters max. including spaces)
	Results showed that less than half of European countries (47 %) implemented publicly-accessible mandatory surveillance of at least one antibiotic-resistant bacterium among the 12 pathogens identified by WHO as in urgent need of new therapies. Clinical Microbiology and Infection. 2019 Dec 5. pii: S1198-743X(19)30620-2. https://doi.org/10.1016/j.cmi.2019.11.020
COMBACTE-MAGNET antimicrobial resistance	Study as part of EPI-NET: Another study was conducted to collect the most recent data on prevalence of AMR from surveillance networks and to test the hypothesis of an association between lower income status and AMR prevalence in invasive infections. Surveillance data were available from 67 countries: 38 (57 %) were high income, 16 (24 %) upper middle income, 11 (16 %) lower-middle income and two (3 %) low income countries The study showed that the prevalence of invasive infections caused by the WHO top-ranked antibiotic-resistant bacteria is inversely associated with gross national income per capita at the global level. Journal of Antimicrobial Chemotherapy, Volume 74, Issue 12, December 2019, Pages 3619–3625, https://doi.org/10.1093/jac/dkz38
COMBACTE-MAGNET antimicrobial resistance	Study as part of EPI-NET: The use of online search behaviour in monitoring and tracking infectious diseases was explored with the example of *Candida auris* cases, an emerging multidrug resistant infectious yeast which is challenging to eradicate and despite available laboratory methods is still difficult to identify especially in less developed countries. The study showed that using Google Trends provides both insight into the known and highlights the unknown, providing potential for surveillance and tracking and hence aid in taking timely precautionary measures. Journal of Fungi 2019, 5(2), 44; https://doi.org/10.3390/jof5020044
COMBACTE-NET antimicrobial resistance	Strengthening of the CLIN-NET network capacity with a total of around 1 004 sites participating, about 355 sites participating in 23 trials enrolling more than 21 000 patients.
DIRECT diabetes	Established the most comprehensively phenotyped cohorts of 2 300 pre-diabetic and 850 early diabetic patients with follow-up for 48 and 36 months, respectively. Collected 40 TB of data that includes fsOGTT, MMTT, MRI-imaging (liver, pancreas fat), physical activity (accelerometry), diet (questionnaire), multiomics: genetic, metabolomics, proteomics, lipidomics, stool sequencing and RNA-seq. This now serves as unique, valuable resource for studying diabetes and its progression.
DIRECT diabetes	Established single site high quality biobank with 300 000 samples, which will be a source for replication/biomarker identification for other diabetic focused initiatives.
EPAD Alzheimer's disease	The Longitudinal Cohort Study (LCS) by end of 2019 had 28 sites enrolling and 1 985 research participants screened of which 1 605 enrolled. The LCS acts as a readiness cohort for the proof of concept (PoC) trial for secondary prevention of Alzheimer's disease, as well as generating data for disease modelling work in the preclinical and prodromal phases of Alzheimer's dementia.
PRECISESADS autoimmune diseases	In total, the samples from a very significant cohort of 2 871 participants (over 2 000 people with various autoimmune diseases and comparison with 600 healthy controls) divided between: ▪ the inception cohort (215 newly diagnosed patients, with baseline and 2 follow up visits); ▪ cross-sectional 1 study (301 participants); ▪ cross-sectional 2 (2 322 participants); were collected, processed and analysed. This important effort resulted in a PRECISESADS catalogue available at: https://bit.ly/2TNeCqa

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
APPROACH osteoarthritis	A common database has been set up on a tranSMART platform, which enables the consortium to access and exploit harmonised data from 8 well-defined and unique existing cohorts of osteoarthritis patients with the aim to define differentiating osteoarthritis phenotypes. These phenotypes are being used in the APPROACH clinical study for patient stratification.
BIOVACSAFE vaccines	The project has made publicly available transcriptomics, proteomics and metabolomics data on vaccine immuno-safety generated by BioVacSafe (Umbrella BioProject; PRJNA515032). This could be useful as a resource for future vaccine safety biomarker benchmarking and research.
BIOVACSAFE vaccines	The project in collaboration with the Clinical Data Interchange Standards Consortium (CDISC) has generated a Vaccines Therapeutic Area User Guide (TAUG-Vax), which is available in the public domain at https://www.cdisc.org/standards/therapeutic-areas/vaccines. This can be used to codify vaccine reactogenicity, and is an essential tool to standardise research on vaccine safety and biomarker identification.
EPAD Alzheimer's disease	The baseline data from the first 1 500 research participants (V1500.0) for the EPAD Longitudinal Cohort Study is available as December 2019 and accessible to all EPAD partners and Trial Delivery Centres for an embargoed period of 6 months, following which access will be opened to the entire research community globally.
iPiE environmental issues	Human active pharmaceutical ingredients (APIs) are used in large quantities, and can partly end up in the environment because they are generally not completely broken down during their passage through the human body and wastewater treatment plants (WWTPs). Pharmaceutical residues are mainly transported into the environment via the effluent of WWTPs. Although concentrations reported are generally low, adverse ecological effects caused by some pharmaceuticals are plausible considering their specific modes of action and high potency. A crucial step in environmental risk assessment of chemicals is the estimation of their environmental exposure potential. The iPiE technical model predicts assists in this estimation by providing concentrations of pharmaceuticals across Europe based on national consumption data. It is available for download at: http://i-pie.org/epie/.
PRECISEADS autoimmune diseases	As part of the sustainability plan, the project database with all processed data is hosted by the Luxembourg ELIXIR Platform, as well as the biobank of the project, which is composed several legacy samples of 2 866 participants according to their signed consent letter (DNA, RNA, cell types, plasma, serum and urine). The consortium members (EU / non-EU affiliates) can continue to exploit the data in relation with non-commercial or commercial research perspectives and to further analyse bio samples. EU researchers outside the consortium can be granted access to data and samples after evaluation of their requests by the sustainability committee, providing they have submitted a research plan for a new study approved by an ethical committee. Non-EU researchers outside the consortium cannot access the bio samples and may only be granted access to aggregated/anonymised data. The PRECISESADS catalogue is accessible at this link: https://bit.ly/2TNeCqa
ULTRA-DD drug development	The project submits its data open source to relevant databases and through its website, for general scientific community use. The consortium has recently initiated a collaboration with the IMI project FAIRplus, to establish tools and guidelines to make life science related data FAIR (findable, accessible, interoperable, reusable). In addition, ULTRA-DD has made available 13 patient-derived cell assay datasets pre-publication.

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

Project title	Description of result(s)
APPROACH osteoarthritis	APPROACH researchers and members of the project's patient council have been invited by different stakeholders (including policy makers) at the national level to present the APPROACH set-up as a good example of patient engagement in clinical research. More information on the patient council's activities and interactions with stakeholders is available in the project website: https://www.approachproject.eu/patient-council
COMBACTE-NET antimicrobial resistance	As part of the building of the clinical network CLIN-NET, GCP (good clinical practice) training organised. In total, 129 of the 132 participants passed the exam of the COMBACTE face-to-face GCP training in 2019. 54 investigators contacts passed the exam of the online COMBACTE GCP training provided by the European Centre for Clinical Research Training.
iABC antimicrobial resistance	Development of lung clearance index (LCI) training programme, e-learning tool (www.MBWtraining.com) and a central LCI reading service completed. At the end of iBEST study, training was completed in 20 sites taking part in LCI sub study and the certification process was completed in 13 sites. LCI is being explored as a novel exploratory endpoint of lung disease severity and response to inhaled antibiotic therapy in patients with cystic fibrosis and bronchiectasis.

Impact on regulatory framework

Project title	Description of result(s)
ZAPI infectious diseases	The final version of the Platform Master File (PfMF) for a fast-track regulatory approval to allow quick availability of vaccines and virus-neutralising reagents and antibodies in emergency situations was agreed among ZAPI partners and shared with National Regulatory Authorities, EMA, OIE (World Organisation for Animal Health), WHO, CEPI. It is considered now for inclusion into the Annexes of the New Veterinary Medicines Regulation, which will be applied in 2022.

Implementation of project results inside industry

Project title	Description of result(s)
CANCER-ID cancer	Industry partners started implementing technologies and respective protocols evaluated in the course of CANCER-ID (e.g. ddPCR, ctDNA extraction).
ULTRA-DD drug development	Chemical probes, antibodies as well as chemical probe screening results from disease-relevant cell assays have been used by industry to guide drug development. ULTRA-DD has, during 2019, a confirmed clinical translation for the initiation of a trial for inflammatory bowel disease (IBD), in part based on supporting results generated within the ULTRA-DD project.
ZAPI infectious diseases	A new technology based on a fungal system has been proved to allow the production of a high number of vaccine doses against Schmallenberg virus (SBV) and Middle-East Respiratory Syndrome coronavirus (MERS-CoV) within 4-6 months at very low costs and with reduced need for fermentation volume capacity. Thus, it represents a suitable platform for the commercial manufacturing of selected key immunogens in the future.

Accessibility of resources/outputs beyond consortium

Project title	Description of result(s)
AETIONOMY Alzheimer's disease and Parkinson's disease	PathMe is a Python package that transforms pathway knowledge from three major pathway databases into a unified abstraction using biological expression language as the pivotal, integrative schema. PathMe is complemented by a novel web application (freely available at https://pathme.scai.fraunhofer.de/) which allows users to comprehensively explore pathway crosstalk and compare areas of consensus and discrepancies.
CANCER-ID cancer	The University Cancer Center Hamburg established 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 database access and a platform for partnering for clinical studies utilising liquid biopsies. The kick-off took place in May 2019. An ELBS legal framework has been worked out in the course of 2019.
COMBACTE-NET antimicrobial resistance	LAB-Net network has developed a 'generic' laboratory manual. This generic manual template represents the backbone of a sample collection and management manual and should be adapted to the study specifics of the given study. www.combacte.com/publications/lab-net-sample-collection-management-manual/
EPAD Alzheimer's disease	The data from the first visit of the first 500 participants of the Longitudinal Cohort Study (LCS) have been made available to the scientific community. The data has been de-identified to protect participants' privacy, and quality controlled. Access is provided via secure online tools; researchers who want to use it have to apply via the EPAD website: http://ep-ad.org/erap/.
iPiE environmental issues	The iPiE ECOdrug database contains information on the evolutionary conservation of human drug targets in over 600 eukaryotic species. The interface allows users to identify human drug targets to 1 000+ legacy drugs and explore integrated orthologue predictions for the drug targets, transparently showing the confidence in the predictions across both methods and taxonomic groups. http://www.ecodrug.org/
ULTRA-DD drug development	Antibodies, chemical and biological probes developed for targets selected in ULTRA-DD are made available to the scientific community either directly or through the project's vendor partners. For example, ULTRA-DD chemical probes have been distributed directly by the project to 48 international research groups and over 200 samples (including entire sets) were distributed through the project's chemical vendor partners. One biological probe is available for purchase from Modiquest and can be used in target and/or biomarker validation studies. A total of 13 patient-derived cell assay datasets have been published up to date on the ULTRA-DD website including access to experimental research protocols. The team has received requests from outside the consortium to further mine these disease-relevant datasets.
ULTRA-DD drug development	The free for use open resource 'Priority index' (atlas of drug target prioritisations in immune-mediated diseases) is a genetics-led drug target prioritisation system developed as a collaborative effort within the ULTRA-DD project. The work was published in Nature Genetics and provides the scientific community with a tool for target discovery. http://pi.well.ox.ac.uk
ULTRA-DD drug development	51 antibodies have been generated that have the potential to detect current and future biomarkers. Specifically, the antibodies produced for tRNA-synthetases hold specific future promise for this purpose. https://ultra-dd.org/antibodies

IMI2 project outputs

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result(s)
ADAPTED Alzheimer's disease	Successfully established a novel two dimensional (2D) co-culture system of human inducible pluripotent stem cell (hiPSC)-derived neurons and astrocytes. These co-cultures will facilitate the study of non-cell autonomous effects of astrocytes with different Apolipoprotein E (ApoE) genotypes on neurons and vice versa.
ADAPTED Alzheimer's disease	Developed a novel method for generating monocytes derived from hiPSCs, and differentiating them into macrophages with a pro- or anti-inflammatory phenotype. The method was implemented by the project to determine the effect of the APOE genotype on inflammation in *in vitro* models of Alzheimer's disease.
BEAt-DKD diabetes	Identification of dicarbonyl and L-xylulose reductase (DCXR) as a therapeutic target in human chronic kidney disease (CKD). Downregulation of DCXR in renal tissue is associated with a poor prognosis in CKD. Therefore enhancing DCXR expression may offer a strategy to counterbalance CKD progression with sodium glucose cotransporter-2 (SGLT2) inhibitors, thereby, having a beneficial effect on DCXR expression levels in renal proximal tubular cells. https://insight.jci.org/articles/view/128120
BEAt-DKD diabetes	Refined and validated protocols to isolate specific cell types, in order to study them individually. Developed insulin-sensitive and -resistant model systems, in which insulin sensitivity mechanisms can be investigated to identify mechanisms and relevant biomarkers.
BEAt-DKD diabetes	Conducted two important large randomised controlled clinical trials, which demonstrated that the endothelin receptor antagonist atrasentan and the sodium-glucose transport protein 2 (SGLT2) inhibitor canagliflozin delayed the progression of kidney function decline in patients with diabetic kidney disease. BEAt-DKD investigators led one of these trials (SONAR; Heerspink et.al. Lancet 2019) and were involved in the leadership of the other trial (CREDENCE; Perkovic New England Journal of Medicine 2019). Although the drugs reduced the risk on a population level, still a substantial number of patients receiving these new drugs showed a progressive loss of renal function decline possibly due to treatment resistance to these drugs.
BEAt-DKD diabetes	Identified canonical pathways associated with atrasentan drug. Sirtuin and ephrin signalling, NRF2-mediated oxidative stress response, thrombin signalling, and acute phase response signalling are among the top ranked pathways. This may allow for better understanding of the drug mechanism of action and possibly better predicting the response.
BEAt-DKD diabetes	Identified gene signature and molecular pathways that are associated with Angiotensin converting enzyme (ACE) response to various renoprotective treatments (Lisinopril, Losartan, Ruxolitinib, Canagliflozin). Ingenuity pathway analysis revealed distinct biological processes known to be associated with DKD pathogenesis, including immune cell expansion and infiltration, inflammation, fibrosis, and homeostasis of the glomerular filtration barrier. This analysis shed light on the common molecular mechanisms in responding to renoprotective drugs. These discovered molecular pathways will facilitate the understanding of response to treatment and the gene signature may help to stratify patients that respond to the drugs even before the treatment.
BEAt-DKD diabetes	Generated mouse models in which key enzymatic regulators of DNA methylation have been knocked out resulting in a severe kidney phenotype. This has allowed to demonstrate that DNA methylation as a key regulatory event of prenatal renal programming, which possibly represents a fundamental link between maternal nutritional factors during gestation and reduced nephron number. (Wanner et al J Am Soc Nephrol. 2019 Jan;30(1):63-78)
BEAt-DKD	Developed novel glomerular cell specific insulin receptor / insulin-like growth factor 1 (IGF-1R) knockout mice that allow investigation of the physiological role of podocyte

Project title	Description of result(s)
diabetes	and/or glomerular endothelial cell insulin resistance in respect to glomerular endothelial cell glycocalyx function.
BEAt-DKD diabetes	Developed insulin sensitive and animal models and insulin-resistant and -sensitive renal cell lines (podocytes, glomerular endothelial cells, mesangial cells, proximal tubular cells) of human and murine origin. Also generated insulin resistant and insulin sensitive human microvascular endothelial cells of non-renal origin and human blood outgrowth endothelial cells (BOECs) as potential carriers of accessible information about the patient's DKD status.
EQIPD data quality, neurodegenerative diseases	Emerging findings of the systematic review of publications related to results from animal studies in the Alzheimer area are available here: https://tinyurl.com/tqo7k9r. It is an important piece of work paving a way towards a quality management system enhancing the robustness and rigor of preclinical studies.
eTRANSAFE safety	The eTRANSAFE consortium has developed a flexible framework supporting predictive modelling. It facilitates the development of machine-learning models, (e.g. quantitative structure-activity relationship -like models), starting from annotated collections of chemical compounds stored in standard formats. The new models can then be transferred into a production environment where they can be used by web services to predict the properties of new compounds.
HYPO-RESOLVE diabetes	Developed animal models to study new hypoglycaemia sensing pathways as well as symptomatic awareness of hypoglycaemia.
IMPRiND neurodegenerative disease	IMPRiND scientists have unravelled the structure of the abnormal tau filaments associated with chronic traumatic encephalopathy (CTE), a type of dementia associated with repeated blows to the head. Moreover, the tau filaments associated with CTE are different to those found in people with Alzheimer's disease. These findings support the hypothesis that the formation and propagation of distinct conformers of assembled tau underlie different neurodegenerative diseases and could pave the way for future treatments for CTE. This discovery resulted in a publication in the journal Nature (March 2019).
INNODIA diabetes	Identified candidate genes related to β cells' response to a pro-inflammatory environment and implicated a role for stimulus-response islet enhancers in T1D. The project has observed that exposure of human islets to pro-inflammatory cytokines unmasks a marked plasticity of the β-cell regulatory landscape. They expanded the repertoire of human islet regulatory elements by mapping stimulus-responsive enhancers linked to changes in the β-cell transcriptome, proteome and 3D chromatin structure. The data indicates that the β cell response to cytokines is mediated by the induction of novel regulatory regions as well as the activation of primed regulatory elements pre-bound by islet-specific transcription factors. They found that T1D-associated loci are enriched in the newly mapped cis-regulatory regions and identified T1D-associated variants disrupting cytokine-responsive enhancer activity in human β cells. www.nature.com/articles/s41588-019-0524-6
INNODIA diabetes	A flexible Gaussian process-based probabilistic modelling framework was developed - a valuable computational tool for longitudinal data analysis. www.ncbi.nlm.nih.gov/pubmed/?term=An+additive+Gaussian+process+regression+model+for+interpretable+non-parametric+analysis+of+longitudinal+data
INNODIA diabetes	Highly sensitive radionuclide imaging technologies for in vivo imaging of CD8 positive cells and PD-L1 have been established in animal models. These technologies are ready for translation and validation in experimental diabetes models.
INNODIA diabetes	Developed a method for preclinical single-photon emission computed tomography (SPECT/CT) imaging of CD8 expressing cells using monoclonal antibodies. This imaging method has been extensively validated in various preclinical tumour models.

Project title	Description of result(s)
INNODIA diabetes	Demonstrated in non-obese diabetic (NOD) mice that systemic inhibition of citrullination through the injection of the pan protein arginine deiminase (PAD) inhibitor BB-Cl-amidine markedly reduced diabetes incidence. This marked decrease was accompanied by a significant increase in the helper T cells' 1 to 2 serum cytokine ratio, elevated frequencies of Treg cells in the spleen and blood, and reduced frequencies of CD4+ and CD8+ effector memory T cells (TEM) in the pancreas, pointing to a role for dysregulated PAD activity and citrullination in the onset and progression of murine T1D. These findings may contribute to the development of alternative/complementary treatment strategies to slow down the progression or aggravation of T1D.
INNODIA diabetes	Developed a new mouse model for coxsackievirus-induced myocarditis by attenuating coxsackievirus b3 virulence in the pancreas. The animals develop myocarditis while attenuating viral infection of the pancreas leads to development of severe pancreatitis. This new animal model will allow the investigation of the pathogenesis of coxsackievirus B3 (CVB3) myocarditis independently of severe systemic CVB3 infection and pancreatitis. It may also be useful to study new treatments in the post-viremia phase of CVB3-induced myocarditis.
INNODIA diabetes	Developed a novel *in vitro* model, Gaussia luciferase-based reporter system, which allows tracing endoplasmic reticulum stress in isolated human beta cells. The model may aid the identification of novel therapeutics aiming at prevention of beta cell stress in human pancreatic islets. https://www.ncbi.nlm.nih.gov/pubmed/30532033
INNODIA diabetes	Discovered molecular pathways and potential targets for the development and testing of new families of molecules for the treatment of enterovirus-associated type 1 diabetes. https://www.ncbi.nlm.nih.gov/pubmed/30799417
ITCC-P4 paediatrics, cancer	Out of the 401 models registered in their R2 Genomics Analysis and Visualization Platform, covering various paediatric tumour types including some rare cancer diagnoses, the consortium fully established 140. Over 50 of these models are fully molecular characterised. Compounds were selected for proof of concept of the preclinical paediatric PDX platform and testing starting. Two genetically engineered mouse models (GEMMs) models established; initial drug testing initiated on paediatric organoids generated from paediatric neuroblastoma patients (from primary and relapse) with matched PDX/organoid drug testing for comparison. 3 paediatric PDX models were successfully established in humanised mice and displayed fast tumour growth kinetics. This is important to explore the potential for the established PDX platform to be used as starting materials for 'humanised' xenografts, aiming for the reinstatement of the human immune counterpart that is typically missed within immune-deficient host mice and to allow for preclinical testing of cancer-immunity molecules.
ITCC-P4 paediatrics, cancer	Wrote a white paper on the role and place of preclinical evaluation on paediatric tumour models. The paper is based on international consensus results from the international multi-stakeholder workshop held in 2018 meeting. It will support discussion with regulatory authorities on the biological and preclinical information required to support a paediatric investigation plan (PIP) for an oncology medicinal product and has been submitted for publication. Collaborations established with the Paediatric Preclinical Testing Consortium of the US National Cancer Institute as well as with the Foundation for the National Institute to foster a global approach to paediatric preclinical testing of cancer therapies.
LITMUS liver disease	Created an atlas of digital images for the harmonisation of non alcoholic fatty liver disease (NAFLD) histological evaluation, using guideline images for each of the semi-quantitative scores for diagnostic features that are included in the liver biopsy report form. Central histological interpretation and scoring of 320 NAFLD liver biopsies has been completed.
NEURODERISK	The project developed a prototype for the NeuroDeRisk toxicity profiling with 3D-pharmacophore models that will allow virtual screening of compounds against a set of

Project title	Description of result(s)
safety	predictive models. The tool includes outputs, chart, tables and scores to assess results. The prototype models are currently in the process of being deployed to members of the consortium for validation. The software environment (KNIME-www.knime.org) used for deployment/development of the prototype tools is freely available to the public. Within this environment, several developers can make available dedicated nodes under the so-called KNIME Hub (https://hub.knime.com). At this stage, the NeuroDeRisk node is not yet available to the public, because it is still under internal validation. All the models derived from public data and internally validated will be publicly available.
NEURODERISK safety	The project developed 3D-pharmacophore models of γ-aminobutyric acid (GABA-A) receptor agonist and antagonist and picrotoxin channel blocker sites.
NEURODERISK safety	The project developed prototypes for datamining tools using the FDA Adverse Event Reporting System (FAERS) database to help with identification of targets, genes and pathways along with scoring and visualisation tools. The prototypes have been used in the project to assist researchers with compound selections for seizure risk and psychological effects for the project.
NEURODERISK safety	The project established a catalogue of tool compounds or drugs associated with neurotoxicity (convulsions/seizures, psychological/psychiatric effects, peripheral neuropathies). This catalogue has been collected from literature. At this stage, the consortium is setting up all procedures necessary to validate the data so that it can be shared with the public later, and used internally in order to further de-risk development candidates.
NGN-PET pain	The consortium has performed a critical re-evaluation of how to prioritise targets for pain drug discovery. In addition, they have established the large-scale production of human sensory neurons, and have devised miniaturised formats for the culture of these sophisticated cellular systems. These are operable in industrial settings for drug screening.
NGN-PET pain	Several assays, including two animal models of neuropathic pain (spinal nerve ligation and chemotherapy-induced neuropathy) have been set up and dose-response curves for reference compounds were obtained. These assays are now being routinely used within the project.
PERISCOPE vaccines	Developed and used an imaging modality to read out pertussis infection effects on vaccinated/challenged baboons that is very valuable to assess vaccine efficacy and impact. 2 most important impacts: ▪ significantly reduce the need for invasive approaches in animal studies; ▪ [18F]-FDG and PET-CT (positron emission tomography–computed tomography) are approved for use in patients, hence there is a strong translational potential for clinical investigation/efficacy trials for new vaccines.
PEVIA Ebola and related diseases	Chimeric and humanised mouse models to assess efficacy of Ebola vaccine candidates were developed. Development of 2 bioassays to evaluate, in biosafety level 2 (BSL2) laboratory, on the one hand the sero-neutralising activity, and on the other hand, the enhancing activity of vaccine candidates.
PHAGO Alzheimer's disease	Demonstrated that in mice with early signs of plaque deposition and a functioning TREM2 (Triggering receptor expressed on myeloid cells 2) gene, microglia cluster around small plaques and cause them to disintegrate but that in mice with more advanced plaque deposition the plaques grew faster in mice with a functioning TREM2 gene than in mice without it. These findings indicate that TREM2 influences the progression of AD in different ways in the early and later stages and that future therapies will need to be applied in a stage-specific manner.
PHAGO	PHAGO was able to identify Galactin-3 (gal3), a molecule involved in microglial activation, as a novel endogenous TREM2 ligand, which is upregulated in Alzheimer's

Project title	Description of result(s)
Alzheimer's disease	disease (AD) patients and is specifically associated with Aβ plaques. As a result, gal3 inhibition may be a potential pharmacological approach to counteract AD.
PHAGO Alzheimer's disease	Described the crystal structures of CD33 alone and bound to a subtype-selective sialic acid mimetic called P22. P22 increased uptake of the toxic AD peptide, amyloid-β (Aβ), into microglial cells. The sialic acid-binding site on CD33 is thus a promising target for developing therapeutics that promote clearance of the toxic Aβ peptide. These results will be of great value in future structure-based drug discovery efforts targeting CD33 in AD.
PRISM neurological disorders	Refined and implemented the RFID-Assisted SocialScan, based on video tracking supported by radio-frequency identification (RFID) for their preclinical studies. RFID-Assisted SocialScan is an automated tracking and analysis tool for long-term behavioural observations of multiple freely moving mice housed in an environment that is relevant to their natural behaviour. The tool will enable increase reproducibility of animal behaviour and better animal welfare.
PRISM neurological disorders	A genome wide analysis in a UK biobank sample (n=342 461) identified a significant genetic component to variation in population levels of sociability, which is relevant to some psychiatric disorders including schizophrenia, but not to bipolar disorder and Alzheimer's disease. 33 robust candidate genes were mapped on a molecular landscape related to social functioning, including several concrete biological pathways for further target discovery.
RESOLUTE drug development	The project has fully characterised the transcriptome, metabolome and proteome of 6 human cancer cell lines, cumulatively covering the expression of about 80% of all human solute carrier proteins. The transcriptome data is already publicly available at Sequence Read Archive (SRA; PRJNA545487).
RHAPSODY diabetes	In collaboration with BEAt-DKD, established a type 2 diabetes progression model that stratifies patients in 5 subgroups with different disease progression rates and development of secondary complications. This may enable application of precision medicine of T2D.
RHAPSODY diabetes	Continued to develop the Beta Cell Diabetes Platform (BCDP) as a fully operational sustainability activity to make available biggest standardised biobank of islet / beta cells, with samples from more than 740 donors (including transcriptomal data) as well as patient centric *in-vivo* models for collaborations and in-house research activities and to serve as a hub for the integration of other diabetes / metabolic disorders data.
RTCure rheumatoid arthritis	An antigen specific model of inflammatory arthritis has been developed in mice for tolerance studies. With this model, it will be possible to assess how T cells respond to various tolerising regimes, the impact of this on the development of arthritis and thus establish the best approaches (treatment, times and locations) to re-establish tolerance in an experimental model.
TransQST safety	A web application was developed to conduct simulations for the hemodynamic effects of drug candidates and reference drugs. The application can be of use to help interpret experimental studies, for instance to determine the most likely mode of action. Furthermore, the application may also be of relevance to guide the design of future studies. The application, which is still under development, can be accessed at www.hemodynamic-simulator.eu .
TransQST safety	The TXG-MAPr web tools available via txg-mapr.eu enable analysis of transcriptomics data from *in vivo* rat liver and primary human hepatocytes, interpretation of regulated processes following drug treatment and comparison of responses to other compounds in the open large-scale toxicogenomics (TG-GATEs) data set. The full versions of the TXG-MAPr web tools are available for the consortium members during the project. When the manuscripts of the TXG-MAPr web tools have been published, the consortium members expect that other members of the scientific community will also want to exploit the tools. Therefore, the consortium will make the tools available to those interested, but likely not the full version, or it will involve a

Project title	Description of result(s)
	license fee. The consortium has plans to keep the tools available after the project end, depending on funding needed for tool maintenance and improvement.
VITAL vaccines	VITAL has developed a programme for specific infectious diseases known to cause a high burden in aging adults, for which sources of information in Europe have been made available. This could be an interesting tool in pre-clinical drug development for those interested in knowing the impact of a specific infectious disease burden.
VSV EBOVAC Ebola and related diseases	3 qualified ELISA (Enzyme-Linked ImmunoSorbent Assay) and validated PRNT (Plaque Reduction Neutralization Test) assays for measuring antibody to Ebola, qualified RT-PCR for measuring vaccine viremia, viruria, synovial fluid virus were developed.

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

Project title	Description of result(s)
AIMS-2-TRIALS autism	Resting state functional magnetic resonance imaging (fMRI) analysis demonstrated that differences in resting brain functional connectivity are related to variation in clinical phenotype, and can replicated internationally across 4 different research networks involving 2 000 subjects. This is being taken forward for development as an enrichment biomarker to optimise patient stratification in clinical trials.
AIMS-2-TRIALS autism	Worked closely with the industry partners to develop a 'wearable' device for measuring symptom change, engaged with autistic individuals (ages 6-45 years) to ensure it is acceptable, and included it in the first clinical trial of the project.
AIMS-2-TRIALS autism	Found that some autistic individuals had differences in the timing of the electrophysiological responses to pictures of upright and inverted faces, (also replicated by the US Autism Biomarker Consortium for Clinical Trials (ABC-CT) consortium part of the project) and that these differences predict clinical outcome ~ 2 years later.
BEAt-DKD diabetes	Generated a signature of 23 renal age-associated genes (RAAGs) based on six different data sources (transcriptomics data and data extracted from scientific literature and dedicated databases). Those RAAGs show concordant regulation in renal aging and CKD progression. The RAAGS were then used as input to computationally screen for compounds with the potential of reversing the RAAG/CKD signature on the transcriptional level. Among the top-ranked drugs, atorvastatin, captopril, valsartan, and rosiglitazone, which are widely used in clinical practice for the treatment of patients with renal and cardiovascular diseases, had positive impact on the RAAG/CKD signature. This was validated in an in-vitro model of renal aging. www.sciencedirect.com/science/article/pii/S2001037019301679?via%3Dihub
BEAT-DKD diabetes	The project has designed a new multiple parameter risk efficacy and safety score, which translates a short-term drug effect based on multiple efficacy and safety parameter into a predicted cardiovascular/renal outcome effect. This new tool is currently tested for validation in the project's large clinical trials and observational cohorts.
BEAt-DKD diabetes	Identified protein candidate biomarkers for kidney disease drug mode of action – atrasentan (10 biomarker candidates); canagliflozin (10 biomarker candidates); satin (11 biomarker candidates); 1 dynamic biomarker for canagliflozin efficacy.
BEAt-DKD diabetes	Validated 17 prognostic protein biomarkers and identified 5 prognostic metabolite biomarkers for eGFR decline.
BEAt-DKD diabetes	Identified a kidney specific 6-gene signature (based on 41 kidney specific genes) that differentiate most macro- from normo- albuminuric individuals.

Project title	Description of result(s)
BEAt-DKD diabetes	Identified 180 epigenetic biomarker candidates based on pilot studies on the blood of diabetic and non-diabetic patients.
BEAt-DKD diabetes	Established DNA methylation as a key regulatory event of prenatal renal programming, which possibly represents a fundamental link between maternal nutritional factors during gestation and reduced nephron number. https://www.ncbi.nlm.nih.gov/pubmed/30518531
BEAt-DKD diabetes	Identified an 8-marker baseline predictive panel and a 19-marker dynamic panel that predicted urinary albumin:creatinine ratio UACR response to atrasentan. Validation of these markers is ongoing.
BigData@Heart big data, cardiovascular disease	The project has published an article on risk factors for incident heart failure in age- and sex-specific strata. Several risk factors for incident heart failure have previously been identified, however this study uses linked electronic health records' datasets, which may provide the opportunity to examine the consistency of risk factors across different subgroups from the general population. The article is freely available at https://doi.org/10.1002/ejhf.1350.
INNODIA diabetes	Identified several novel circulating small RNAs (piRNAs) as differentially expressed in plasma of new-onset T1D patients as compared to non-diabetic controls, which may, if validated, become a diagnostic marker for the disease.
INNODIA diabetes	Discovered novel beta cell targets of the autoimmune attack in diabetes (insulin granule proteins, citrullinated proteins, mRNA and peptide splice variants). This may enable future medicines development for type 1 diabetes.
INNODIA diabetes	Identified a new circulating biomarker of islet inflammation and type 1 diabetes severity, miR-409-3p. This may, if validated, become a diagnostic and/or prognostic marker for the disease. https://www.ncbi.nlm.nih.gov/pubmed/31659408
LITMUS liver disease	17 shortlisted fibrosis and fibrogenesis serum protein markers are being validated in an independent cohort. 3 new collagen markers and 2 non-collagen (matricellular) have been included in the list. 10 protein markers have already been validated in independent cohorts.
MACUSTAR eye disease	Active recruitment by the 20 clinical sites (in 7 EU countries) to the observational study that aimed 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). The recruitment was closed end of 2019 for all patients (no AMD, early AMD, iAMD), except late AMD patients that will be closed in January 2020. In December the number of patients enrolled was: intermediate iAMD: 578/600, no AMD: 54/50, early AMD: 34/50, late AMD: 34/50. This is an important milestone towards the overall goal to develop and validate appropriate clinical endpoints for future clinical trials and drug development in iAMD. In May 2019, results from a preliminary analysis of the navigation performance including 31 subjects was presented at the ARVO conference as a poster. Early results suggested that transient reducing light levels are significantly more difficult for people with AMD resulting in an average 11% decrease in walking speed and increased incidence of mobility errors (bumps, disorientation).
MOBILISE-D digital health	Algorithms for digital mobility outcome assessment have been identified, optimised and are now being tested on existing datasets for refinement. The protocol for the technical validation of the device/algorithm solution in clinical populations has been finalised and ethics approval is in place now to start the study. The EMA qualification advice procedure for the use of digital mobility outcome as endpoints has been initiated.

Project title	Description of result(s)
PERISCOPE vaccines	Established a controlled human infection model to investigate efficacy of vaccination against *Bordetella pertussis* colonisation. Novel immunological methods have been developed and implemented for identification of biomarkers possibly associated with protection against colonisation.
PRISM neurological disorders	In the PRISM clinical study the mobile app BEHAPP profiles distinguished three distinct subgroups of Alzheimer's disease and schizophrenia patients which did not yield a one to one mapping onto underlying diagnostic labels of participants, and were not confounded by participant age. These distinctions could be used for building a diagnostic/stratification algorithm that incorporates endpoints derived from BEHAPP.
RESCEU respiratory disease	A model to predict locally and globally epidemic months of the most common viruses associated with acute lower respiratory infections in young children and elderly (influenza virus and respiratory syncytial virus, parainfluenza virus and metapneumovirus) has been developed. The model is helpful in predicting the local onset month and in particular the month-by-month activity of influenza and respiratory syncytial virus epidemics. The seasonality information has important implications for health services planning, the timing of passive prophylaxis and the strategy of vaccination.
RHAPSODY diabetes	Identified biomarker candidates of T2D progression: 4 protein biomarker candidates, 3 metabolites, several lipid species.
TransQST safety	An *in vitro/in silico* system to predict drug-induced liver injury (DILI) in relation to oral doses and blood concentrations has been established and published (Albrecht et al., 2019, Arch Toxicol).
TransQST safety	The cardiac work package has developed two biomarkers, which could help predict pro arrhythmia in man - these are also accessible in *in vivo* nonclinical studies.
TRISTAN safety	TRISTAN demonstrated that a novel 89Zr-chelator (DFOcyclo*), shows improved *in vitro* and *in vivo* stability compared to desferrioxamine (DFO), the current gold standard to label antibodies for immunoPET with 89Zr. This suggests that DFOcyclo* could be a promising candidate chelator for clinical studies.
TRISTAN safety	Organic-anion-transporting polypeptides (OATPs) and multidrug resistance-associated protein 2(MRP2) are liver uptake and export transporters, respectively, which play an important role in the liver toxicity of drugs and in liver mediated drug-drug interactions. TRISTAN developed MRI data acquisition protocols and associated documentation for 3D dynamic scanning of free breathing animals' and patients' livers with the goal to determine OATP and MRP2 transport rate constants. Use of this imaging biomarker may support early detection and management of a drug candidate's liver toxicity. The documentation is available for download at: https://www.imi-tristan.eu/en/download-area.php
Vac2Vac vaccines	Physicochemical methods based on circular dichroism and fluorescence spectroscopy have been developed. Those methods demonstrated suitability for replacement of the rabbit or guinea pig serology assay currently used as a test for vaccine batch-to-batch consistency of monovalent tetanus vaccines. They have the required sensitivity to detect altered samples in the pre-adjuvanted state of the vaccines; their use appears to be also feasible when applied to model (adjuvanted) monovalent tetanus vaccines with three different adjuvants used in the veterinary vaccine industry.
Vac2Vac vaccines	An assay based on the analysis of the B cell response in human peripheral blood mononuclear cells eliciting a recall response to tetanus toxoid has been developed. This method can be used to demonstrate that a tetanus toxoid vaccine antigen is capable of triggering the expected antigen-specific B cell response. It may therefore be a valuable tool to complement physicochemical and immunochemical methods and/or to replace the currently performed *in vivo* potency assays.

Project title	Description of result(s)
VITAL vaccines	VITAL has developed a flow cytometry staining panel including 19 biomarkers in 1 tube to determine cell subset constitution and analyse this in the context of vaccination response.
VSV EBOVAC Ebola and related diseases	Transcriptomic and metabolomic profiles of human immune response to rVSV-ZEBOV vaccination (the Ebola virus disease vaccine under licensing by MSD, this vaccine is the first FDA-approved vaccine for the prevention of Ebola virus disease) were identified in samples collected at multiple time points in 3 different cohorts in subjects vaccinated with different doses. A panel of genes whose expression levels after vaccination are associated with long-term antibody response was identified.
HYPO-RESOLVE diabetes	*In-silico* mathematical model is in final stages of development to quantify how much hypoglycaemia frequency and duration in people with diabetes is determined by behavioural factors.

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
AMYPAD Alzheimer's disease	Developed a new deep learning algorithm for performing attenuation correction with positron emission tomography/ magnetic resonance (PET-MR) scanners. The algorithm achieves increased overall accuracy and generalisability of results. The tool overcomes the need (as opposed to the multi-atlas method available to date) to disclose a magnetic resonance/computed tomography dataset of the same individuals to perform the correction facilitating the performance of imaging clinical studies.
COMBACTE-CDI antimicrobial resistance	Completion of the analysis on the samples obtained from sites testing both in-patients and community in 12 countries (total of 3 163 samples obtained from the 2 sampling periods). The data provides new knowledge on the diagnosed burden of *Clostridium difficile* infection (CDI) across Europe and both hospital and community settings, as well the types of strains circulating. The preliminary data were presented at ECCMID 2019 and the poster was one of the six top-rated posters from the 5 000 abstracts submitted ('Detection of *Clostridium difficile* infection across whole healthcare economies in Europe: results from COMBACTE-CDI'; Davies et al.) Comparison between assays for testing diarrhoeal faecal samples was completed using novel ultra-sensitive toxin detection assays (SIMOA, BioFire gastro intestinal molecular panel and cell-cytotoxin neutralisation assay). Results on the difference in testing sensitivity may provide potential value for clinical practice. (preliminary data were presented as abstract presented at ECCMID 2019) Completion of the case/control study (total 689) providing more insight on the risk factors for developing CDI, and outcomes of CDI between those diagnosed within a hospital setting and those in the community. These results will feed the CDI transmission model. This has important implications for guideline development in terms of testing and treatment.
COMBACTE-CDI antimicrobial resistance	Completion of a survey of (155 European centres/facilities from 12 different European countries responded) providing information on the current knowledge/practices (awareness and compliance to guidelines) for CDI diagnosis, treatment and management across European and different settings (in and out of the hospital setting).
DO-IT big data	To facilitate the uptake of their core outcome sets (COS), the DO-IT consortium held a public webinar on outcomes standardisation. The COS and their role in harmonising outcomes generated in real world settings were presented via webinar. A presentation of the toolkit gave methodological and practical guidance on developing COS, including for use in real world settings. Explanations of experiences from the different BD4BO

Project title	Description of result(s)
	projects including, for example, on involving patient perspectives in the standardisation of outcomes
GetReal Initiative relative effectiveness	Think tank set up (structure, mandate) including establishment of the core group members that include key opinion leaders in the area of real-world evidence (RWE) from regulatory bodies, health technology assessment bodies, industry, academic groups and clinical experts, payer organisations, patient organisations, with the role of driving the acceptability of the RWE and the uptake of the outputs of GetReal and GetReal Initiative.
INNODIA diabetes	Established a master protocol that will serve as a backbone for INNODIA clinical trials. This master protocol is fully aligned with the time points of the ongoing natural history collection in the project. The protocol allows adaptive trial design and has been finalised and presented for Scientific Advice (at SAWP EMA) in 2019.
MOPEAD Alzheimer's disease	A big challenge for clinical trials in Alzheimer's disease is patient recruitment. New strategies are needed for finding 'hidden Alzheimer's disease' in the general population. The online citizen science campaign completed successfully its recruitment: 1 400 citizens across all MOPEAD sites took the online memory test, suggesting the huge potential value of this sort of application for citizens in Europe.
PREFER patient involvement in R&D	The patient preference studies in several diseases areas and stage of development are being finalised: ▪ for the 3 core clinical case studies, in rheumatoid arthritis, neuromuscular disorders and lung cancer the qualitative data collection phase has been completed and quantitative data collection phase near to completion; ▪ for the additional 5 academic cases studies (diabetes, multiple myeloma, gene therapy in Haemophilia, rheumatoid arthritis, rye tracking) nearly all have completed the quantitative data collection phase; ▪ The 3 additional industry led case studies completed in chronic obstructive pulmonary disease, myocardial infarction and chronic pain. All studies gather data on the use of discrete choice experiments (DCE) as the prioritised methodology, with comparisons of a number of other methods for the elicitation of patient preferences as well as answer research questions in a clinical context. These clinical case studies are important as together they address the methodological research questions identified in the first phase of the project and their results are being integrated in the final recommendations to guide industry, regulatory authorities, HTA bodies and reimbursement agencies on how patient preferences can be assessed and used to inform medical product decision making. They will also provide data to support the EMA/EUnetHTA qualification procedure initiated. More information on the case studies is available at www.imi-prefer.eu/digitalAssets/585/c_585658-l_1-k_print-imi-prefer-case-studies_final.pdf
RADAR-AD Alzheimer's disease	Remote monitoring technology (RMT) is very promising for quantitative and sensitive measuring of functional decline in people with mild cognitive impairment (MCI) or mild Alzheimer's disease dementia (AD). Meaningful areas of function that may be potentially important to measure for clinical decision making have to be identified first. The consortium established 6 focus groups with 40 participants (individuals with MCI, AD and carers) across 3 European countries (United Kingdom, Greece and the Netherlands) and identified and sorted for relevance activities of daily living (ADL) to consider for monitoring. There was a general acceptance of, and enthusiasm for, the idea of monitoring function using RMT across groups.
RADAR-CNS neurological disorders	RADAR-CNS researchers identified factors that could aid or hinder patient acceptance of wearable devices for measurement and management of depression. 25 patients across three countries were interviewed to establish their concerns about the use of mobile technologies. The main themes included motivation, potential impact on mood and anxiety, aspects of inconvenience, and ease of use. The study was published in

Project title	Description of result(s)
	JMIR Mhealth and the results will be used to prepare guidance on how to design feasible and acceptable cross-cultural mHealth tools.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s)
PERISCOPE vaccines	PERISCOPE has developed preclinical *Bordetella pertussis* (Bp) vaccination models, these models have been tested and the consortium provided evidence that these models can predict protection by acellular (aP) and whole-cell pertussis (wP) vaccines. In addition, the human challenge model enables to highlight differences between symptomatic and non-symptomatic subjects evaluated by antibody analyses and high-dimensional flow cytometry. Such differences could be surrogates for efficacy biomarkers, to be further tested in the second phase of the human challenge study.

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

Project title	Description of result(s)
PERISCOPE vaccines	Following vaccination with acellular pertussis vaccine, there is an increase in antibodies that, together with human complement, kill *Bordetella pertussis*. The serum bactericidal antibody titres obtained correlate with anti-pertactin IgG concentration determined in multiplexed immunoassay. There is no correlation with antibody concentrations to other acellular vaccine antigens. This work paves the way to improve the efficacy and safety of *Bordetella pertussis* vaccine.
PRISM neurological disorders	Initial results of the PRISM clinical study showed that subgroups of Alzheimer's disease and schizophrenia patients, distinguished by different BEHAPP social functioning profile, map onto different underlying biology. Thus clustering participants across classical diseases classification, using digital social functioning parameters, obtained from BEHAPP, has biological meaning. It might be a new approach for the development and application of medicine in a personalised therapy setting.
VITAL vaccines	Using the flow cytometry staining panel, VITAL is exploring whether the cell subset constitution data which could assist in better stratification of the participants in vaccination studies.

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

Project title	Description of result(s)
AIMS-2-TRIALS autism	To facilitate large multi-site clinical trials in autism, the AIMS-2-TRIALS clinical trials network (CTN) has expanded to 118 sites across 37 countries with access to >20 000 new patients per year organised around 3 lead regional 'hubs' and with a single point of contact. Within the CTN, work has been done to identify and train sites for the first clinical trial and to link to another network in north America in order to increase the study size.
AIMS-2-TRIALS autism	Showed, in a first study, that the repurposed drug arbaclofen can affect electrophysiological and imaging biomarkers in a dose dependant manner in people with autism. This is a first demonstration that these biomarkers have potential as markers for response to treatment in people with autism.
AMYPAD	Amyloid imaging is an important tool for patient diagnosis, but its value in guiding patient management is not clear. The diagnostic and patient management study

Project title	Description of result(s)
Alzheimer's disease	(DPMS) is fully activated in eight sites including Geneva, Amsterdam, Toulouse, Barcelona, London, Stockholm and Lausanne (new one added within 2019), with a total of 636 patients at the end of December 2019, and 429 amyloid PET scans have been performed. The target of 300 mild cognitive impaired individuals (MCIs) has been reached, and the focus is now to be put on subjective cognitive decline individuals (SCDs) and dementia patients. The tracer balance between vizamyl and neuraceq is stable at 45 % vs. 55 % respectively.
AMYPAD Alzheimer's disease	Amyloid imaging is an important tool for identifying patients with Alzheimer's disease for clinical trials. The prognostic and natural history study (PNHS) expanded by engagement of additional sites and parent cohorts to reach out to study participants target and efficiently deliver on several objectives without exposing de novo participants (n=2 000). The finalisation and the approval of the study protocol has been done in Amsterdam, Edinburgh, Barcelona, Toulouse, Geneva, and Stockholm. Within 2019, 12 additional sites have been approached to come on board to strengthen the study, all receiving approvals also in 2019. As of December 2019, 383 participants have been recruited, at least 295 of whom have been scanned.
AMYPAD Alzheimer's disease	Centiloid values are a new innovative way to measure the burden of amyloid in the brain. The first descriptive report on amyloid PET scan quantification has been delivered, including 122 subjects from the PNHS and 222 from the DPMS with Centiloid values as a primary outcome measure. The results show that both trials are effectively recruiting the target populations and that both amyloid tracers used in the project are providing similar results.
BEAt-DKD diabetes	One of the main objectives of the project is to gather all existing prospective observational and intervention cohorts of diabetic patients with kidney disease in one unique network. To achieve this objective, the project has intensified collaborations with two large international consortia in US and in Asia (the NIDDK at NIH - National Institute of Diabetes and Digestive and Kidney Diseases - funded Kidney Precision Medicine Program (KPMP) and the Singaporean Research Program DYNAMO – Diabetes study of nephropathy and other microvascular complications) to secure access to large population cohorts, including other ethnicities for replication purposes.
C4c paediatric clinical trials	The pan-European paediatric clinical trial network being set up. This includes the establishment of 19 paediatric national hub trials; of national coordinators of trial sites to oversee site activity related to trials; the identification of a single Point of Contact (SPoC) for all sponsors; the availability of network procedures, principles & tools ready for use. Four non-industry proof-of-viability studies have been selected to test the appropriateness of the set up procedures and the efficiency of the network using performance metrics. Integration of c4c into the wider paediatric community by including clinical and methodology experts and patients (children and young people)/parents' associations to contribute to advice during the study development; A Call for expression of interest to join an experts group was launched. More than 300 experts have been appointed into 24 standing expert groups (16 clinical and 8 innovative methodology expert groups) to provide to provide high quality advice on paediatric study design and paediatric medicine development strategy A Call was also launched for children, young people and families to become members of the pool of patient/YPAG experts.
DRIVE vaccines	For the clinical networks, DRIVE liaises with different public health institutes of Europe, and integrates them as associated partners in the project. These include Austria, Denmark, Luxembourg and Iceland.

Project title	Description of result(s)
	DRIVE releases annual tenders to increase the European capacity to analyse influenza vaccine effectiveness. Those sites that have sufficient potential to produce important results are included in the project as DRIVE Research collaborators or study sites. These activities enable the consortium to meet DRIVE's objectives, in determine the seasonal flu vaccine effectiveness by brand.
EBOVAC2 Ebola and related diseases	The work of EBL 2002 clinical trial in Africa was mainly possible due to the involvement of existing clinical networks or facilities in Africa, PAC-CI managed a network of sites in Ivory Coast. For this clinical trial, a total of 4 cohorts were created in Africa.
HARMONY big data, cancer	In 2019 several data providers from across the EU uploaded their data (including the NOVARTIS RATIFY clinical trial) making a total of 10 975 data records, from both acute myeloid leukaemia and multiple myeloma patients, that have already been included the HARMONY data platform.
IMI-PAINCARE pain	The clinical study PROMPT NIT-2 (which will be the data source for outcomes of acute and chronic pain in observational studies) has recruited 934 patients in Germany, Italy and France, and is completed. The study is contributing to the validation of robust patient outcome measures for the transition from acute to chronic pain.
INNODIA diabetes	Created INNODIA clinical trial network - 16 clinical centres in 5 different countries. All centres are accredited and ready for upcoming clinical trials.
NECESSITY Sjögren's syndrome	In its first year, NECESSITY has obtained clinical and biological data (from blood and tissue samples) from all available longitudinal cohorts and clinical trials on primary Sjögren's syndrome (pSS) in Europe in the last 10 years. These data will be re-analysed and used to (i) identify and evaluate biomarkers for patient stratification; and (ii) develop a new clinical endpoint for use in future clinical trials in pSS.
PERISCOPE vaccines	Developed a clinical network in the UK, Finland and the Netherlands to perform booster studies with aP vaccines in children and adults in different age groups and analysed serological, cellular and molecular responses. Developed a central data base with all clinical and laboratory data and a clinical network to analyse the effects of maternal immunisation with aP vaccine on aP/wP infant responses.
PIONEER big data, cancer	79 databases of patients with prostate cancer have been identified, the project has access to 22 and conversion of data records into the platform is ongoing.
PRISM neurological disorders	The clinical study on the biological underpinnings of social withdrawal in Alzheimer's disease and schizophrenia has enrolled 165 individuals (initial target of 144), composed of 56 schizophrenia patients, 52 Alzheimer's disease patients and age-matched healthy subjects. This final sample for the PRISM1 clinical study is sufficient to detect real effects of diagnosis or of social withdrawal and this is the first large-scale study to apply the research domain criteria (RDoC) principles, proposed by the US National Institute of Mental Health.
RHAPSODY diabetes	The project established a biomarker prioritization matrix combining data from protein localisation, target druggability, disease association & novelty screening and a web-based prioritisation tool. These two new tools enable: ▪ to systematically evaluate biomarker candidates with relation to high quality and relevant external data sources; ▪ to place candidate biomarkers in the context of all RHAPSODY data generated and visualise results across multiple experiments. Those tools are currently shared with other IMI2 projects such as Beat-DKD.
RTCure rheumatoid arthritis	A new registry with information on individuals at risk of developing rheumatoid arthritis (RA) has been organised. It contains more than 2 400 individuals at risk of developing RA and more than 9 000 patients with established RA. This registry is the first in the world to explore the state of the disease in multifaceted way and it will be an important base for recruitment of individuals for clinical trials.

Project title	Description of result(s)
VITAL vaccines	VITAL is performing a clinical vaccine study to understand the mechanisms underlying vaccine response in different age groups. VITAL included 326 healthy participants across 3 age groups: adults (age 25-49), middle aged adults (aged 49-54) and older adults (aged >65) and collected data and biological samples (serum, cells, faeces, saliva, nose- and oropharyngeal swabs) to measure vaccine immune responses before and at several moments after influenza vaccination (2 days, 1 week and one month). In total, VITAL has performed over 1 300 blood draws, stored isolated cells in 8 000 vials and performed 854 real time analyses of cell constitution.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
BEAt-DKD diabetes	Established a federated database, where data from 6 different cohorts are linked to as local nodes. All data from 24 630 patients have been harmonised and formatted to a CDISC and SDTM format. With the ongoing integration of multi-omics data from cell, animal and human studies, it will help to identify baseline and dynamic predictive biomarkers for potential first drugs.
BigData@Heart big data, cardiovascular disease	A BigData@Heart community has been created on the European Medical Information Framework (EMIF) platform and datasets relating to cardiovascular diseases (i.e. atrial fibrillation, heart failure and acute coronary syndrome) are being tested. This open access catalogue (emif-catalogue.eu/c/bigdata) details available datasets and associated variables in the consortium enabling current and potential users to explore and understand the datasets. Ultimately, big data can be used to improve our understanding of cardiovascular diseases aetiology and advance treatments to become more individualised.
BigData@Heart big data, cardiovascular disease	The project has developed a globally agreed atrial fibrillation standard set of outcomes. This is expected to enable measurement and comparison of important outcomes in a consistent manner with other countries around the world. It is available at www.ichom.org/portfolio/atrial-fibrillation/
C4c paediatric clinical trials	Harmonisation and standardisation of data terms commonly collected in paediatric clinical trials and initial version of cross-cutting data dictionary developed (based on CDISC standards) has been completed.
DO-IT big data	The DO-IT project has developed a toolkit for the identification, selection, and measurement of outcomes including in real-world settings The toolkit proposes six main stages to develop core outcome sets (COS), from scoping to dissemination, with a focus on stakeholder input across all stages to ensure a wide range of perspectives are taken into account. Whilst the toolkit highlights any existing best practice to developing COS, it importantly also presents a range of methodological options which BD4BO projects can consider depending on the scope of the work and resources available. The toolkit is freely available at: bd4bo.eu/index.php/toolkit/
DRIVE vaccines	A secured big data infrastructure has been produced where data is uploaded, pre-analysed and a short quality report for the sites is produced. This enables to harmonise the data standard across study sites in the project. In addition, different statistical approaches are being explored in order to obtain comparable seasonal flu vaccine effectiveness across countries. A quality control and assurance committee is also looking into the quality of the data and the standardisation of the results.
EHDEN big data	The EHDEN project ran its first data partner call in 2019. 29 eligible applications were received, of which 20 were selected by the EHDEN Data Source Prioritisation Committee. Combined, the 20 selected data partners represent over 150 million

Project title	Description of result(s)
	patient records, originating from various care settings. Geographically, they cover 8 countries: France, Denmark, the UK, Finland, Spain, Serbia, Portugal and the Netherlands. Harmonisation of their data by the certified SMEs should begin in early 2020.
EHDEN big data	Results of the first EHDEN study-a-thon were reported in 2019. In the largest study of its kind, a team of researchers used existing data on more than 250 000 individuals, to assess the relative merits of unicompartmental and total knee replacement in less than five days. The results were reported in The Lancet Rheumatology. This event showcased the possibility to harness clinical data (such as electronic health records) from different sources and use it to generate information that could help patients and doctors to make better decisions about their care. The second EHDEN study-a-thon will take place in early 2020.
EQIPD data quality, neurodegenerative diseases	Data from 770 historical studies conducted by consortium members have been pooled (Open Field (282), Irwin (36), EEG measurements (452)).These are now being analysed by the project to establish any interactions between study design features and observed outcomes.
eTRANSAFE safety	The project has developed solutions for endpoints currently not covered in the SEND format (e.g. proposal of new domains: treatment-related, pharmacological target) and identified about 400 varied data resources which could be integrated within the eTRANSAFE platform to address certain use cases.
HARMONY big data, cancer	To comply with the General Data Protection Regulation (GDPR) and national data protection legislation, HARMONY has developed and implemented a ‘de-facto’ anonymisation procedure. It consists of a safeguarded two-step brokerage procedure, complemented by a third ‘hash’ coding step, along with additional organisational, contractual, and top-level security measures. It provides the required anonymisation warranties and de-identification level by technical and organisational means, as well as the ability to identify data records stemming from the same patient to be able to track disease, update, and extend datasets.
HYPO-RESOLVE diabetes	The key objective of Hypo-RESOLVE is the creation of a secure, sustainable database with data from more than 100 clinical trials. Analysing these data will offer tremendous statistical power to establish the glucose threshold(s) below which hypoglycaemia constitutes a risk for clinical outcomes as well as determine risk factors for hypoglycaemia. Thus far, anonymisation of trials and subsequent standardisation and harmonisation of clinical trial and CGM data have been completed for demographics, vital signs and glucose and other laboratory measurements for 71 (out of >100) trials, comprising over 45 000 individuals.
NEURODERISK safety	The project developed a NeuroDeRisk toxicity profiling tool that can screen very large sets of compound data against a large number of predictive models in parallel.
PERISCOPE vaccines	CDISC standards for the multiplex immunoassay (MIA) and enzyme-linked immune absorbent spot (ELISpot) are developed with the project. Data standards are implemented in a central database (tranSMART). Findings already led to adjustments in the approach for RNAseq and to savings in the single-cell RNAseq data analysis.
RADAR-CNS neurological disorders	The RADAR-BASE software platform, made open-source in 2018 has since been used to facilitate over 13 additional studies involving greater than 13 500 participants. Examples include the monitoring of emerging infectious disease in Africa, and the UNFOLD mental health study which will track how recovery from mental ill health may ‘unfold’ over time.
RHAPSODY diabetes	Established a federated database with 10 nodes across Europe covering ~50 000 diabetic patients from 10 cohorts, with clinical, genetics, plasma omics data. The federated database design allows interrogating the database as a single virtual cohort.

Project title	Description of result(s)
ROADMAP Alzheimer's disease	IMI's ROADMAP project has released its Data Cube, an online, three-dimensional 'heat map' that allows users to visualise how different data sources capture different Alzheimer's disease outcomes at different disease stages. Furthermore, users can switch between the perspectives of people with dementia, carers, and health professionals. The Data Cube makes it easy to see what data sources are available, and where there are gaps. It comprises information from 65 data sources, including electronic health records, clinical trials, and cohorts, but does not provide access to any underlying data. According to the project, 'Enabling the visualisation of the AD-related data availability in different types of European data sources and the intrinsic gaps has proven to be a powerful tool for the design, planning and validation of the models and strategies used to guide future recommendations to enhance AD research.

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

Project title	Description of result(s)
AMYPAD Alzheimer's disease	AMYPAD is liaising with ongoing efforts by the European Association of Nuclear Medicine (EANM), the umbrella organisation for nuclear medicine in Europe to create procedures and guidelines for the standardisation of brain positron emission tomography (PET) imaging in the clinic. To this end, a collaboration agreement will be sought between AMYPAD and the EARL (EANM Research Ltd) initiative to promote multicentre nuclear medicine and research.
BEAt-DKD diabetes	BEAt-DKD is collaborating with the education trailing programme PROMINENT that will provide training for 16 early stage researchers, in 1) disease mechanism; 2) drug development; 3) drug registration; and 4) drug application for personalised medicine in diabetic chronic disease management. In addition, 8 PhD students and 31 postdoctoral fellows are involved in the BEAt-DKD project, allowing them to learn and grow academically within this international collaboration. BEAt-DKD results will have an impact on clinical and research training by expanding new basic and clinical research options for trainees.
C4c paediatric clinical trials	Establishment of the c4c Academy for Paediatric Clinical Trials – an e-learning platform (www.academyc4c) with developed for short courses and training modules courses. The online course is currently available to the c4c network's site staff and healthcare professionals involved in the c4c supported clinical trials.
CARDIATEAM diabetes	A webinar on imaging procedures to address the diagnosis and evaluation of diabetic cardiomyopathy has been recorded and is available for all the clinical centres involved in the CARDIATEAM clinical study. A translational network on diabetic cardiomyopathy has been created in France and involves many CARDIATEAM partners (1 meeting in June 2019, next in March 2020).
EBODAC Ebola and related diseases	Training has been delivered by the EBODAC consortium in 2019 for the use of biometric tools, community engagement, rumour management, use of remote training platforms for community health workers in Sierra Leone, Uganda, DRC, Rwanda. In total 9 892 people received training from the EBODAC consortium in 2019.
EBOVAC1 Ebola and related diseases	For the EBOVAC-Salone trial (EBL3001: (Ebola vaccine phase 2b safety and immunogenicity trial carried out in Sierra Leone), 44 training events were conducted during 2019, on various trial-related topics, including: ▪ Protocol amendments ▪ General Data Protection Regulation (GDPR) ▪ Procurement ▪ Rave software package ▪ Pharmacy manual ▪ Paediatric refresher training

Project title	Description of result(s)
	▪ Serious Adverse Events reporting ▪ Sub-store management For Sierra Leone PREVAC (currently conducting a Phase 2 clinical trial in Guinea, Liberia, Sierra Leone and Mali to evaluate three Ebola vaccination strategies in people aged one year and older), 40 training events were conducted during 2019, on various trial-related topics, including: ▪ Electronic Case Report Form ▪ PREVAC clinical trial protocol ▪ Biometrics ▪ Quality control ▪ Verbal autopsies ▪ General Data Protection Regulation (GDPR) ▪ Sample transport ▪ Data cleaning ▪ Informed consent documentation
EBOVAC3 Ebola and related diseases	In Sierra Leone, the project conducted 35 training events for EBOVAC staff and stakeholders on the following topics: ▪ Standard Operating Procedures (SOPs) ▪ Informed consent ▪ The EBL3005 clinical trial protocol ▪ Data management ▪ Safety reporting ▪ Good Clinical Practice (GCP) ▪ Participant messaging ▪ Quality control ▪ Human resource policies ▪ General Data Protection Regulation (GDPR) In Guinea the project conducted 14 training events for EBOVAC staff and stakeholders on the following topics: ▪ The EBL2005 clinical trial protocol and its subsequent amendments ▪ Standard Operating Procedures (SOPs) ▪ Dry runs ▪ Infant medical conditions In the Democratic Republic of the Congo the project conducted 5 training events for EBOVAC staff and stakeholders on the following topics: ▪ Good Clinical Practice (GCP) ▪ The EBL2007 clinical trial protocol ▪ The EBL2007 clinical trial investigator's brochure (IB) ▪ Data collection ▪ Standard Operating Procedures (SOPs)
EHDEN big data	The EHDEN project launched its first call for data harmonisation service providers in 2019. 11 SMEs were successful in the call, and all 11 have now been trained and fully certified to carry out the harmonisation for the data partners identified in the data partner calls. Full details of the SMEs are available at: https://www.ehden.eu/business-directory/. Further SME calls will take place in 2020 and future years.
EQIPD data quality, neurodegenerative diseases	The EQIPD 2019 summer school took place at Radboud University Medical Center, Nijmegen, the Netherlands, on 16-19 September 16th -19 2019: involved were 7 PhD students, 3 post-docs, 1 assistant researcher, 1 physician scientist,1 biomedical advisor and 1 MSc student (14 in total). Teachers involved in the training programmes: 9 from EQIPD, 3 external teachers. Further information, incl. the programme, can be found at: quality-preclinical-data.eu/learning-environment/summer-school/
HARMONY	Organised a masterclass for the HARMONY patient cluster (a group of 7 European patient umbrella organizations working in the different areas of haematological

Project title	Description of result(s)
	diseases) to build a solid relationship with this stakeholder group and to learn about their information and communication needs from the project, how they can contribute, and which kind of data could be gathered from patients that may be helpful in HARMONY. www.harmony-alliance.eu/for-patients-carers/learn-more-about-the-harmony-patient-cluster
MACUSTAR eye disease	Training performed as well as certification of clinical sites and imaging technicians to ensure quality of the readings. As of 31 August 2019 a total of 467 certificates were obtained by technicians on different imaging modalities.
PERISCOPE vaccines	Organized the 10th EuroFlow-PERISCOPE education & training workshop dedicated to database training for automated data analysis. This workshop took place in Salamanca, Spain on April 2, 2019. Nineteen people from 7 institutes attended this workshop.
PRISM neurological disorders	Delivered six educational videos about PRISM science, available on YouTube for the public, via prism-project.eu/en/ecnp-prepared-a-series-of-six-videos-to-show-what-prism-is-about/
RESCEU respiratory disease	On 31/08/2019 at Wilhelmina Children's Hospital in Utrecht, the 'RESCEU for You' symposium was organised with the aim to inform patients about the results of the RESCEU study in which they contributed. All the Dutch participants (350 out of 1000 patients recruited in total for the older adult cohort study) that were followed during two winter seasons to see how often an infection with RSV occurred have been invited and 70 adults aged 60 to 93 years participated to the event.

Impact on regulatory framework

Project title	Description of result(s)
AIMS-2-TRIALS autism	The Federal Food and Drug Administration (FDA) accepted into the biomarker development programme the consortium finding (jointly with the ABC-CT network (USA)) on the potential utility of N170 as an enrichment biomarker in autism. N170 is a component of the event-related potential that reflects the neural processing of faces, familiar objects or words, which is different in people with/without autism.
DRIVE vaccines	DRIVE arose as the regulatory need to assess brand specific influenza vaccine effectiveness. Therefore discussions between DRIVE and EMA staff occur on a regular basis especially regarding the involvement of EMA's Vaccine Working Party before submission of brand specific data to NCAs (national competent authorities).
EBOVAC1, EBOVAC 2 and EBOVAC3 Ebola and related diseases	The EMA showed high levels of flexibility in the marketing authorisation applications submission process of the Ebola virus disease vaccine developed by Janssen. Janssen was allowed to submit the current data package and safety database on the basis of an immunobridging approach rather than clinical efficacy data. In the absence of clinical efficacy data, the likelihood of clinical benefit needs to be inferred by bridging human immunogenicity data (Phase2/3trials) to the relationship between immunogenicity and survival outcome (efficacy) in the non-human primate Ebola virus challenge model.
GetReal initiative relative effectiveness	Reference made in the EMA Committee for Medicinal Products for Human Use (CHMP): Work Plan 2019 to explore the ADDIS decision-making tool developed during the training of assessors on regulatory decision-making and structured benefit-risk assessment of medicines for assessors.
HYPO-RESOLVE diabetes	Innovation Task Force meeting with the EMA took place to exchange/discuss views on the definition of hypoglycaemia in diabetes.

Project title	Description of result(s)
IMI-PAINCARE pain	The consortium started (informal) interactions with the Federal Drug & Food Administration (FDA) and met on May 8, 2019 with the EMA Innovation Task Force to present the project work of regulatory relevance. The regulators expressed interest and provided first feedback on the potential patient reported outcome measures (PROMs) and functional biomarkers selection and plans for their further qualification/validation.
INNODIA diabetes	The project has undergone a formal Scientific Advice procedure with the EMA to obtain a qualification advice regarding the INNODIA's Trial Master Protocol.
LITMUS liver disease	Letters of Intent (LOI) were submitted in June 2019 to FDA and EMA with 3 contexts of Use (COUs) and 3 biomarkers.
NECESSITY Sjögren's syndrome	The consortium has initiated informal dialogue with EMA in order to obtain early advice on the development of the project's clinical protocol for further validation of new clinical endpoints in primary Sjögren's syndrome (pSS). The ultimate goal from a regulatory perspective is to obtain qualification of a novel methodology (new clinical endpoints) developed in NECESSITY for its future use in clinical trials.
PREFER patient involvement in R&D	The consortium has initiated a first joint EMA/EUnetHTA qualification procedure for a framework and the discrete choice experiments (DCE) method for performing patient preference studies to support medical decision-making. This will provide the proof of concept that patient preference methods can be qualified as well as a blueprint for the qualification of further methods by other applicants.
PRISM neurological disorders	The consortium met on June 17, 2019 with the EMA Innovation Task Force (EMA ITF) to discuss the results obtained with the BEHAPP app in the PRISM clinical study. Overall, the EMA ITF clearly supported the progression of the BEHAPP social functioning assessment via the biomarker qualification process.
TransQST safety	The project is initiating dialogue with regulators concerning the qualification of models relative to ICH E14 and S7B and the current Q&A process.
VHFMODRAD Ebola and related diseases	The preparation for registration of a rapid diagnostic test for detection of Ebola antigen requires new capacity as this test is classified in the new European *in vitro* diagnostic device (IVD). The consortium is working in order to succeed in the registration processes of the rapid diagnostic tests.
WEB-RADR 2 pharmacovigilance	The WEB-RADR consortium published its findings on the suitability of social media for detecting new safety issues in marketed medicines in the journal Drug Safety. As part of this publication, the team studied some 4.2 million tweets and Facebook posts as well as over 42 000 posts from over 400 online patient fora. Overall, they conclude that social media, such as Facebook and Twitter, are not recommended for detecting potential safety issues. However, social media may prove useful in certain niche areas, such as exposure to medicines during pregnancy and the abuse (or misuse) of medicines. Furthermore, advances in technology could mean that social media could be used as a source of information on ADRs in the future.
WEB-RADR 2 pharmacovigilance	In 2019, facilitated through a collaboration with the WHO and local regulatory authorities, the Med Safety app developed in the WEB-RADR project was launched in Armenia, Ghana, Ethiopia, Botswana and Cote d'Ivoire with the support of the World Health Organisation (as reported in the WHO newsletter). The app is now available in 11 countries. Many more launches will follow in 2020.

Implementation of project results inside industry

Project title	Description of result(s)
EBOVAC1, EBOVAC 2 and EBOVAC3 Ebola and related diseases	The clinical trial results generated in these 3 projects (aiming at developing a vaccine against Ebola virus disease) contributed to the vaccine licensure package that Janssen filed in the EU and will contribute to the one Janssen will prepare for filing in US. Experience has been gained via EBOVAC2 in conducting clinical studies in sub-Saharan Africa and more specifically in a resource-limited setting. The lessons learned in EBOVAC2 have contributed to developing a clinical guideline that includes an optimised operating model with better oversights from the R&D company towards local clinical trial conduct.
EQIPD data quality, neurodegenerative diseases	The EQIPD preclinical study quality management system (QMS) is in a pilot stage, including a pilot trial at Janssen. Pilot trials are also ongoing at contract research organisation (CRO) and academic labs. These pilot trials already provided useful feedback and helped to continuously refine and improve the QMS. The outcome of these trials will determine the utility of the QMS for the sites that implemented it.
NEURODERISK safety	In the context of toxicity profiling and datamining tools, the project established industry level standard operating procedures (SOPs) and quality assurance measures for the NeuroDeRisk database that will be populated with data generated in this project. The established industry level standard operating procedures and QA measures are already used for data collection and curation in order to build up the database. All partners in the consortium (academic, SME, EFPIA) are committed to the SOPs and QA measures.
PERISCOPE vaccines	4 Immunoassays have been implemented inside the industry. There are lab tests to evaluate immune response to vaccines. Impact: PERISCOPE assays have been used to evaluate the ability of novel industry vaccine formulations to engender functional antibody/T-cell response. The preclinical read out with bioimaging improved the understanding of pathogenesis/vaccines protection.
PRISM neurological disorders	The industry partners have implemented in house three of the project's technology platforms, namely two preclinical technology platforms (social behaviour and electroencephalography (EEG) assessments) and one clinical platform (BEHAPP smartphone application).
TransQST safety	In 2019, the consortium finalised the first version of the liver (DILI) TXG-MAPr and made it available for consortium members via the new website txg-mapr.eu The TGX-MAPr web tools are being evaluated by EFPIA partners.
TransQST safety	The cardiac models are being evaluated and used within EFPIA partners and the haemodynamics Shiny simulation tool is also being evaluated for use with EFPIA partners.
VHFMODRAD Ebola and related diseases	The Ebola-Ag K-SeT developed by Coris BioConcept is prepared for registration. Cepheid cartridges open to in-house reagents for bedside diagnostics, developed and evaluated during VHFMODRAD have the potential to be licensed, FDA-approved and commercialized by Cepheid.
VSV-EBOVAC and VSV-EBOPLUS Ebola and related diseases	The detailed analyses of immune and molecular signatures of immune responses, elicited by rVSV-ZEBOV in humans, conducted within these 2 projects provide relevant information on VSV-ZEBOV Ebola vaccine immunogenicity and support its development by the industry partner (MSD).

Accessibility of resources/outputs beyond consortium

Project title	Description of result(s)
AMYPAD Alzheimer's disease	Has developed and tested methods for the refinement of amyloid quantification. The resulting algorithms are integrated in the NiftyPET software which is publicly available at niftypet.readthedocs.org. Acknowledgements to AMYPAD can be found at niftypet.readthedocs.io/en/latest/ackn.html
AMYPAD Alzheimer's disease	The code for the new deep learning-based magnetic resonance (MR) to computed tomography (CT) synthesis algorithm for performing attenuation correction with positron emission tomography/MR (PET-MR) scanners is publicly available as part of NiftyNet (github.com/NifTK/NiftyNet.git), and can be obtained from /NiftyNet/niftynet/contrib/deep_boosted_regression.
EBiSC2 stem cells	From March 2019 onwards, 20 EBiSC induced pluripotent stem cells (iPSC) lines have been expanded and banked and an additional 17 lines have undergone QC testing. Deposition of 53 iPSC lines generated within EBiSC1 has been completed and additional lines made available to users via the EBiSC catalogue since the end of the first project period in 2017. 41 customer orders have been completed since March 2019 to date, with 47 vials distributed to 23 users across 13 countries. These numbers demonstrate that the iPSC repository is under expansion, which is an essential prerequisite for reaching the self-sustainability of the banking entity and fulfil the expected future demands from both industry and the research community.
DO-IT big data	The DO-IT project has developed template harmonised informed consent forms (ICF) to facilitate the secondary use of personal data The freely available templates cover all information required by the General Data Protection Regulation (GDPR) within a traditional (non-electronic) informed consent document to be signed by patients or healthy volunteers before participating in a clinical study. The ICFs aim to address the processing of personal data for (a) the conduct of a clinical study within a drug development programme (Part 1); and (b) future scientific research on personal data and biosamples collected in clinical studies, i.e. research beyond of the original drug development programme.
DRIVE vaccines	DRIVE has produced a number of public deliverables accessible on DRIVE website. These include the study protocols, SOPs, a guideline for the interpretation of the IVE results, a research agenda, a standard set of analytical methods to measure influenza vaccine effectiveness, and a generic statistical analysis plan, that is revaluated yearly. These are accessible at www.drive-eu.org/index.php/results/deliverables/
FAIRplus big data	The first draft of a key project output the open FAIR 'Cookbook' with 'recipes' for the FAIRification of different types of data was made publicly available at https://is.gd/cpWIAX. This cookbook will continue to grow throughout the project. The cookbook was applied to the first four FAIRified datasets, which are now in the IMI Data Catalogue https://is.gd/6eY8el The datasets are: ▪ OncoTrack: Oncology biomarker development data ▪ ND4BB: Antimicrobial compounds database ▪ Resolute: Solute carriers as drug targets ▪ eTOX: Preclinical toxicology data
PERISCOPE vaccines	The PERISCOPE biobank will stay available at RUMC (coordinating entity) beyond the project. https://periscope-project.eu/
PIONEER big data, cancer	A policy paper has been published which is freely available on CORDIS and the project website as deliverable 6.16: prostate-pioneer.eu/wp-content/uploads/2019/07/D6.16-Policy-Paper-1.pdf

Project title	Description of result(s)
	This policy paper attempts to identify the key issues and make recommendations for next steps that will support action and alignment for the prostate cancer evidence framework.
PREFER patient involvement in R&D	Glossary of terms relevant to patient preference publicly available. This glossary provides working definitions for PREFER to helps researchers with a common taxonomy for day-to-day interactions www.imi-prefer.eu/about/glossary/
RESOLUTE drug development	The project has made publicly available the DNA sequence of approximately 400 solute carrier proteins, which regulate basic functions of human cells and are involved in diseases. The DNA has been codon-optimised to improve the sequence, thus make it easier for cells to produce higher amounts of it. These reagents are powerful tools, which are expected to allow the scientific community to work more efficiently with this family of proteins and, ultimately, make use of them as targets for drug development. The DNA reagents are available at Addgene.org (www.addgene.org/depositor-collections/re-solute/) for a small fee, which covers quality control and shipping costs.
RESOLUTE drug development	The project has published the RESOLUTE knowledge base (re-solute.eu/knowledgebase), an online database that brings together in one place information on solute carrier proteins. The knowledge base, which is freely accessible to the scientific community, comprises high quality, reliable information from publicly available sources allowing researchers to rapidly get an overview on the current knowledge on any human SLC. In the coming years, the project intends to add further information to the knowledge base from public resources as well as data generated by RESOLUTE.
TransQST safety	The cardiac virtual assay software from UOXF is available for license. Virtual assay is available for free for academic purposes and for a fee for commercial purposes through Oxford University Innovation. The haemodynamics simulation tool has been made publicly available via https://www.cs.ox.ac.uk/ccs/virtual-assay.
TransQST safety	BioModels Parameters is publicly available under the BioModels domain at /www.ebi.ac.uk/biomodels/parameterSearch/ and linked via the TransQST platform. Any researcher or modeller can access this data without registration.
TransQST safety	The DisGeNET database (www.disgenet.org/) is available under the Attribution-NonCommercial-ShareAlike 4.0 International License, and can be accessed in several ways: through the web interface, the Resource Description Framework (DisGeNET-RDF) representation via the SPARQL endpoint, the DisGeNET Cytoscape App, the disgenet2r package, the SQLite database, and a REST API.
TransQST safety	The iPath tool is freely accessible through this URL sbi.imim.es/data/ipath.tgz Data are planned to be published in international scientific journals, and through that, will become publicly accessible for free.
TransQST safety	The project is searching for suitable model parameters from published literature and models is an essential yet laborious task. The project developed a new service, BioModels Parameters which is released and publicly accessible at www.ebi.ac.uk/biomodels/parameterSearch/. All data can also be freely downloaded. A manuscript is currently under review at Bioinformatics. The tool can facilitate easy search and retrieval of parameter values such degradation rate, production rate, Kcat and Michaelis-Menten constant. Quantitative systems toxicology (QST) modellers can directly search for an entity (e.g. a protein or drug) to extract data.
TransQST safety	The TGX-MAPr web tools are available for free to consortium partners (TransQST, eTRANSAFE, EUTOXRISK) at https://txg-mapr.eu/ Access details need to be requested.

Annex 4 - Publications from projects

Hot publications in 2019

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

- Cossarizza, A et al. (2019) Guidelines for the use of flow cytometry and cell sorting in immunological studies (second edition), EUROPEAN JOURNAL OF IMMUNOLOGY 49: 1457
- Parikh, AR et al. (2019) Liquid versus tissue biopsy for detecting acquired resistance and tumor heterogeneity in gastrointestinal cancers, NATURE MEDICINE 25: 1415
- Pantel, K et al. (2019) Liquid biopsy and minimal residual disease - latest advances and implications for cure, NATURE REVIEWS CLINICAL ONCOLOGY 16: 409
- Falcon, B et al. (2019) Novel tau filament fold in chronic traumatic encephalopathy encloses hydrophobic molecules, NATURE 568: 420

2019 publications featured in in the top 10 Journals

- Schapira, Matthieu et al. (2019) Targeted protein degradation: expanding the toolbox, NATURE REVIEWS DRUG DISCOVERY 18: 949
- Keller, Laura et al. (2019) Unravelling tumour heterogeneity by single-cell profiling of circulating tumour cells, NATURE REVIEWS CANCER 19: 553
- Heitzer, Ellen et al. (2019) Current and future perspectives of liquid biopsies in genomics-driven oncology, NATURE REVIEWS GENETICS 20: 71
- Wohlfahrt, Thomas et al. (2019) PU.1 controls fibroblast polarization and tissue fibrosis, NATURE 566: 344
- Culemann, Stephan et al. (2019) Locally renewing resident synovial macrophages provide a protective barrier for the joint, NATURE 572: 670
- Piot, Peter et al. (2019) Immunization: vital progress, unfinished agenda, NATURE 575: 119
- Falcon, Benjamin et al. (2019) Novel tau filament fold in chronic traumatic encephalopathy encloses hydrophobic molecules, NATURE 568: 420

Highly-cited publications in 2019

- Pantel, K et al. (2019) Liquid biopsy and minimal residual disease - latest advances and implications for cure, NATURE REVIEWS CLINICAL ONCOLOGY 16: 409
- Danne, T et al. (2019) International Consensus on Risk Management of Diabetic Ketoacidosis in Patients With Type 1 Diabetes Treated With Sodium-Glucose Cotransporter (SGLT) Inhibitors, DIABETES CARE 42: 1147
- Albrecht, W et al. (2019) Prediction of human drug-induced liver injury (DILI) in relation to oral doses and blood concentrations, ARCHIVES OF TOXICOLOGY 93: 1609
- Siravegna, G et al. (2019) Plasma HER2 (ERBB2) Copy Number Predicts Response to HER2-targeted Therapy in Metastatic Colorectal Cancer, CLINICAL CANCER RESEARCH 25: 3046
- Rothwell, DG et al. (2019) Utility of ctDNA to support patient selection for early phase clinical trials: the TARGET study, NATURE MEDICINE 25: 738
- Falcon, B et al. (2019) Novel tau filament fold in chronic traumatic encephalopathy encloses hydrophobic molecules, NATURE 568: 420
- Bolte, S et al. (2019) The contribution of environmental exposure to the etiology of autism spectrum disorder, CELLULAR AND MOLECULAR LIFE SCIENCES 76: 1275
- Bennett, DL et al. (2019) THE ROLE OF VOLTAGE-GATED SODIUM CHANNELS IN PAIN SIGNALING, PHYSIOLOGICAL REVIEWS 99: 1079
- Lianidou, E et al. (2019) Liquid biopsies, GENES CHROMOSOMES & CANCER 58: 219
- McDermott, LA et al. (2019) Defining the Functional Role of Na(v)1.7 in Human Nociception, NEURON 101: 905

- Schewe, M et al. (2019) A pharmacological master key mechanism that unlocks the selectivity filter gate in K+ channels, SCIENCE 363: 875
- Zhang, WJ et al. (2019) Heparin-induced tau filaments are polymorphic and differ from those in Alzheimer's and Pick's diseases, ELIFE 8: -
- Kas, MJ et al. (2019) A quantitative approach to neuropsychiatry: The why and the how, NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS 97: 3
- Porcelli, S et al. (2019) Social brain, social dysfunction and social withdrawal, NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS 97: 10
- Scott, R et al. (2019) Loss of Cntnap2 Causes Axonal Excitability Deficits, Developmental Delay in Cortical Myelination, and Abnormal Stereotyped Motor Behavior, CEREBRAL CORTEX 29: 586
- Gerlag, DM et al. (2019) Effects of B-cell directed therapy on the preclinical stage of rheumatoid arthritis: the PRAIRI study, ANNALS OF THE RHEUMATIC DISEASES 78: 179
- Frangou, E et al. (2019) REDD1/autophagy pathway promotes thromboinflammation and fibrosis in human systemic lupus erythematosus (SLE) through NETs decorated with tissue factor (TF) and interleukin-17A (IL-17A), ANNALS OF THE RHEUMATIC DISEASES 78: 238
- Steen, J et al. (2019) Recognition of Amino Acid Motifs, Rather Than Specific Proteins, by Human Plasma Cell-Derived Monoclonal Antibodies to Posttranslationally Modified Proteins in Rheumatoid Arthritis, ARTHRITIS & RHEUMATOLOGY 71: 196
- Ge, CR et al. (2019) Structural Basis of Cross-Reactivity of Anti-Citrullinated Protein Antibodies, ARTHRITIS & RHEUMATOLOGY 71: 210
- Church, RJ et al. (2019) Candidate biomarkers for the diagnosis and prognosis of drug-induced liver injury: An international collaborative effort, HEPATOLOGY 69: 760
- Parhizkar, S et al. (2019) Loss of TREM2 function increases amyloid seeding but reduces plaque-associated ApoE, NATURE NEUROSCIENCE 22: 191
- Heitzer, E et al. (2019) Current and future perspectives of liquid biopsies in genomics-driven oncology, NATURE REVIEWS GENETICS 20: 71
- Cunningham, F et al. (2019) Ensembl 2019, NUCLEIC ACIDS RESEARCH 47: D745
- Mendez, D et al. (2019) ChEMBL: towards direct deposition of bioassay data, NUCLEIC ACIDS RESEARCH 47: D930
- Scheer, S et al. (2019) A chemical biology toolbox to study protein methyltransferases and epigenetic signaling, NATURE COMMUNICATIONS 10: -
- van Overbeeke, E et al. (2019) Factors and situations influencing the value of patient preference studies along the medical product lifecycle: a literature review, DRUG DISCOVERY TODAY 24: 57
- Schuetz, DA et al. (2019) Predicting Residence Time and Drug Unbinding Pathway through Scaled Molecular Dynamics, JOURNAL OF CHEMICAL INFORMATION AND MODELING 59: 535
- Pavlidis, S et al. (2019) T2-high in severe asthma related to blood eosinophil, exhaled nitric oxide and serum periostin, EUROPEAN RESPIRATORY JOURNAL 53: -
- Shrine, N et al. (2019) Moderate-to-severe asthma in individuals of European ancestry: a genome-wide association study, LANCET RESPIRATORY MEDICINE 7: 20
- Atkinson, MA et al. (2019) The challenge of modulating beta-cell autoimmunity in type 1 diabetes, LANCET DIABETES & ENDOCRINOLOGY 7: 52
- Roep, BO et al. (2019) Antigen-based immune modulation therapy for type 1 diabetes: the era of precision medicine, LANCET DIABETES & ENDOCRINOLOGY 7: 65
- Colombo, M et al. (2019) Serum kidney injury molecule 1 and (2)-microglobulin perform as well as larger biomarker panels for prediction of rapid decline in renal function in type 2 diabetes, DIABETOLOGIA 62: 156

Annex 5 - Patents from projects

Since the start of IMI2 programme, IMI projects have been patenting developed technologies. The statistics below encompass 7 patent applications and 1 patent awarded from the beginning of IMI2 until 31 December 2019.

FILODAG – 1 patent application

- Superparamagnetic particles

About FILODIAG: A quick Ebola test that will allow health workers to rapidly isolate infected individuals has the potential to stop an outbreak from ballooning into a major epidemic. FILODIAG created an ultra-fast molecular test that can detect Ebola in a blood sample in a fraction of the time it typically takes in the lab. The technology is based on pulse-controlled amplification and a specific set of reagents.

MOFINA – 2 patent applications

- Filovirus detector

About MOFINA: MOFINA 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

About EBOVAC1 & 2: Between them, the 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

About PHAGO: 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. 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. PHAGO 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.

PEVIA – 2 patent applications

- Immunogenic epitopes and immunogenic peptides

About PEVIA: There are a number of promising Ebola vaccines in development, and studies suggest that they are both safe and effective. Nevertheless, their large-scale deployment could be limited by issues such as the fact that they need to be stored at extremely low temperatures (-80°C). The goal of PEVIA is to develop second-generation Ebola vaccines based on the proteins found on the surface of the virus. The project team is using the prime-boost approach, in which one vaccine is given to prime the immune system, and a second (different) vaccine is given to boost the immune response.

Annex 6 - Scoreboard of Horizon 2020 common KPIs

Table I[53] - 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 2019
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
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	[On average, 20 publications per EUR 10 million funding (for all societal challenges)]	22.28%

53 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 2019
				bibliometric databases.		
	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	7 patent applications 1 patent awarded
	16	Number of prototypes testing activities and clinical trials[54]	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: 14 - Testing Activities: 53 - Clinical Trials: 48
	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]	123 23.16 %
	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: 18 -New Processes: 10 -New Methods: 13
EVALUATION	**NA**	Time to inform (TTI) all applicants of the outcome of the evaluation of their application from the final date	To provide applicants with high quality and timely evaluation results and feedback after each evaluation step by implementing	Number and % of information letters sent to applicants within target	153 calendar days	No. of Short Proposal information letters: 78 (100 % on time) No. information letters for Full Proposals: 23 (100 % on time) Average TTI: 73 days

54 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 2019
		for submission of completed proposals	and monitoring a high scientific level peer reviewed process	Average TTI (calendar days) Maximum TTI (calendar days)		Statistics refer to letters sent out in 2019 (SPs for IMI2 – Calls 15, 17 and 18; FPs for IMI2 – Calls 14 and 15 and single stage proposals for IMI2 – Calls 16 and 19). Letters for IMI2 – Call 17 FPs will be sent out in 2020.
	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		2 redress request. The review committee evaluated the complaints and found no grounds to re-evaluate the proposals.
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 < 245 days (as % of GAs signed)	27 out of 29 (93 %) were signed within the target Average TTG: 210 days. Maximum TTG: 289 days

	Correspondence to general Annex 1	Key Performance Indicator	Definition / responding to question	Type of data required	Target at the end of H2020	Results in 2019
	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 29 (0 %) was signed within the target.[55] Average TTS: 151 days Maximum TTS: 219 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: 57 days (100 % on time) Final payments: 65 days (100 % on time)
HR	**NA**	Vacancy rate (%)		% of post filled in, composition of the JU staff		Overall vacancy rate: 5.35 % TAs: 2.56 % CAs: 6.67 % 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	99.17 % CA to total budget 96.33 % PA to total budget

55 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 2019
	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)		1 111 payments of which 46 were late (4 %)

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[56] - 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 2019
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: 4724 Applicants:1708 Beneficiaries: 1832 Country — Participations (Participants) Austria — 37 (17) Belgium — 178 (60) Croatia — 1 (1) Czechia — 8 (6) Denmark — 68 (23) Estonia — 4 (2) Finland — 31 (12) France — 230 (100) Germany — 285 (119) Greece — 9 (6) Hungary — 6 (5) Ireland — 18 (13) Italy — 109 (66)

56 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 2019
					Latvia 1 (1) Luxembourg 28 (6) Netherlands 198 (68) Poland 5 (5) Portugal 17 (16) Romania 2 (2) Slovenia 4 (4) Spain 110 (60) Sweden 76 (18) United Kingdom 407 (121) **Total EU-28: 1832 (731)** (Cumulative figures as of 31/12/2019)
		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 27.8 (2.8%) Belgium 58.4 (5.9%) Croatia 0.1 (0.0%) Czechia 2.3 (0.2%) Denmark 16.9 (1.7%) Estonia 1.9 (0.2%) Finland 11.5 (1.2%) France 106.8 (10.8%) Germany 115.3 (11.7%) Greece 2.8 (0.3%) Hungary 2.8 (0.3%) Ireland 16.7 (1.7%) Italy 75.4 (7.6%) Latvia 0.3 (0.0%) Luxembourg 11.3 (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 2019
					Netherlands 140.9 (14.3%) Poland 1.2 (0.1%) Portugal 5.6 (0.6%) Romania 1.5 (0.2%) Slovenia 0.5 (0.1%) Spain 102.9 (10.4%) Sweden 30.3 (3.1%) UK 253.0 (25.7%) **Total EU-28**: 986.3 (Cumulative figures as of 31/12/2019)
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: - Applications: 358 - Applicants: 146 - Beneficiaries: 152 Country — Participations (Participants) Iceland 1 (1) Israel 15 (8) Norway 16 (10) Serbia 2 (2) Switzerland 117 (35) Turkey 1 (1) Associated Countries: 152 (57) (Cumulative figures as of 31/12/2019)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2019
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 (%) Iceland: 0.1 (0.2%) Israel: 3.1 (5.8%) Norway: 5.3 (9.9%) Serbia: 0.8 (1.4%) Switzerland: 44.4 (82.3%) Turkey: 0.2 (0.5%) Associated Countries: 54.0 (Cumulative figures as of 31/12/2019)
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: 230 out of 1457 (15.8 %) Participants: 159 out of 705 (22.6 %) EU funding: EUR 113.8 million (10.6 %) (Cumulative figures as of 31/12/2019, beneficiaries receiving EU funding only)
6	Gender	6.1 Percentage of women participants in H2020 projects	Gender of participants in H2020 projects	YES	51% 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	27 women out of 89 project coordinators for IMI2 projects in 2019
		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 %)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2019
					Expert evaluators: 62 out of 134 experts (46.27%) Interim review experts: 29 out of 58 experts (50 %)
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) Canada 1 (1) Gabon 2 (1) Japan 1 (1) Senegal 2 (1) Sierra Leone 3 (2) Singapore 1 (1) South Africa 2 (2) Tanzania 1 (1) United States 66 (34) Third countries 83 (48) (cumulative figures as of 31/12/2019)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2019
		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 0.9% (0.3) Benin 1.7% (0.6) Brazil 0.9% (0.3) Burkina Faso 11.1% (3.8) Canada 0.0% (0.0) Gabon 2.4% (0.8) Japan 0.0% (0.0) Senegal 1.1% (0.4) Sierra Leone 65.8% (22.3) Singapore 0.0% (0.0) South Africa 1.9% (0.6) Tanzania 1.5% (0.5) United Sates 12.8% (4.3) Third Countries (33.9) (cumulative figures as of 31/12/2019)
9	Bridging from discovery	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.		0

57 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 2019
		9.2 Within the innovation actions, share of EU financial contribution focused on demonstration and first-of-a-kind activities	Topics properly flagged in the WP; follow-up at grant level		n/a
NA		Scale of impact of projects (High Technology Readiness Level)	Number of projects addressing TRL[58] between (4-6, 5-7)		-1 project TRL5 -3 projects TRL9
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: 809 out of 2067(39.1 %) Participants: 294 out of 836 (35.1 %) (Cumulative figures as of 31/12/2019)
		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 120.8 million out of EUR 1 074.2 million (11.2 %) (Cumulative figures as of 31/12/2019)
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 1 062.2 million (total cash contribution EC at the end of 2019)
		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		EFPIA & Associated Partners contribution (EUR 1 097.3 million) divided by EU contribution (EUR 1 062.2 million) = leverage of 1.03.

58 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 2019
			- additional activities (i.e. research expenditures/investment of industry in the sector, compared to previous year)		
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: 7 441 -Total funding amounts: EUR 6 617 045 -Number of people reached: 149 694 539
14	Participation patterns of independent experts	14.2 Proposal evaluators by country	Nationality of proposal evaluators		30 countries[59] (134 experts)
		14.3 Proposal evaluators by organisations' type of activity	Type of activity of evaluators' organisations	YES	49 – HES: higher or secondary education establishment 18 – REC: research organisations 18 – PUB: public bodies 25 – PRC: private for-profit entities 24 – OTH: other type of organisations

59 Austria (2), Belgium (9), Bulgaria (1), Croatia (4), Czechia (2), Denmark (3), Finland (3), France (7), Germany (13), Greece (3), Hungary (4), Iceland (1), Ireland (3), Israel (2), Italy (14), Lithuania (3), Malta (1), Netherlands (5), Norway (2), Poland (5), Portugal (3), Romania (1), Slovakia (2), Slovenia (1), Spain (8), Sweden (5), Switzerland (5), Turkey (1), United Kingdom (20), United States (1).

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2019
NA	Participation of RTOs and Universities	Participation of RTO[60]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: 367 (17.8 %) HES: 682 (33.0 %) % budget allocated: Res. Org: EUR 296.8 million (27.6 %) HES: EUR 544.6 million (50.7 %) (Cumulative figures as of 31/12/2019)
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)[61]		0% of proposals not granted because non-compliance with ethical rules/proposals invited to grant Time to ethics clearance in line with Grant Agreement Preparation timelines.
NA	Audit	Error rates	% of common representative error; % residual error		Representative error rate: 0.58 % Residual error rate: 0.28 %
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		Cases implemented 7 (58 %) Amount: EUR 459 815

60 RTO: Research and Technology Organisation
61 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[62] - KPIs specific to each single JU

Reporting methodology: cumulatively reporting from the beginning of IMI2 until 31/12/2019.

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).

KPI	Definition	Comment	Relates to	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'	12	11 out of 12 (11 out of 12 SRA priority areas are addressed by IMI2 projects) Number of projects: 66 Budget committed: EUR 1 846 613 930	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 clinical relevance and approved by regulators'	50	54	131

62 Table III presents the KPI specific for each JU, as transmitted by the Programme Offices or the operational services.
In this table, the budgets given include the EFPIA and Associated Partner contributions to the projects.

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
			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'	10 (for completed procedures)	10 completed procedures: -CE mark: 2 -Inclusion in regulatory guidelines: 1 -Regulatory qualified opinion : 6 -Submission for qualification opinion: 1 Number of projects: 6 Budget committed: EUR 132 419 117	28 completed procedures: -CE mark: 2 -Inclusion in regulatory guidelines: 9 -Regulatory letter of support: 6 -Regulatory qualified opinion : 9 -Submission for qualification opinion: 2 Number of projects: 19 Budget committed: EUR 665 651 664

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
4	New taxonomies of diseases and new stratifications (such as the definition of patient subpopulations, development, validation and use of new diagnostics) developed.	- Expressed as net figure. - 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.	IMI2 Regulation objectives b3 and b4: 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'	30	15 Number of projects: 6 Budget committed: EUR 138 233 409	25 Number of projects: 10 Budget committed: EUR 230 626 170
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.'	EUR 300 million	EUR 182.1 million (AP: EUR 149.3 million. Partners in Research: EUR 32.8 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'	50%	43.48% Number of projects: 20 Budget committed: EUR 500 250 728	61.62% Number of projects: 61 Budget committed: EUR 1 839 749 246

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
7	Co-authorships and cross-sector publications between European researchers on IMI2 projects (sectors include academia, small and mid-sized companies, pharma, regulators, patient organisations, etc.).	- Expressed as net figure - Complemented by the number and budget of grant agreements that delivered them.	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…'	1 500	123	1 453
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'	50	44 Number of projects: 22 Budget committed: EUR 547 888 944	228 Number of projects: 57 Budget committed: EUR 1 874 566 703
9	Share of projects involving patient organisations and healthcare professionals' associations (as consortium partners, members of advisory boards, members of	- 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 importance to the Union's competitiveness and industrial leadership…' b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'	80 %	63.79% Number of projects: 37 Budget committed: EUR 981 781 741	55.56% Number of projects: 65 Budget committed: EUR 1 798 529 323

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
	stakeholder groups etc.).					
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'	20 %	SME participations: 15.8 % (230 out of 1457) (IMI2 cumulative figures until 31/12/2019, beneficiaries receiving EU funding only)[63]	SME participations: 15.9 % (428 out of 2699) (IMI1 and IMI2 cumulative figures until 31/12/2019, beneficiaries receiving EU funding only)

63 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	31.12.2019	31.12.2018
NON-CURRENT ASSETS			
Intangible assets	*2.1*	*46*	*63*
Property, plant and equipment	*2.2*	*126*	*127*
Pre-financing	*2.3*	*244 200*	*217 790*
		244 372	**217 980**
CURRENT ASSETS			
Pre-financing	*2.3*	*113 577*	*78 451*
Exchange receivables and non-exchange recoverables	*2.4*	*25 584*	*49 739*
		139 161	**128 190**
TOTAL ASSETS		**383 533**	**346 170**
CURRENT LIABILITIES			
Payables and other liabilities	*2.5*	*(241 139)*	*(185 996)*
Accrued charges and deferred income	*2.6*	*(156 186)*	*(133 404)*
		(397 324)	**(319 400)**
TOTAL LIABILITIES		**(397 324)**	**(319 400)**
NET ASSETS		**(13 791)**	**26 770**
Contribution from Members	*2.7*	*2 290 993*	*1 957 247*
Accumulated deficit		*(1 930 477)*	*(1 625 988)*
Economic result of the year		*(374 306)*	*(304 489)*
NET ASSETS		**(13 791)**	**26 770**

Statement of financial performance

EUR '000

	Note	2019	2018
REVENUE			
Revenue from non-exchange transactions			
Recovery of expenses	*3.1*	*2 721*	*1 188*
Other		*1*	*4*
		2 722	**1 192**
Revenue from exchange transactions			
Other		*51*	*22*
		51	**22**
Total revenue		**2 773**	**1 214**
EXPENSES			
Operational costs	*3.2*	*(368 441)*	*(297 476)*
Staff costs	*3.3*	*(4 644)*	*(4 573)*
Finance costs		*–*	*(3)*
Other expenses	*3.4*	*(3 994)*	*(3 651)*
Total expenses		**(377 080)**	**(305 703)**
ECONOMIC RESULT OF THE YEAR		**(374 306)**	**(304 489)**

Cash flow statement[64]

EUR '000

	2019	2018
Economic result of the year	*(374 306)*	*(304 489)*
Operating activities		
Depreciation and amortization	*65*	*35*
(Increase)/decrease in pre-financing	*(61 536)*	*(63 319)*
(Increase)/decrease in exchange receivables and non-exchange recoverables	*24 155*	*26 579*
Increase/(decrease) in payables	*55 143*	*11 829*
Increase/(decrease) in accrued charges & deferred income	*22 782*	*(1 432)*
Increase/(decrease) in cash contributions	*198 265*	*179 400*
Increase/(decrease) in in-kind contributions	*135 481*	*151 524*
Investing activities		
(Increase)/decrease in intangible assets and property, plant and equipment	*(47)*	*(126)*
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 31.12.2017	**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**
Allocation 2018 economic result	*–*	*(304 489)*	*304 489*	*–*
Cash contribution	*198 265*	*–*	*–*	*198 265*
Contribution in-kind	*135 481*	*–*	*–*	*135 481*
Economic result of the year	*–*	*–*	*(374 306)*	*(374 306)*
BALANCE AS AT 31.12.2019	**2 290 993**	**(1 930 477)**	**(374 306)**	**(13 791)**

64 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. 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 same materiality criteria are applicable to the FP7 and H2020 programmes.

The IMI2 JU 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 lessons learnt from previous audits were taken in account for defining the 2 % threshold. Progress towards this objective is to be (re)assessed annually, in view of the results of the implementation of the ex-post audit strategy. As long as the residual error rate is not (yet) below 2% at the end of a reporting year within the programme's life cycle, a reservation would (still) be made. Nevertheless, apart from the residual error rate, the Executive Director may also take into account other management information at his disposal to identify the overall impact of a weakness and determine whether or not it leads to a reservation.

When deciding whether or not something is material, qualitative and quantitative terms have to be considered.

- 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, in order to make a judgement on the significance of a weakness, 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 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 calculation of the residual error rate subsequently uses the representative error rate as the starting point.

The representative error rate for a population from which one or more samples have been drawn is calculated according to the following formula:[65]

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

- n = total sample size
- err_i = error rate (in %) in accepted IMI contributions detected on individual transactions from the sample (in range [0, 100%]; i.e. only errors relating to overpayments are counted)
- SI_i = sampling interval used for selecting transactions from the sample
- P = total accepted 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[66]:

$$\mathbf{ResER\% = \frac{(RepER\% * (P-A) - (RepERsys\% * E)}{P}}$$

Where:

- **ResER%** = residual error rate, expressed as a percentage;
- **RepER%** = representative error rate, or error rate detected in the representative JU sample, calculated as described above;
- **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 of the auditable population relating to accepted IMI contributions, expressed in euros;
- **A** = total value of audited accepted IMI contributions, expressed in euros;
- **E** = total non-audited amounts of accepted 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 up to the date of the last sample of which audit results are available for the error rate calculation.

65 Based on the Horizon 2020 Ex-post Audit Strategy (2016 – 2025).
66 Based on the Horizon 2020 Ex-post Audit Strategy (2016 – 2025).

Annex 11 – Media highlights

- Technology Networks (UK), 5 December 2019
  The Power of Collaboration: Tackling Pharmaceutical Challenges
- European Files (EU), 26 November 2019
  Harnessing the power of partnerships to develop life-saving vaccines
- Pharmaceutical Technology (UK), 25 November 2019
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- PMLiVE Blogs (UK), 25 November 2019
  Is competition the enemy of progress and collaboration the ally of success?
- Ärzteblatt (Germany), 25 November 2019
  Europaweite Studie soll personalisierte Therapie bei Autoimmunerkrankungen verbessern
- MedPage Today (US), 23 November 2019
  Ebola Vax Seems to Work in Kids, Too
- Pink Sheet (UK), 21 November 2019
  Remote Decentralized Clinical Trials Could Solve RCT Problems
- Ledger Insights (Cyprus), 20 November 2019
  Novartis to go live with blockchain network in 2020
- CNN Monday (Switzerland), 14 November 2019
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- European Biotechnology News (EU), 6 November 2019
  AMR: ENABLE selects Mutabilis candidate
- Multiple Sclerosis News Today (US), 6 November 2019
  European 3TR Project Unites Experts in Effort to Make Treatment More Personal and Effective
- BioWorld (US), 6 November 2019
  EU's new IHI program aims to 'push the boundaries,' expand innovation in health care
- Labiotech (Germany), 31 October 2019
  European Project Launches to Tailor Autoimmune Disease Treatments
- Telegraph (UK), 23 October 2019
  Parents urged to vaccinate children against whooping cough as number of cases rises four-fold
- Irish Examiner (Ireland), 23 October 2019
  Whooping cough bacteria 'can hide in noses and throats of healthy people'
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- PharmaFile (UK), 23 October 2019
  Damage control: How will pharma manage the health economic impacts of Brexit?
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  Health research is where the EU can leave a mark, lawmakers agree
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- Pharma Times (UK), 30 September 2019
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  Under the microscope: Improving hit discovery efficiency at Europe´s leading screening centre
- MedPage Today (US), 3 September 2019
  ICDs Still Save Lives in HF - But underuse shown in Swedish study affirming mortality benefit persists
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  Advanced Therapy Medicinal Products: The Right Time for Hope?
- Pharmaceutical Technology (UK), 24 July 2019
  J&J launches research consortium for new drugs against TB
- Bio-IT World, 2 July 2019
  MELLODDY Using Federated Learning To Improve Drug Development
- EurActiv (EU), 28 June 2019
  New pharma boss: Next EU Commission should be clear on how to protect innovation
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  New IMI Funding For EU Research Into ATMPs, Health Outcomes & Drug Info
- Scribd (US), 22 June 2019
  How Europe is building a sweeping system to study medication safety in pregnant and lactating women

- Business News Wales (UK), 17 June 2019
  International Partnership to Tackle Research Gaps in Medication Safety for Pregnant and Breastfeeding Women
- The Lancet (UK), 15 June 2019
  Pharma blockchains AI for drug development
- La Repubblica (Italy), 15 June 2019
  Harmony, i big data contro i tumori del sangue
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  Huit femmes enceintes sur dix prennent des médocs
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  Pharma groups combine to promote drug discovery with AI
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  Dix géants de la pharmacie s'allient pour optimiser les IA de découverte de médicaments
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  IMI to Boost Patient Involvement in its Activities
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  Researchers in international drive to develop safer drugs
- Wearable Technologies (Germany), 16 April 2019
  European Researchers Team Up with Pharma Companies to Develop Gait Detecting Sensor
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  Forschungsprojekt untersucht Ursachen von Neurodermitis und Schuppenflechte
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  Scotland's universities warn Brexit threatens world-leading dementia work that could transform lives around the globe
- EurActiv (EU), 1 April 2019
  Andriukaitis: I like blows from anti-vaxxers, it means I'm doing my job
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  Blockchain's Potential In Clinical Research
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  Irish scientists secure EU funding for Parkinson's research project
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- PharmaBoardroom (UK), 22 February 2019
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- Berlingske (Denmark), 13 February 2019
  Lundbeck og Novo Nordisk går sammen om at snyde hjernen
- Quotidiano Sanità (Italy) 11 February 2019
  Antibiotico resistenza. Farmindustria, ecco come arginarla in cinque mosse
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  Pharmaceutical industries: a healthier future for Europe?
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- Clinical Informatics News (US), 14 January 2019
  Blockchain Enthusiasts Finding Their Partners

Annex 12 - List of acronyms

Acronym	Meaning
AAR	Annual Activity Report
ABAC	Accrual Based Accounting System
ABC-CT	Autism Biomarker Consortium for Clinical Trials
ACE	Angiotensin converting enzyme
AD	Alzheimer's disease
ADL	Activities of daily living
AI	Artificial intelligence
ALDE	Group of the Alliance of Liberals and Democrats for Europe
ALS	amyotrophic lateral sclerosis
AMD	Age-related macular degeneration
AMR	Antimicrobial resistance
AP	Associated Partner
ApoE	Apolipoprotein E
APS	Antiphospholipid syndrome
ARES	Advanced Records System
ASD	Autism spectrum disorder
ATM-AVI	Aztreonam-avibactam
ATMP	Advanced therapy medicinal product
AWP	Annual Work Plan
BARDA	Biomedical Advanced Research and Development Authority
BBMRI	Biobanking and BioMolecular Resources Research Infrastructure
BCDP	Beta Cell Diabetes Platform
BD4BO	Big Data for Better Outcomes
BE	Bronchiectasis
BMGF	Bill and Melinda Gates Foundation
BOEC	Blood outgrowth endothelial cell
Bp	*Bordetella pertussis*
CA	Commitment appropriations
CA	Contract agent
CAFS	Commission's Anti-Fraud Strategy
CAS	Common Audit Service
CDI	*Clostridium difficile* infection
CDISC	Clinical Data Interchange Standards Consortium
CEN	European Committee for Standardisation
CEO	Chief Executive Officer

Acronym	Meaning
CEPI	Coalition for Epidemic Preparedness Innovations
CF	Cystic fibrosis
CFS	Certificate on Financial Statements
CHMP	Committee for Medicinal Products for Human Use
CIC	Common Implementation Centre
CKD BioCon	Chronic kidney disease biomarkers consortium
CF	Cystic fibrosis
CKD	Chronic kidney disease
CMPA	Candidate mechanism perturbation amplitude
COMPASS	H2020 workflow tool providing harmonisation between business processes & validation workflows
CORDA	Common Research Data Warehouse
COS	Core outcome set
CRO	Contract research organisation
CRS	Common representative sample
CSA	Coordination and support action
CSC	Common Support Centre
CSF	Cerebrospinal fluid
CT	Computed tomography
CTC	Circulating tumour cell
ctDNA	Circulating tumour DNA
CTE	Chronic traumatic encephalopathy
CTN	Clinical trials network
CVB3	coxsackievirus B3
CVD	Cardiovascular disease
DAS	Declaration of Assurance
DCE	Discrete choice experiment
DCXR	Dicarbonyl and L-xylulose reductase
DFO	Desferrioxamine
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 RTD	European Commission Directorate-General for Research and Innovation
DG SANTE	European Commission Directorate-General for Health and Food Safety
DILI	Drug-induced liver injury
DKD	Diabetic kidney disease

Acronym	Meaning
DKFZ	German Cancer Research Centre
DMO	Document Management Officer
DoA	Description of Action
DOI	Digital object identifiers
DORA	Document Registry Application
DoW	Description of Work
DPMS	Diagnostic and patient management study
DRC	Democratic Republic of the Congo
DW	Data warehouse
EANM	European Association of Nuclear Medicine
EARL	EANM Research Ltd
EC	European Commission
ECA	European Court of Auditors
ECCMID	European Congress of Clinical Microbiology and Infectious Diseases
ECRIN	European Clinical Research Infrastructure Network
ECSEL JU	Electronic Components and Systems for European Leadership Joint Undertaking
EEAS	European External Action Service
EEG	Electroencephalogram
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHA	European Hematology Association
ELBS	European Liquid Biopsy Society
EMA	European Medicines Agency
eMA	Electronic Missions Application
EMBARC	EU bronchiectasis registry
ENSO	Exploring New Scientific Opportunities
EPP	European People's Party
ERC	European Research Council
ERM	Enterprise risk management
EU	European Union
EUnetHTA	European Network for Health Technology Assessment
EVD	Ebola virus disease
FAERS	FDA Adverse Event Reporting System
FAIR	Fraud and Irregularity in Research
FAIR	Findable, accessible, interoperable, reusable
FC	Financial contribution
FDA	US Food and Drug Administration
FG	Function group

Acronym	Meaning
FNIH	Foundation for the National Institutes of Health
FTE	Full time equivalent
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
GAP	Global Alzheimer's Platform
GB	Governing Board
GCP	Good clinical practice
GDPR	General Data Protection Regulation
GEMM	genetically engineered mouse model
GWAS	Genome-wide association study
H2020	Horizon 2020
HALE	healthy aging lifestyle education
HAP	hospital-acquired pneumonia
hiPSC	Human induced pluripotent stem cell
HR	Human resources
HTA	Health technology assessment
IAI	Intra-abdominal infections
iAMD	Intermediate age related macular degeneration
IAS	Internal Audit Service of the European Commission
IB	Investigator's brochure
IBD	Inflammatory bowel disease
ICF	Internal Control Framework
ICF	Informed consent forms
ICT	Information and communication technology
ICU	Intensive care unit
IGLO	Informal Group of R&I Liaison Offices
IGF	Insulin-like growth factor 1 receptor
IKC	In-kind contribution
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
iPSC	Induced pluripotent stem cell
ISO	International Organization for Standardization

Acronym	Meaning
IT	Information technology
ITF	Innovation Task Force
IVD	*In vitro* diagnostic device
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
KLK6	kallikrein-related peptidase 6
KPI	Key performance indicator
KPMP	Kidney Precision Medicine Program
LCI	Lung clearance index
LCS	Longitudinal Cohort Study
LT	Long-term contract
mAb	monoclonal antibody
MCI	Mild cognitive impairment
MCI	Multicomponent intervention
MCTD	Mixed connective tissue disease
MEP	Member of the European Parliament
MERS-CoV	Middle East respiratory syndrome coronavirus
MIA	Multiplex immunoassay
MMV	Medicines for Malaria Venture
MoU	Memorandum of Understanding
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCP	National Contact Point
ND	Neurodegenerative disorders
ND4BB	New Drugs for Bad Bugs
NICE	National Institute for Health and Care Excellence
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
NOD	Non-obese diabetic
NSCLC	Non-small cell lung cancer

Acronym	Meaning
NTM	Non-tubercular mycobacteria
OAC	Obesity Action Coalition
OATP	Organic-anion-transporting polypeptide
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
OLAF	European Anti-Fraud Office
ORR	Operating Risk Register
PA	Payment appropriations
PA	Physical activity
PAD	protein arginine deiminase
PBPK	physiologically-based pharmacokinetic
PD	Parkinson's disease
PDX	patient derived xenografts
PET	Positron emission tomography
PF&S	Physical frailty and sarcopaenia
PIP	paediatric investigation plan
PiR	Partner in Research
PLoS	Public Library of Science
PMO	Paymaster Office
PoV	Proof of viability
PPP	Public-private partnership
PRO	Patient reported outcome
pSS	Primary Sjögren's Syndrome
QC	Quality control
QMS	Quality management system
R&D	Research and development
RA	Rheumatoid arthritis
RAAG	Renal age-associated genes
RAE	Risk assessment exercise
RAFS	Common Research Family Anti-fraud Strategy
RAL	Rest a liquider
RDoC	Research domain criteria
REEFAR	Spanish Network of Excellence in Drug Discovery
RepER	Representative error rate
ResER	Residual error rate
RFID	Radio-frequency identification
RIA	Research and Innovation Action

Acronym	Meaning
RMIC	Risk Management and Internal Control manager
RMT	Remote monitoring technology
RSV	Respiratory syncytial virus
RTO	Research and Technology Organisation
RWE	Real-world evidence
S&D	Group of the Progressive Alliance of Socialists and Democrats in the European Parliament
SAD	systemic autoimmune diseases
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SBV	Schmallenberg virus
SC	Scientific Committee
SCD	Subjective cognitive decline
SEP	Staff establishment plan
SEP	H2020 IT tool for submission and evaluation of proposals
SFARI	Simons Foundation Autism Research Initiative
SGG	Strategic Governing Group
SGLT2	Sodium glucose cotransporter-2
SIRD	Severe insulin resistant diabetes
SjS	Sjögren's Syndrome
SLC	Solute carrier
SLE	Systemic lupus erythematosus
SME	Small and medium-sized enterprise
SNE	Seconded national expert
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SPECT	Single-photon emission computed tomography
SPOC	Single Point of Contact
SRA	Strategic Research Agenda
SRG	States Representatives Group
SRR	Strategic Risk Register
SSc	Systemic sclerosis
SSI	Surgical site infection
ST	Short-term contract
SyGMa	H2020 IT tool for grant management
T1D	Type 1 diabetes
T2D	Type 2 diabetes

Acronym	Meaning
TA	Temporary agent
TAUG-Vax	Vaccines Therapeutic Area User Guide
TB	Tuberculosis
TTG	Time to Grant
TTI	Time to inform
TTP	Time to pay
TTS	Time to sign
UACR	Urinary albumin:creatinine ratio
UCTD	Undifferentiated connective tissue disease
UK	United Kingdom
US	United States
UTI	Urinary tract infections
VaDER	Variational deep embedding with recurrence
VAMBN	Bariational autoencoder modular bayesian networks
VAP	Ventilator-associated pneumonia
WHO	World Health Organisation
WWTP	wastewater treatment plant

Annex 13 – Table of IMI projects

(As of 31 December 2019)

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	drive-ab.eu	antimicrobial resistance
EBiSC	European bank for induced pluripotent stem cells	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		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	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		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		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
3TR	Identification of the molecular mechanisms of non-response to treatments, relapses and remission in autoimmune, inflammatory, and allergic conditions	3tr-imi.eu	Autoimmune diseases
AB-Direct	Antibiotic distribution and recovery in tissue		Antimicrobial resistance
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
BIOMAP	Biomarkers in atopic dermatitis and psoriasis	biomap-imi.eu	skin diseases
C4C	conect4children - Collaborative network for European clinical trials for children	conect4children.org	Paediatric clinical trials
CARDIATEAM	Cardiomyopathy in type 2 diabetes mellitus	cardiateam.eu	diabetes
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
COMBINE	Collaboration for prevention and treatment of MDR bacterial infections	amr-accelerator.eu/project/the-imi-amr-accelerator	antimicrobial resistance
CONCEPTION	Building an ecosystem for better monitoring and communicating of medication safety in pregnancy and breastfeeding: validated and	www.imi-conception.eu	medicines safety

Project acronym	Full project title	Website	Subject area
	regulatory endorsed workflows for fast, optimised evidence generation		
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
EBISC2	EBiSC2 – A sustainable European bank for induced pluripotent stem cells	ebisc.org	
EBODAC	Communication strategy and tools for optimizing the impact of Ebola vaccination deployment (Compliance with vaccine regimens)	www.ebovac.org/ebodac	Ebola and related diseases
EbolaMoDRAD	Ebola virus: modern approaches for developing bedside rapid diagnostics	www.ebolamodrad.eu	Ebola and related diseases
EBOMAN	Manufacturing and development for rapid access Ebola vaccine	www.ebovac.org/eboman	Ebola and related diseases
EBOVAC1	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	www.ebovac.org	Ebola and related diseases
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: Phase II	www.ebovac2.com	Ebola and related diseases
EBOVAC3	Bringing a prophylactic Ebola vaccine to licensure	www.ebovac.org/ebovac-3	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
ERA4TB	European regimen accelerator for tuberculosis	era4tb.org	antimicrobial resistance
ESCULAB	European screening centre; unique library for attractive biology	www.europeanleadfactory.eu	drug discovery
eTRANSAFE	Enhancing translational safety assessment through	etransafe.eu	safety

Project acronym	Full project title	Website	Subject area
	integrative knowledge management		
EU-PEARL	EU patient-centric clinical trial platform	www.eu-pearl.eu	clinical trial design
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
GNA NOW	Novel Gram-negative antibiotic now	amr-accelerator.eu/project/gna-now/	
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
IDEA-FAST	Identifying digital endpoints to assess fatigue, sleep and activities in daily living in neurodegenerative disorders and immune-mediated inflammatory diseases	ideafast.eu	digital health
IM2PACT	Investigating mechanisms and models predictive of accessibility of therapeutics (IM2PACT) into the brain	im2pact.org	drug delivery
IMI-PainCare	Improving the care of patients suffering from acute or chronic pain	www.imi-paincare.eu	pain
IMMUCAN	Integrated immunoprofiling of large adaptive cancer patients cohorts	immucan.eu	cancer
Immune-Image	Specific imaging of immune cell dynamics using novel tracer strategies	www.immune-image.eu	imaging
ImmUniverse	Better control and treatment of immune-mediated diseases by exploring the universe of microenvironment imposed	www.immuniverse.eu	autoimmune diseases

Project acronym	Full project title	Website	Subject area
	tissue signatures and their correlates in liquid biopsies		
IMPRiND	Inhibiting misfolded protein propagation in neurodegenerative diseases	www.imprind.org	neurodegenerative disease
imSAVAR	Immune safety avatar: nonclinical mimicking of the immune system effects of immunomodulatory therapies		autoimmune diseases, cancer
INNODIA	Translational approaches to disease modifying therapy of type I diabetes: an innovative approach towards understanding and arresting type I diabetes	innodia.eu	diabetes
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
MELLODDY	Machine learning ledger orchestration for drug discovery	www.melloddy.eu	machine learning
MOBILISE-D	Connecting digital mobility assessment to clinical outcomes for regulatory and clinical endorsement	mobilise-d.eu	digital health
MOFINA	Mobile filovirus nucleic acid test		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	www.necessity-h2020.eu	Sjögren's syndrome
NEURODERISK	Neurotoxicity de-risking in preclinical drug discovery	neuroderisk.eu	safety
NEURONET	Efficiently networking European neurodegeneration research	imi-neuronet.org	neurodegenerative disease
NGN-PET	Modelling neuron-glia networks into a drug discovery platform for pain efficacious treatments	ngn-pet.com	pain

Project acronym	Full project title	Website	Subject area
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
PD-MIND	Parkinson disease with mild cognition impairment treated with nicotinic agonist drug	www.pd-mind.org	Parkinson's disease
PD-MitoQUANT	PD-MitoQUANT – A quantitative approach towards the characterisation of mitochondrial dysfunction in Parkinson's disease	www.pdmitoquant.eu	Parkinson's disease
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
PharmaLedger	PharmaLedger	pharmaledger.eu	blockchain
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

Project acronym	Full project title	Website	Subject area
RESOLUTE	Research empowerment on solute carriers	re-solute.eu	drug development
RespiriNTM	Progress novel assets (one FIH start) for non-tubercular mycobacteria that may act synergistically with bedaquiline and cytochrome bc drugs	respiritbntm.eu	antimicrobial resistance
RespiriTB	Progress new assets (one pre-new molecular entity and one first-time-in-human start) for tuberculosis that act synergistically with bedaquiline, cytochrome bc or cytochrome bd inhibitors	respiritbntm.eu	antimicrobial resistance
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
STOPFOP	Saracatinib trial to prevent FOP	www.stopfop.com	rare / orphan diseases
TransBioLine	Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease	transbioline.com	safety
TransQST	Translational quantitative systems toxicology to improve the understanding of the safety of medicines	transqst.org	safety
Trials@Home	Center of excellence – remote decentralised clinical trials	trialsathome.com	digital health
TRIC-TB	Boosting Ethionamide efficacy and lowering the dose with a small molecule transcriptional modulators, to overcoming MDR-TB infections and define a new place for Ethionamide in 1st-line TB treatments	amr-accelerator.eu/project/tric-tb	antimicrobial resistance
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

Project acronym	Full project title	Website	Subject area
VALUE-Dx	The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use	value-dx.eu	diagnostics
VHFMoDRAD	Viral haemorrhagic fever: modern approaches for developing bedside rapid diagnostics	vhfmodrad.eu	Ebola and related diseases
VITAL	Vaccines and infectious diseases in the ageing population	vital-imi.eu	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 23 of the IMI2 JU Financial Rules states that *"The authorising officer shall report annually to the governing board on the performance of his or her duties for year N-1 in the form of a consolidated annual activity report"*

Article 23 of the IMI2 JU Financial Rules further specifies that *"No later than 1 July each year, the governing board shall send the consolidated annual activity report together with its assessment of it to the Court of Auditors, the Commission, the European Parliament and the Council."*

Analysis

The Innovative Medicines Initiative Annual Activity Report 2019 (Authorising Officer's report) was presented to the IMI2 JU Governing Board at the end of February 2020 and it is planned to have it approved by the Governing Board in June 2020.

The Governing Board is of the opinion that the IMI2 JU AAR 2019 covers well the main activities and achievements of the IMI2 JU in 2019 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 2019 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 2019 together with the draft Budget 2019 was approved by the Governing Board on 12 December 2018 (Decision IMI2-GB-DEC-2018-32), first amended by the Governing Board on 21 June 2019 (Decision IMI2-GB-DEC-2019-12), and second amended on 13 December 2019 (Decision IMI2-GB-DEC-2019-23).
- In 2019, the JU implemented the final stage (grant agreement signature) of the IMI2 Calls for proposals 13 and 16, and two Calls were at various stages of the evaluation and granting process (IMI2 - Calls 14 and 15) initiated under the Horizon 2020 Framework Programme. The JU launched three new Calls under Horizon 2020, IMI2 Calls 17, 18 and 19. Those Calls represent the commitment of €135,652,000 of EU contribution; €117,486,760 of contribution from EFPIA companies; and €11,493,139 of contribution from Associated Partners to Call 17 (topics 1 and 2), Call 18 (topic 2, 3 and 6) and Call 19 (topic 1).
- The Governing Board takes note of the return of €139 million of commitment appropriation to the EU budget, which originated from EFPIA's request to lower the total industry commitment under IMI2 JU. The limited capacity of EFPIA companies to absorb the funds available in 2019 was caused by a combination of several factors, including major projects launched in 2018 and early 2019 under the Think Big themes that significantly drew on available industry resources. Having evaluated various options available in mid-2019 and the uncertainties about the potential to use remaining 2019 appropriations if moved to 2020, the Governing Board opted for handing back the commitment appropriations to the European Commission with a view of supporting additional collaborative health projects under Horizon 2020, where immediate absorption capacity was available.
- In 2019, the JU signed 29 new grant agreements from IMI2 Calls 13, 14, 15, 16 initiated under Horizon 2020. As on 31 December 2019, the IMI portfolio of projects represented a total of 16 projects from the first phase of IMI (initiated under Framework Programme 7) of which 11 still running, plus Grant Agreements signed from IMI2 Calls 1 to 16 (initiated under Horizon 2020) of which 79 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 2019, 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 16 projects in 2019. 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) New taxonomies of diseases and new stratifications of patient sub-populations; (e) Development of cohorts, registries and clinical networks for clinical studies and trials; (f) Big data solutions to leverage knowledge / implementation of data standards; (g) Education and training for new and existing R&D scientists and stakeholders; (h) Impact on regulatory framework; (i) Implementation of project results inside industry; (j) Accessibility of resources/outputs beyond consortium.
- By 31 December 2019, IMI2 projects had led to 7 patent applications and 1 patent award (no change from 2018), and IMI1 and IMI2 projects had produced 5837 publications in peer reviewed journals, around 16% of which (944) were published in year 2019. The latest biblio-metric analysis demonstrated that the citation impact of papers associated with IMI projects is at 1.99 (slight increase from 1.98 in 2018), twice the world average (baseline of 1), and almost twice the EU‘s average (1.10). Also, 32.64% (increased from 24.64% in 2018) of IMI publications are published in top 10 % of publications. This confirms, like for previous year 2018, 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 2019, the IMI2 JU States Representatives Group met 3 times. The IMI2 JU Scientific Committee held 3 meetings. The IMI2 JU Scientific Committee is composed of 11 members, as well as additional experts. Notably, this Committee prepared two position papers with recommendations, on ‘Public private partnership funding – what makes a topic ultimately suitable for this kind of funding model?’, and on ‘lessons learnt from IMI in view of a public private partnership continuation in a new EU framework programme’. In addition, it has agreed on a future work plan with a view to providing recommendations to the IMI Governing Board on matters important to the IMI objectives. 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 1 to 4 times plus several teleconferences.
- In 2019, 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. IMI2 JU Programme Office held the Stakeholder Forum in June 2019 with the theme of ‘Brain health and disease in the digital era – 2020 & beyond’, which attracted almost 400 attendees. In addition, the communication office promoted IMI with 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 2019, IMI2 JU conducted 22 interim reviews of projects from the IMI2 Calls 2, 3, 5, 6, 7, 8, 9 and 10. Overall, the reviewers were generally satisfied with the progress made by these projects, and no major issue was identified with the reviewed projects, except for the IMI2 Call 8 project PEVIA (Pan Ebola vaccine innovative approach), which requires appropriate follow up and the IMI2 Call 7 project BigData@Heart which was facing considerable delays in 2019. In addition, the experts provided a number of constructive recommendations to the projects.
- The “Time To Pay” is similar to 2018 and below the maxima foreseen for the Horizon 2020 Programme, with 9 days for pre-financings, 57 days for interim payments, and 65 days for final payments. The “Time

To Grant" (210 days) also improved from 2017 and 2018, and is below the maximum foreseen for the Horizon 2020 Programme.

- For IMI projects (operating under Framework Programme 7), 74.1% of the €965.7 million EU contribution committed in total have been claimed, validated and paid, while 70.5% of the €977.1 million EFPIA contributions committed in total have been reported and validated, as on 31 December 2019. For IMI2 projects (operating under Horizon 2020), 16.04% of the €1,062.2 million JU contribution already committed have been claimed, validated and paid, while 20.02% of the €1,097.3 million EFPIA and Associated Partners contributions already committed have been reported and validated, as on 31 December 2019.
- In total, 269 ex-post audits of beneficiaries under Framework Programme 7 have been launched since 2011, out of which a total of 258 have been finalised, of which 22 during the year 2019. 65 ex-post audits of beneficiaries under Horizon 2020 have been launched since 2016, out of which a total of 29 have been finalised, of which 13 during the year 2019. In 2019, the cumulative residual error rate from the finalised audits was 0.66% for operational expenditure under Framework Programme 7, and was 0.52 % 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 2019, the declared in-kind contribution of 20 EFPIA companies participating in IMI projects (operating under Framework Programme 7) had been audited ex-post, altogether covering 90% 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 2018, which nevertheless 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. The JU has in particular improved their implementation of the 2018 budget (which reached 87% compared to 72% in 2017), and took measures to stabilise the staff turnover.
- In 2019, the Commission Internal Audit Service (IAS) issued the 2019-2021 Strategic Internal Audit Plan for IMI2 JU. The plan is based on the results of IAS risk assessment conducted in December 2018 and the IMI GB took note of the plan on 13 December 2019. In addition, IMI continued implementing one recommendation in the action plan stemming from the audit report on "*Coordination with the Common Support Centre and implementation of CSC tools and services in the IMI2 JU*", issued on 9 March 2018. The IAS acknowledged the conclusions of the exploratory work conducted by IMI2 and CSC IT development team and closed this recommendation.
- In relation to the use of human resources, the IMI2 JU staff assigned to the activities carried out in 2019 has been used for their intended purpose. On 31 December 2019, 53 of the 56 positions as in the Staff Establishment Plan of the IMI2 JU were occupied. Eight positions were filled during 2019, three temporary agents and five contract agents.

During 2019 the monitoring tools were fully operational and the IMI2 JU AAR 2019 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 2019 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 2019 in a realistic way.

The Governing Board considers that the following aspects require improvements:

- The Governing Board is recommending that efforts must be continued in 2020 to execute all the remaining commitment appropriations.
- By the end of 2019, SMEs accounted for 15.8% (15.6% in 2018) of all EU funded beneficiaries, receiving 10.3% (9.45% in 2018) of the EU funding. SMEs should be encouraged to participate in the remaining calls and supported during project execution.

Assessment

The declaration of the Executive Director and the IMI2 JU AAR 2019 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 2019.

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 2019 of the authorizing officer. This analysis and assessment will be included into the IMI2 JU AAR 2019.

Brussels, on 19 JUIN 2020,

For the Governing Board of the Innovative Medicines Initiative 2 JU

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