Annual Activity Report 2020

In accordance with Article 17 of the Statutes of IMI2 JU annexed to Council Regulation (EU) No 557/2014 of 06.05.2014 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-2021-09 of the Innovative Medicines Initiative 2 Joint Undertaking on 25.06.2021

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	Chair: Olivier Laureau Vice-chair: Irene Norstedt Full list of members: www.imi.europa.eu/about-imi/governance/governing-board
Other bodies	States Representatives Group (SRG): 27 European Union (EU) Member States and 16 countries associated to the Horizon 2020 Framework Programme Scientific Committee: 12 members including ad hoc members Stakeholder Forum: 954 registrations in 2020 Strategic Governing Groups (SGGs): 7 groups
Staff	Total posts: 56 (39 Temporary Agents, 15 Contract Agents, 2 Seconded National Experts) Posts filled: 53 (37 Temporary Agents, 15 Contract Agents, 1 Seconded National Expert)
2020 budget	Commitment appropriations: EUR 276 538 561 Payment appropriations: EUR 241 559 114
2020 budget implementation	Commitment appropriations: EUR 272 839 982 (98.66 %) Payment appropriations: EUR 234 511 515 (97.08 %)
Grants	19 grants signed in 2020 for a total value of EUR 382 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'.

Call implementation in 2020	Calls launched: 4 Proposals submitted under two-stage Calls: ▪ Short proposals submitted: 83 ▪ Eligible proposals submitted: 79 ▪ Full proposals submitted: 6 ▪ Proposals selected for funding: 6 (Call 20 only) Proposals submitted under single-stage Calls: ▪ Proposals submitted: 152 ▪ Eligible proposals submitted: 128 ▪ Proposals selected for funding: 11 Global project portfolio in 2020: 103 projects running during 2020 (11 under IMI1, of which 3 ended by 31 December 2020; and 92 under IMI2, of which 6 ended by 31 December 2020)
Participation, including SMEs	Beneficiaries receiving EU funding in IMI1 and IMI2 projects represent a range of different types of organisations, including universities, research organisations, small and medium-sized enterprises (SMEs) and patient organisations. For the IMI2 programme, SMEs account for 16.1 % of EU funded beneficiaries (by participations), 24.3 % of EU funded beneficiaries (by participants), and receive 11.9 % of EU funding so far.

Unless stated otherwise, all data in this factsheet reflects the situation as of 31 December 2020.

Foreword

The year 2020 will unfortunately be remembered for one thing only, the global pandemic caused by a simple virus of the coronavirus family, SARS-CoV-2, which causes the disease COVID-19. In what would be a very challenging year for IMI in normal times, with the final allocation of funding for IMI2 JU and the beginning of the transition preparations for the new programme under Horizon Europe, the pandemic turned our priorities upside down.

IMI[1] was able to rapidly implement a new programme dedicated to COVID-19 following swift decision making by the Governing Board. On 3 March, we launched a Call for proposals which focused on new diagnostics and therapeutics for COVID-19 and other coronaviruses. IMI received over 140 submissions which had to be evaluated in record time by experts in 6 parallel panels, meeting virtually due to lockdowns being in place from mid-March. Eight projects mobilising over EUR 115 million are now up and running and already producing interesting results.

The resilient staff of IMI were equal to this challenge and more. Indeed, in 2020 we launched no fewer than 4 Calls, ending with IMI2 - Call 23 which included important topics in rare diseases, cancer and neurodegenerative diseases that complete the IMI2 Strategic Research Agenda. We fulfilled our 2020 budgetary commitments fully (committing EUR 264 million) and signed new Grant Agreements for projects with a total combined budget of over EUR 380 million.

It was also a year in which past investments in the IMI project portfolio really came to the fore and demonstrated the real impact of a public-private partnership.

The IMI1 project ZAPI (Zoonosis Anticipation and Preparedness Initiative) was designed in 2014 and set up in 2015 with of course no knowledge of what was to hit the globe in 2020. This project was designed to accelerate the design and production of new vaccines and virus neutralising agents (like monoclonal antibodies). It has produced a myriad of tools and potential products that are in clinical assessment for treatment of COVID-19 as we go to press. The project also engaged very early on with the European Medicines Agency (EMA), who has accepted the principle of platform technology as proposed by ZAPI in its platform master file (PfMF) for completing the annexes of the New Regulation on Veterinary Medicines. It should be pointed out that ZAPI was the only ‘one health’ project in the IMI portfolio and it was led by the animal health industry.

Many other IMI projects have had major impacts on COVID-19, like COMBACTE NET, a project focussed on antimicrobial resistance that has built a pan European network of hospitals and clinical laboratories that can deliver high quality clinical trials. This network has now been repurposed for clinical assessments for COVID-19 interventions. The reader will find more examples of these projects in the AAR.

IMI has again demonstrated that the project outputs and impacts cover the full spectrum of activities from our excellent research output as demonstrated by the bibliometrics statistics (both the quantity and quality of IMI research publications is of outstanding dimensions), to the impact on regulatory science and ultimately new products like the Janssen Ebola vaccine which received EC authorisation in July 2020. The technology developed for the Ebola vaccine is now the basis of one of the COVID-19 vaccines which has since received conditional marketing authorisation from the European Commission.

We also worked with our pool of patient experts to integrate patient expertise into more of our activities, including reviews of project proposals and ongoing projects.

As always, I would like to close this foreword by thanking the many people whose hard work and dedication make IMI a PPP success story. Firstly, our project participants - the researchers, patients, regulators and other experts who deliver high-quality, sound results that are making a difference in so many fields.

[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.

Secondly, our governing bodies, the IMI Governing Board, Scientific Committee, States Representatives Group and Strategic Governing Groups are full of people whose dedication, experience and ideas help to improve IMI in so many ways. We also benefit from a positive working relationship with our day-to-day contacts in the European Commission and EFPIA.

Finally, I would like to thank my colleagues in the IMI Programme Office. Every year, they work hard to make IMI a success, and in 2020 they rose magnificently to the challenges of working from home and running IMI remotely, while also handling the increased workload brought on by our Call for proposals on coronaviruses. It is thanks to their dedication and commitment that IMI continued to function as normal and deliver the strong operational and administrative results presented in this report.

Pierre Meulien

IMI Executive Director

Executive summary

IMI highlights in 2020

- Launched a fast-track Call for proposals on coronavirus treatments and diagnostics. This resulted in eight projects which are already starting to deliver results. Meanwhile many existing IMI projects contributed knowledge and resources to combating the COVID-19 pandemic.
- Launched three additional Calls for proposals featuring topics on rare diseases, infectious diseases, cancer, neurodegenerative diseases and autoimmune diseases.
- Signed 19 new Grant Agreements for projects with a total combined budget (i.e. EU + EFPIA + Associated Partner commitments) in excess of EUR 380 million, bringing the total IMI portfolio to 167 projects. The new projects focus on cancer, diabetes, obesity, digital health, artificial intelligence, advanced therapies, drug discovery, and environmental issues.
- Thanks to the flexibility and commitment of all staff, strong support from the IT team, and regular internal communication, the IMI Programme Office adapted rapidly to the requirement to work from home and organise meetings and events (including Call evaluations and our Stakeholder Forum) remotely.
- 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.

Contributing to the fight against COVID-19

On 30 January 2020, the WHO declared the outbreak of the then novel coronavirus (COVID-19) a public health emergency. In response, and in line with the European Commission's wider response to COVID-19, IMI quickly decided to reallocate EUR 45 million of IMI's 2020 budget to a fast-track, single stage Call for proposals on the subject. The Call, which was launched on 3 March, focused on two things:

- the development of treatments to rapidly respond to the current COVID-19 outbreak and/or future coronavirus outbreaks;
- the development of diagnostic tests to rapidly and reliably identify people infected with COVID-19, and for use in clinical trials of new drugs.

Preventive vaccines were not included in the Call, as IMI did not want to duplicate the work of other organisations in this area.

The Call attracted 144 proposals, and a review of the strongest prompted the IMI Governing Board to increase the IMI funding pot to EUR 72 million. This allowed IMI to fund 8 projects under the Call – 3 on treatments, and 5 on diagnostics. EFPIA companies, IMI Associated Partners and other organisations are contributing over EUR 45 million to the projects.

The IMI team worked hard to get the Grant Agreements signed rapidly, and the first projects were up and running by the summer.

By the end of the year, the projects had already started delivering results. For example, the COVID treatment project CARE has screened libraries of small

IMI in 2020 at a glance

New projects

19 Grant Agreements signed launching new projects with a combined budget of over **EUR 380 million** from…

EU: EUR 200 million

EFPIA: EUR 162 million

Associated Partners: EUR 19 million

molecules and identified some ‘hits’ which have the potential to be transformed into drugs.

Fellow COVID treatment project MAD-COV 2 has shown that a low dose combination of the antiviral remdesivir and a drug called APN01 (hrsACE2) can stop the virus from multiplying in cells. They hope their findings will pave the way for clinical trials.

Diagnostics project RAPID-COVID has carried out field trials of its prototype point of care diagnostic instrument, in preparation for a larger clinical validation study.

Meanwhile, as COVID-19 spread around the world, many IMI projects working in other areas applied their skills, resources and expertise to the challenge of tackling this new disease.

Most notably, IMI’s ZAPI project had developed antibodies which block the spike protein of the MERS (Middle East Respiratory Syndrome) coronavirus, which is closely related to the SARS-CoV-2 virus. These antibodies are now being assessed as potential COVID-19 treatments as part of the EU-funded MANCO (Monoclonal antibodies against COVID-19) project.

Meanwhile the EHDEN, ConcePTION and ADVANCE/VAC4EU projects were selected to help the European Medicines Agency (EMA) gather real world data on COVID-19 vaccines and treatments once they are approved and being used in day-to-day clinical practice.

EHDEN also responded rapidly to the outbreak by harmonising data from 1 million people who had been tested for COVID-19. Harmonising the data makes it easier to analyse for insights that could help to improve patient care. EHDEN scientists also played a leading role in a COVID-19 study-a-thon held in the early days of the pandemic. The EMA subsequently cited one of the papers generated by the study-a-thon in its communications on the side effects of chloroquine and hydroxychloroquine.

For its part, antimicrobial resistance (AMR) project COMBACTE made its extensive network of clinical and laboratory sites available to the REMAP-CAP (Randomised, embedded, multi-factorial, adaptive platform trial for community-acquired pneumonia) project. REMAP-CAP is running adaptive clinical trials of COVID-19 treatments, and COMBACTE is contributing to the project by ensuring the rapid participation of hospital sites that are experienced in clinical trials.

Cancer in the spotlight

The decision to make cancer one of the five missions under Horizon Europe reflects the serious and lasting impact cancer has on the lives of many Europeans. In 2020, IMI gave its cancer portfolio a significant boost by launching three Call topics that address key questions in the cancer field, and also reflect IMI’s shift towards sectors beyond the pharmaceutical industry.

One addresses the immense challenge posed by cancers that have spread to other parts of the body, which are notoriously hard to treat. The topic focuses on ‘drug tolerant persister’ cells which are behind drug resistance, a major cause of cancer mortality.

Another topic asks whether proton therapy is better than radiotherapy for treating certain cancers. Today, radiation therapy is widely used in cancer treatment, but the dose used has to be kept low because of the damage caused to surrounding organs. Proton therapy delivers a higher dose of

Disease areas

Coronavirus treatments

CARE
Impentri
MAD-CoV 2

Coronavirus diagnostics

COVID-RED
DECISION
DRAGON
KRONO
RAPID-COVID

Cancer

SISAQOL-IMI
HARMONY PLUS

Diabetes

INNODIA HARVEST

Obesity

SOPHIA

Other sectors

Digital health

H2O
Gravitate-Health

Artificial intelligence

BIGPICTURE

radiation that is focused more precisely on the tumour, something that limits damage to healthy tissues.

Finally, IMI2 - Call 23 included a topic that will deliver a decision support tool based on artificial intelligence that will make it easier for physicians to select the right treatment for each patient.

2020 also saw the signature of Grant Agreements for new projects that will advance cancer research. For example, SISAQOL-IMI aims to develop recommendations on how to analyse and interpret data on health-related quality of life (HRQOL) and patient reported outcomes (PROs) in cancer clinical trials.

Another new project, T2EVOLVE, addresses key challenges in the development of engineered T cell therapies, a type of advanced therapy in which the body's immune cells are 'engineered' to seek out and destroy cancer cells.

Between them, these topics and projects place IMI firmly at the cutting edge of cancer research, and ensure our contribution to the wider cancer mission.

Care for rare diseases

There are some 5 000 to 8 000 rare diseases and between them, they affect up to 36 million people in the EU alone. Yet despite ongoing research, fewer than 10 % of patients receive any treatment and just 1 % have a treatment specifically approved for their condition. One of many challenges facing rare disease patients is getting a diagnosis; this takes an average of 8 years.

A new topic launched through IMI2 – Call 23 aims to speed up the time to diagnosis. Its strategy is based around two key elements. Firstly, the genetic screening of new-born babies, as around three quarters of rare diseases (excluding rare cancers) are genetic in origin and a majority of rare disease patients are children. Secondly, the development of artificial intelligence algorithms to identify rare disease patients via electronic health records (EHRs). Ultimately, the topic should enable the development of a broad rare disease 'symptom checker' to help undiagnosed rare disease patients to find their way to a diagnosis.

Rare diseases (specifically those caused by a single gene mutation) are also the focus of the ARDAT project, which aims to deliver the knowledge, tools and standards needed to speed up the development of advanced therapy medicinal products (ATMPs).

IMI project results punch above their weight in scientific journals

IMI projects publish prolifically in scientific journals, which are a key channel for the dissemination of project results. In 2020 alone, IMI projects published 1 052 articles, bringing the total number of articles published by IMI to 6 963. Furthermore, other researchers regularly cite IMI research in their own work; the citation impact for IMI papers stands at 1.99, compared to 1.10 for the EU and the baseline of 1 for the world. Some 25 % of IMI project papers are classified as 'highly cited', meaning they are in the top 10 % of papers by journal category and year of publication.

Cross-cutting issues

Advanced therapies

ARDAT
T2EVOLVE

Drug discovery

EUbOPEN

Environmental issues

PREMIER

New Call topics

4 Calls for proposals launched with a total of 14 topics and a budget of:

EU: EUR 264 million

EFPIA: EUR 157 million

Associated Partners: EUR 30 million

Infectious diseases

Accelerating vaccine development and manufacture

Innovation and treatment for tuberculosis

Treatments and diagnostics to combat coronavirus infections

Modelling the impact of monoclonal antibodies and vaccines on

The impact of IMI projects

Despite the immense challenges posed by COVID-19, IMI's projects continued to deliver results that clearly demonstrate the added value of a public-private partnership in health research. Some of the most significant results are presented below, but many more can be found elsewhere in this report, as well as on the IMI website. What is notable is the number of projects whose outputs are recognised by regulators in various ways. Regulatory recognition shows that the tools, resources and protocols developed by IMI projects are good enough to be used widely in drug development.

IMI-supported Ebola vaccine regimen gets green light

In July, the European Commission officially granted market authorisation for an IMI-supported Ebola vaccine regimen, which represents a vital tool in the fight against the deadly disease. The marketing authorisation was for Janssen, a Johnson & Johnson company, for its two-dose 'prime-boost' Ebola vaccine regimen. It is specifically designed to induce long-term immunity against the Ebola virus in adults and children aged one year and up. As such, it can be used to support preventive vaccination in countries most at risk of outbreaks. A number of organisations contributed to the development of the vaccine regimen, including IMI through the Ebola+ programme. Janssen used its AdVac® vaccine technology platform in the development and manufacture of its Ebola vaccine. Now, they are using the same AdVac® technology to develop a COVID-19 vaccine.

One step closer: digital readouts of walking as a measure of health

Reduced walking speed is a sign of many health conditions. The MOBILISE-D project wants to make continuous digital measurements of the way a person walks, gathered using wearable sensor technology, accepted as valid indicators of their state of health, much in the same way as blood pressure readings or oxygen levels are. In 2020, the project received a letter of support for their working methods and plans from the European Medicines Agency (EMA). The letter of support – an intermediary sign of encouragement from the EMA on the way to full qualification - is important because it demonstrates the promise of the innovation.

INNODIA diabetes trial protocol gets nod from regulators

Before a clinical trial can start, the organisers have to submit the protocol of their study to regulatory authorities for approval. Preparing this protocol takes a lot of time. To speed up the process, INNODIA has developed a master protocol for certain clinical trials of treatments that could potentially stop type 1 diabetes. In 2020, the EMA gave its support to the master protocol. By the end of the year, the project had launched four clinical trials designed to test treatments to prevent and cure type 1 diabetes in people who have just been diagnosed.

IMI-supported antibiotic passes Phase I clinical trials

IMI's ENABLE project set up an antibiotic development platform to provide researchers with the expertise, resources and support needed to advance promising early research stage antibiotics into Phase 1 clinical trials in humans. In 2016, Swiss SME Juvabis started working with ENABLE on a potential antibiotic called EBL-1003. This work demonstrated the safety and efficacy of in the antibiotic in pre-clinical tests, and a Phase I clinical trial in healthy volunteers started in 2019. The results of that trial are now in, and they show that EBL-1003 is both safe and well tolerated. The Juvabis team now plans to run a further Phase I trial in patients with complicated urinary

antimicrobial resistance (AMR)

Cancer

Understanding the rare cancer cells behind drug resistance

Is proton therapy better than radiotherapy for treating certain cancers?

Using artificial intelligence (AI) to select the best cancer treatment

Rare diseases

Towards faster diagnosis for rare diseases

Autoimmune diseases

Improving the lives of people with psoriatic arthritis

Neurodegenerative diseases

A platform to advance neurodegenerative disease biomarker research

Medicines quality

Focus on the quality of drugs based on proteins

tract infections – one of the disease areas where EBL-1003 shows the most promise.

EMIF research reveals three variants of Alzheimer's disease

A study funded in part by IMI's EMIF project reveals three distinct subtypes of Alzheimer's disease. Writing in the journal Brain, the team explains how they arrived at this discovery after analysing 1 500 proteins in the cerebro-spinal fluid of 400 people with Alzheimer's disease. Today, Alzheimer's is treated as one single disease. However, the information on the new subtypes suggests that a treatment that would benefit patients with one subtype may actually be harmful to patients with another subtype. The findings therefore represent an important step towards more personalised treatments for people with Alzheimer's disease.

Coping with COVID at IMI

When the Belgian government placed the country in lockdown in mid-March 2020, the IMI staff switched to full time teleworking. Thanks to strong support from the IT team, this move went smoothly, with staff able to access all the files, tools and resources they needed from day one. The switch to working from home was also facilitated by the fact that IMI had adopted a number of the European Commission's standard tools, such as ARES, SYSPER and the full set of H2020 programme management IT tools.

The staff amply demonstrated their dedication, creativity and flexibility in the following months, organising entire Call evaluations remotely (including the mammoth evaluation of over 100 proposals submitted in response to the coronavirus Call), as well as project reviews, meetings of our governance bodies, and more. The team also ran IMI's first virtual Stakeholder Forum, which focused on paediatric cancers and attracted over 500 registrations.

Meanwhile IMI and the other joint undertakings (JUs) who work in the same building agreed on a single set of rules for staff who exceptionally have to work at the office. These rules are designed to ensure staff safety and wellbeing, and also outline a phased return to the office, as and when that becomes possible.

Sound financial management in hindsight and foresight

Despite the challenges posed by COVID-19 and its dramatic impact on the way we work, the IMI Programme Office remained focused and ensured adherence to sound financial management principles and effective internal control in all its activities. This is recognised by the European Court of Auditors (ECA), which again gave IMI an unqualified ('clean') opinion on the reliability of the 2019 accounts as well as on the legality and regularity of the revenue and payments underlying the annual accounts.

IMI maintained high levels of operational excellence throughout 2020 and demonstrated an exceptional performance on the execution of the operational budget.

The execution rate for operational commitment appropriations reached 99.58 %, meaning the annual budget has effectively been fully executed. On operational payment appropriations, execution hit 98.89 %, which is even higher than the figure for 2019 (97.33 %), which is in turn far higher than the rate in 2018 (87 %) and 2017 (72 %).

Patient engagement

Returning clinical trial data to participants

Understanding patient adherence to treatment

Building on the results of IMI projects

Residual error rates remained below the 2 % materiality threshold for both the IMI1 and IMI2 programmes.

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: 67 days (target: 153 days)
- Time to grant agreement signature (TTG): 190 days (target: 245 days)
- Time to pay (TTP)
  - pre-financing: 6 days (target: 30 days)
  - interim payments: IMI1: 66 days | IMI2: 63 days (target: 90 days)
  - final payments: IMI1: 52 days | IMI2: 72 days (target: 90 days)

1 Achievements of the year

1.1 Key objectives for 2020

The key objectives for IMI in 2020 were set out in the Annual Work Plan (AWP) 2020 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: Complete the execution of the 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.

- Even though IMI moved to remote working during 2020, four Calls for proposals were launched, including one focused on addressing the coronavirus pandemic:
  - IMI2 – Call 20 (two stages, 6 topics, launched 21 January) covered the AWP priorities of infection control including vaccines, oncology, immunology, and other enablers of research topics.
  - IMI2 – Call 21 (one stage, 1 topic, launched 3 March) was launched as an emergency Call in response to the coronavirus pandemic.
  - IMI2 – Call 22 (one stage, launched 23 June) was a Restricted Call to maximise the impact of IMI2 JU objectives and specific priorities.
  - IMI2 – Call 23 (two stages, 6 topics, launched 23 June) covered the AWP priorities of neurodegeneration and other neuroscience priorities, infection control including vaccines, big data, digital health, clinical trials and regulatory research, oncology, facilitating rare disease therapies (including advanced therapy medical products) reaching patients in Europe, and other enablers of research topics
- 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.
- The pool of patient experts to further increase patient involvement in IMI's activities became fully operational.

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.

- For the operational payment appropriations maintained a high execution rate of 98.89 %.
- On Call and grant management, IMI achieved the official targets for:
  - Time to inform (TTI): 67 days out of a target of 153 days
  - Time to grant (TTG): 190 days out of a target of 245 days
  - Time to pay (TTP) pre-financing: 6 days out of a target of 30 days
  - TTP interim payments: 63 days out of a target of 90 days
  - TTP final payment: 72 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 2020, IMI held 14 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.

- Continued to disseminate IMI project results and success stories 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.
- Implemented an editorial calendar to highlight the links between IMI research and some of the biggest health challenges facing society today.
- Looking to the future, the theme of IMI's Stakeholder Forum was 'Broader horizons: growing Europe's health partnership', and the event brought together diverse stakeholders in an open, wide-ranging conversation that discussed how to build together a world leading research partnership.

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 sectors other than the pharmaceutical industry. These include IBA (Ion Beam Applications SA), a world leader in the design and production and marketing of innovative solutions for the diagnosis and treatment of cancer and other serious illnesses. IBA has been one of the pioneers in proton beam therapy. Varian Medical Systems Particle Therapy (GmbH) is a world-leading innovator and manufacture for radiation oncology that develops, manufactures and install proton therapy equipment. They are participating in Call 20, topic 5 (Proton versus photon therapy for oesophageal cancer – a trimodality strategy).
- Links2Trials is a company specialising in patient recruitment, preselection and retention services in clinical trials. It is participating in IMI2 - Call 23, topic 6 (Behavioural model of factors affecting patient adherence).
- A number of companies from other sectors opted to contribute to IMI as EFPIA Partners in Research by committing to IMI Calls for proposals in 2020. In total, 12 Partners in Research companies committed EUR 13.5 million to IMI Calls for proposals in 2020, including Apeiron Biologics, bioMérieux, Illumina, JLP Health, Lonza, Owlstone Medical, Medidata, Psychogenics, Stemcell Technologies, Svar Life Science, Transgene, and Vironova.
- IMI continued to work closely with ECSEL, the joint undertaking on electronic components and systems, to exploit obvious synergies. In 2020 ECSEL launched a Call seeking to complement IMI's Trials@Home project. Unfortunately, the call did not identify any fundable proposals but was a valuable learning experience in how the two JUs can work together.

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 Global Health Drug Discovery Institute, (GHDDI) is an innovative PPP jointly founded by the Bill and Melinda Gates Foundation, Tsinghua University and Beijing Municipal Government in 2016. It is an independent and not-for-profit research organisation committed to improving global health through accelerated development of new drugs and innovative technologies to tackle diseases that disproportionately affect populations in the developing world. It is contributing to IMI2 - Call 21 (Development of therapeutics and diagnostics combatting coronavirus infections).
  - DZIF (the German Centre for Infection Research) was established in 2012 as a registered association with 35 member institutions in Germany. DZIF is a non-profit association with a mission to align translational research with unmet global medical needs caused by infectious diseases. The centre coordinates infections research work in Germany to address national as well as global challenges with great societal impact as defined by the WHO Health Agenda. It is participating in IMI2 - Call 20, topic 3: (Academia and industry united innovation and treatment for tuberculosis - UNITE4TB).

- Klinikum of the Ludwig-Maximilians-Universität München is an institution under public law of the free state of Bavaria with a mission to provide excellent medical services for patients and conduct research for new diagnostic and treatment procedures with the aim to continuously improve services. It is also participating in IMI2 - Call 20, topic 3.
- The JDRF, the leading global organisation funding type 1 diabetes (T1D) research, has continued its engagement and support of IMI projects by contributing to a new proposal selected for funding for INNODIA HARVEST under IMI2 - Call19, a restricted call to maximise impact of the IMI2 JU objectives and scientific priorities.
- The Leona and Harry B Helmsley Charitable Trust, aspires to improve lives by supporting exceptional efforts in the U.S. and around the world in health and select place-based initiatives. The Trust has also continued its engagement and support of IMI projects by contributing to a new proposal selected for funding for INNODIA HARVEST.
- The Bill and Melinda Gates Foundation works to help all people lead healthy, productive lives. The Foundation has extended its participation in IMI2 by contributing to IMI2 - Call 21 on the development of therapeutics and diagnostics combatting coronavirus infections.
- The University of Dundee has extended its participation in IMI2 by contributing to IMI2 - Call 21 on the development of therapeutics and diagnostics combatting coronavirus infections.

- In addition, many IMI projects actively seek to collaborate with other international initiatives, building productive links and accelerating the international outreach of the programme. Some of the recent examples are highlighted below:
  - The IMI-PainCare project in collaboration with NIH HEAL (National Institutes of Health Helping to End Addiction Long-term Initiative) established INTEGRATE-Pain, the 'IMI-NIH Transatlantic Emphasis Group on Research and Translation-to-care Efforts for Pain'. The objectives of the collaboration are transatlantic knowledge sharing, harmonising of standards, combination of infrastructures, coordination of data collection to improve the statistical power of data interpretation in future meta-analyses, and joint dissemination.
  - The project AIMS-2-TRIALS, through close collaboration with US partners from the National Institutes of Health (NIH) Autism Biomarker Consortium-Clinical Trials (ABC-CT), has been able to replicate their EEG (electroencephalogram) signal biomarker in an independent cohort of autistic young people. The two consortia have leveraged data and knowledge to support parallel submissions of this EEG biomarker to the EMA, and to the FDA biomarker development programme, facilitating regulatory alignment between the EU and US. In addition, the IMI project is collaborating with partners in Australia to replicate and ascertain the prognostic validity of cognitive subgroups as potential stratification markers for social-communication difficulties in autism.
  - The AMYPAD project has started interaction with the US IDEAS project to explore synergies associated with the expertise developed during the course of AMYPAD in the field of amyloid PET (positron emission tomography) image quantification.
  - c4c and the European Joint Programme on Rare Diseases (EJP RD) have established a Joint Steering Committee in order to coordinate activities, promote synergies and avoid redundant work. With respect to the US, c4c is working with iACT (the Institute for Advanced Clinical Trials for Children) on specific activities (a CDA with iACT has been executed relating to collaboration in global interoperability and education). iACT is a US independent non-profit organisation formed by the Critical Path Institute (C-Path).
  - INNODIA representatives have been invited, through their collaboration with C-Path, to be part of the steering committee of an initiative of FDA with support of EMA on the use of C-peptide as endpoint in intervention trials in type 1 diabetes (T1D). INNODIA has set up collaboration with the Global Platform for the Prevention of Autoimmune Diabetes (GPPAD) to enhance synergies between both initiatives. The project has also embarked on collaborations with the IMI project SOPHIA on obesity; with TOMI (Trial Outcome Markers Initiative in T1D, an initiative of JDRF and C-Path) on data sharing; with T1D UK, to perform clinical trials together; and with a new Australian T1D network (JDRF Australia).

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

- The report of a study of the socio-economic impacts of 44 IMI1 projects that had finished was published in 2020.
- During 2020, IMI held close-out meetings on 10 projects that had finished. The results and impacts were summarised on the IMI website and promoted. The number of close out meetings was reduced in 2020 due to consortia requesting no-cost extensions as work plans were disrupted by the COVID-19 pandemic.
- 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 and innovation results

The overarching goal of the IMI1 programme 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 key performance indicators (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 2 of this report. Figures on the KPIs can be found in Annex 1.

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.

What is notable is the number of projects whose outputs are recognised by regulators in various ways. Regulatory recognition shows that the tools, resources and protocols developed by IMI projects are good enough to be used widely in drug development. This in turn increases their impact.

1.2.1 Infectious diseases – tackling a serious threat to public health

Despite advances in research infectious diseases continue to pose a serious threat to public health worldwide. While the focus in 2020 was understandably on COVID-19, challenges like antimicrobial resistance, tuberculosis and Ebola have not gone away. As these findings show, IMI projects are making progress in all these fields.

ASPIRE study puts spotlight on bug behind intensive care pneumonia

Patients in intensive care units (ICU) are at risk of developing pneumonia caused by bacteria like *Staphylococcus aureus*. The COMBACTE-NET team studied almost 2 000 ICU patients in 30 hospitals in 11 European countries in a bid to understand how common *S. aureus* intensive care-acquired pneumonia (SAIP) is and the risk factors that mean a patient may be more likely to develop it. *S. aureus* lives harmlessly on the skin and in the respiratory tract of around a quarter of healthy people, but if the conditions are right, it can quickly become a problem. The ASPIRE study showed that the daily risk of developing SAIP is 3.6 times higher for people who are already carriers of *S. aureus*.

Writing in the journal JAMA Network Open, they explain: 'These findings suggest that SAIP incidence may be higher than initially perceived, and future interventions to prevent SAIP should focus on patients colonized with *S. aureus* to achieve a higher efficacy.'

COMBACTE-MAGNET launches AMR travel tool

COMBACTE-MAGNET has launched a new, freely accessible online tool that allows healthcare professionals and the public to assess the risk of international travellers acquiring (and spreading) antimicrobial-resistant bacteria.

Travel plays a major role in the spread of AMR, and the new AMR Travel Tool will make it easier for healthcare professionals to evaluate patients' travel history and associated AMR risk factors. The healthcare professional's section of the website highlights differences in resistance levels between the travel destination and the host country, for example.

Meanwhile, travellers can enter their travel destination and receive general advice on infection control as well as pathogen-specific advice on the infection risks related to their destination (and tips on how to avoid them).

Regulators cite ZAPI master file on vaccines and treatments

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 project outputs is a master file designed to facilitate the fast-track regulatory approval of vaccines and treatments. In 2020, the European Medicines Agency (EMA) accepted the principle of platform technology as proposed by ZAPI in its Platform Master File (PfMF) for completing the annexes of the new regulation on veterinary medicinal products. This officially endorses the regulatory concept of the platform for the development and manufacture of vaccines and opens the way for accelerated registration of vaccines against emerging zoonotic and animal viral diseases.

Project links up data on little-known lung disease

Bronchiectasis refers to a group of diseases in which the airways become damaged and scarred. It is more common among older people, affecting 3 in 1 000 among the over 75s. Patients experience regular respiratory infections, but treatment options are limited. The iABC project set up a Europe-wide registry of bronchiectasis patients to facilitate research into the condition. Now the registry, dubbed EMBARC, has enrolled over 19 000 patients in Europe. Partnerships with registries in Australia and India mean that the registry now offers access to data from 23 000 patients, making EMBARC the largest data resource of its kind in the world. Access to the data is open to anyone with a valid research question.

TRIC-TB gives boost to development of potential new TB drug

Tuberculosis (TB) is a major public health threat. In 2017 alone, over 10 million people developed active TB and it killed 1.7 million, making it one of the top 10 causes of death worldwide. Treatment is via a six-month course of four antibiotics.

IMI's TRIC-TB project is advancing the development of molecules designed to boost the infection-fighting ability of the TB drugs Ethionamide (Eto) and Prothionamide (Pto). In 2020, the US Food and Drug Administration (FDA) gave Qualified Infectious Disease Product (QIDP) designation to one of the compounds (BVL-GSK098) in a fixed combination with Ethionamide for the treatment of pulmonary TB. QIDPs are eligible for priority and fast track review by the FDA. This will therefore help TRIC-TB to speed up the development of the compound.

At the end of the year, the project announced the start of a Phase 1 clinical trial of BVL-GSK098. The trial, which involves healthy volunteers, aims to assess the safety and tolerability of the drug as well as its behaviour in the body.

Although Eto and Pto are potent weapons in the fight against TB, they can cause severe side effects. If approved for use, BVL-GSK098 could allow doctors to reduce the efficacious dose of Eto or Pto, and along with it the side effects they cause.

IMI-supported Ebola vaccine regimen gets green light

In July 2020, the European Commission officially granted market authorisation for an IMI-supported Ebola vaccine regimen, which represents a vital tool in the fight against the deadly disease. The marketing authorisation is for Janssen, a Johnson & Johnson company, for its two-dose 'prime-boost' Ebola vaccine regimen.

The two-dose regimen (Ad26.ZEBOV, MVA-BN-Filo) is designed to induce long-term immunity against the Ebola virus in adults and children aged one year and up. As such, it can be used to support preventive vaccination in countries most at risk of outbreaks. Studies indicate that it is well tolerated, inducing robust and durable immune responses to the Zaire strain of the ebolavirus. A number of organisations contributed to the development of the vaccine regimen, including IMI through the Ebola+ programme.

Janssen used its AdVac® vaccine technology platform in the development and manufacture of its Ebola vaccine. They used the same AdVac® technology to develop a COVID-19 vaccine.

IMI-supported antibiotic passes Phase I clinical trials

IMI's ENABLE project set up an antibiotic development platform to provide researchers with the expertise, resources and support needed to advance promising early research stage antibiotics into Phase 1 clinical trials in humans. In 2016, Swiss SME Juvabis started working with ENABLE on a potential antibiotic called EBL-1003. This work demonstrated the safety and efficacy of in the antibiotic in pre-clinical tests, and a Phase I clinical trial in healthy volunteers started in 2019. The results of that trial came in in 2020, and they show that EBL-1003 is both safe and well tolerated. The Juvabis team now plans to run a further Phase I trial in patients with complicated urinary tract infections – one of the disease areas where EBL-1003 shows the most promise.

1.2.2 Collaborating on COVID

At the start of 2020, IMI was a well-established public-private partnership in health research with an extensive infectious disease portfolio. This meant that we were well place to rapidly launch an urgent, fast-track Call for proposals on treatments and diagnostics for COVID-19 and future coronavirus outbreaks which resulted in eight projects. The first IMI coronavirus projects were launched by the summer and started to deliver results before the end of the year. Meanwhile other, older IMI projects have applied their skills, expertise and resources to the challenge of tackling COVID-19. A selection of examples is given below, but many more can be found on the IMI website.

IMI COVID projects deliver early results

By the end of the year, the projects had already started delivering results. For example, the COVID treatment project CARE has screened libraries of small molecules and identified some 'hits' which have the potential to be transformed into drugs.

Fellow COVID treatment project MAD-COV 2 has shown that a low dose combination of the antiviral remdesivir and a drug called APN01 (hrsACE2) can stop the virus from multiplying in cells. They hope their findings, published in the journal EMBO Molecular Medicine, will pave the way for clinical trials.

Diagnostics project RAPID-COVID has carried out field trials of its prototype point of care diagnostic instrument, in preparation for a larger clinical validation study.

ZAPI – knowledge and tools for a rapid response to a coronavirus outbreak

IMI's ZAPI project was set up to deliver a platform and technologies to facilitate a rapid response to future disease outbreaks, and some of its findings related to the coronavirus that causes Middle East respiratory syndrome (MERS) were potentially relevant to SARS-CoV-2, the virus that causes COVID-19. A ZAPI paper published in the journal Nature Communications shows that a human monoclonal antibody neutralises SARS-CoV-2 in the lab. This finding was picked up by AbbVie for further development. The work is also being taken forward in the MANCO project, which is funded by the European Commission under its emergency coronavirus Call. MANCO aims to carry out further preclinical work on the antibodies, e.g. studying their safety and efficacy, and hopefully advance one antibody into a Phase 1 clinical trial. For its part, the IMI coronavirus project CARE is building on ZAPI's methodology for the discovery, generation and characterisation of monoclonal antibodies that neutralise the virus by targeting SARS-CoV-2's spike protein.

EHDEN, ConcePTION and ADVANCE - helping the EMA gather real-world data on COVID-19 treatments and vaccines

The EHDEN and ConcePTION projects plus the ADVANCE/VAC4EU initiative are helping the European Medicines Agency (EMA) gather real world data on COVID-19 vaccines and treatments once they are approved and being used in day-to-day clinical practice.

EHDEN is collaborating with the EMA on the creation of a framework for multicentre cohort studies on the use of medicines in COVID-19 patients. ConcePTION is working on a project that will collect data on the impact of COVID-19 in pregnancy and follow up the baby to monitor long-term outcomes in order to guide decision-making about vaccine indications, vaccination policies and treatment options for COVID-19 in pregnant women.

The international association VAC4EU (Vaccine Monitoring Collaboration for Europe) is set to work with the EMA to prepare for the monitoring of the benefits and risks of COVID-19 vaccines in Europe. VAC4EU was born out of IMI's ADVANCE project, which drew on lessons learnt from the 2009 swine flu pandemic to create an ecosystem for monitoring vaccine benefits and risks.

The outcomes of the projects feed into the work of the COVID-19 EMA pandemic Task Force (COVID-ETF) and EMA's scientific committees, to ensure that the evidence is translated into scientific opinions on the optimal use of the medicines and vaccines concerned.

COMBACTE – access to a clinical trial network specialised in infectious disease studies

IMI's COMBACTE projects have set up a pan-European network of 1 000 hospitals and 800 laboratories for clinical studies and trials on antimicrobial resistance (AMR). In 2020, the project embarked on a collaboration with the EU-funded RECOVER project, making its established clinical and laboratory networks available for RECOVER's clinical trials of COVID-19 treatments.

EHDEN – harmonising clinical data to facilitate reuse and advance research

In April 2020, EHDEN launched a data harmonisation Call for organisations with patient data relating to COVID-19. Harmonising patient data (while preserving patients' privacy) makes it easier to aggregate and jointly analyse data from different sources, something that is essential if we are to stop the outbreak and save lives. EHDEN selected 25 data partners in 10 countries; between them, the partners have data from 1 million SARS-COV-2-tested patients; 228 000 of whom tested positive. EHDEN immediately started work on harmonising the data to a common data model so that meaningful insights and evidence can be generated that will ultimately improve patient care.

Elsewhere, EHDEN partners were also active in the COVID-19 'study-a-thon' hosted by the Observational Health Data Sciences and Informatics (OHDSI) community. The virtual event drew on diverse data from 37 healthcare databases, some of which included COVID-19 data. This showed that standardising data can facilitate fast analysis and so support evidence-based decision-making. So far, the study-a-thon has resulted in a number of papers, and the EMA subsequently cited one of these in its communications on the side effects of chloroquine and hydroxychloroquine.

RADAR-CNS uses wearable tech to study physical and mental health impacts of COVID-19

One of the most important outputs of the RADAR-CNS project is the RADAR-Base platform, which allows projects to gather and manage data from wearable devices (like smart watches) and smartphones. In 2020, the RADAR-Base team used the platform to create COVID Collab, a citizen science project in which participants will provide data and information on both COVID-19 and the psychological impacts of the outbreak and the measures used to control it.

1.2.3 Neurodegeneration – advancing research in a highly complex field

Brain diseases affect millions of people worldwide, yet we still lack treatments for most brain disorders, and where treatments exist, they do not work for all patients. One reason for this is the highly complex nature of the brain and nervous system. IMI projects are exploring the underlying causes of brain disorders, and developing tools and resources to facilitate research into these complex diseases.

EMIF research reveals three variants of Alzheimer's disease

A study funded in part by IMI's EMIF project reveals three distinct subtypes of Alzheimer's disease. Writing in the journal Brain, the team explains how they arrived at this discovery after analysing 1 500 proteins in the cerebro-spinal fluid of 400 people with Alzheimer's disease. Today, Alzheimer's is treated as one single disease. However, the information on the new subtypes suggests that a treatment that would benefit patients with one subtype may actually be harmful to patients with another subtype. The findings therefore represent an important step towards more personalised treatments for the people with Alzheimer's disease.

Super agers' skills point to potential treatments for neurodegeneration

As we age, our cognitive skills (i.e. our ability to think, remember, and pay attention) gradually decline, even if we remain generally healthy and free of neurodegenerative diseases like Alzheimer's disease. However, some people maintain high levels of cognitive skills well into old age. What mechanisms protect the brains of these 'super agers' from cognitive decline, and could that information help us to understand neurodegenerative diseases?

To find out, the AMYPAD project studied brain scans from three groups of over 80s (super agers, 'normal' agers, and people with mild cognitive impairment or MCI), and compared them to brain scans from a control group of younger, cognitively normal people. They focused specifically on the levels of amyloid and tau in the brain – a build-up of these proteins is a hallmark of neurodegenerative diseases. They found that compared to the younger control group, MCI patients had high levels of both tau and amyloid in their brains, while the 'normal' agers had higher tau levels. However, the brains of the super agers showed no increased tau or amyloid burden compared to the younger control group. The researchers conclude that these super agers must have some resistance to the build-up of tau and amyloid, and this allows them to remain cognitively sharp. The next step would be to carry out further research to find out what drives this resistance, as this could inspire new treatments for neurodegenerative diseases. The findings are published in the Journal of Nuclear Medicine.

PHAGO partner looks to patent new culturing technique for deriving microglia from stem cells

An SME partner in the IMI PHAGO project has filed a patent application with the European Patent Office for an improved protocol for generating high numbers of human microglia, cells which are implicated in Alzheimer's disease, from induced pluripotent stem cells (iPSCs).

Microglia are thought to play an important role in the development and progression of Alzheimer's. To understand more about their function, researchers in PHAGO looked at genetically distinct iPSCs generated from the blood of patients with Alzheimer's, and microglia derived from them. This technique is technically challenging and cumbersome.

LIFE & BRAIN GmbH, who is co-leading the project's work package on iPSC models, has now developed an improved method that involves new types of material, using patient cells collected by the team at King's

College London. The new method enables bioreactor-based expansion and can yield very high numbers of iPSC-derived microglia.

This technique not only facilitates biomedical research; it might also offer new perspectives for a possible immunotherapeutic approach to treat patients with a genetic disposition to Alzheimer's. In the PHAGO project, 40 iPSC lines have already been generated from donors that carry several different genetic mutations in the TREM2 or CD33 gene. PHAGO is working with the IMI initiative EBiSC (European Bank for Induced Pluripotent Stem Cells) to make these cell lines accessible to researchers via the EBiSC catalogue.

1.2.4 Making progress on diabetes and metabolic disorders

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 an extensive diabetes portfolio, covering research into the underlying causes of diabetes, the risk factors for developing complications such as heart disease, and clinical trials. IMI also works on other metabolic diseases, such as the liver disease NASH (non-alcoholic steatohepatitis).

INNODIA speeds up launch of clinical trials for type 1 diabetes

Before a clinical trial can start, the organisers have to submit the protocol of their study to regulatory authorities for approval. Preparing this protocol takes a lot of time. To speed up the process, INNODIA developed a master protocol for certain clinical trials. The idea of a master protocol is that rather than starting off with a new protocol every time you want to do one of these studies, you have a protocol that can be re-used for different studies – a recyclable protocol. The basic design would always be the same, but what would change would be the annex describing the drug (or drugs) under investigation and the minor modifications needed to assess safety and efficacy.

The INNODIA clinical trial master protocol is specifically designed for phase 2 clinical trials of people who have just been diagnosed with type 1 diabetes. Most significantly, in 2020, the European Medicines Agency (EMA) gave its support to the master protocol, and INNODIA and its sister project INNODIA HARVEST used it to launch four clinical trials at the end of the year.

The trials are designed to test treatments to prevent and cure type 1 diabetes in children, adolescents and adults aged from 5 to 45 years who have been diagnosed with type 1 diabetes within the past 6 weeks.

The trials focus on people who have just been diagnosed as research has shown that in the newly-diagnosed, half of the cells in the pancreas that produce insulin are still working (this is known as the honeymoon). The hope is that by treating these people with drugs designed to protect these cells, they will retain the ability to produce their own insulin, and be spared the need to inject themselves with insulin.

The INNODIA developments and resources are of high interest to T1D community around the world; for example, T1D networks in Australia and Israel have approached the team with a view to learning from INNODIA and implementing its master protocol for their own clinical trials.

Type 1 diabetes – one name but two diseases?

In type 1 diabetes, the immune system attacks the beta cells in the pancreas which are responsible for producing the hormone insulin. Insulin plays a vital role in managing blood sugar levels, and as they lack functioning beta cells, people with diabetes have to inject themselves with insulin to keep their blood sugar levels stable. Now research supported in part by IMI through the INNODIA and INNODIA HARVEST projects suggests that type 1 diabetes may be a case of one name, but two diseases.

A study published in Diabetologica analyses the role of immune cells called T cells in type 1 diabetes. They found that in patients whose diabetes appears at an early age, T cells appear to be the main drivers of the disease. However, in older patients, while the T cells are still involved, problems in the beta cells themselves

appear to be the main factor behind the disease. The researchers conclude that while these two groups have similar symptoms, they may benefit from different, more targeted treatments.

RHAPSODY study links prediabetes with heart disease

It is well known that people with diabetes are at greater risk of complications such as heart disease, eye problems and kidney disease. But what about people with prediabetes? Globally, an estimated 352 million people globally have prediabetes, meaning that although they do not meet the threshold to be diagnosed as officially diabetic, their blood sugar levels are not well regulated.

In a study published in Nature Communications, RHAPSODY researchers explored whether people with prediabetes also face a greater risk of certain complications associated with diabetes, namely coronary artery disease, stroke and chronic kidney disease.

They found that prediabetes does appear to cause coronary artery disease, but not kidney disease or stroke. This suggests that preventing diabetes-related coronary artery disease may be more effective if treatment is started before the patient develops diabetes. It would also explain why it is so hard to prevent coronary artery disease in people who have already been diagnosed with diabetes.

LITMUS liver disease tool tells patients' side of the story

Non-alcoholic fatty liver disease (NAFLD), which occurs when fat builds up in the liver, affects around 20-30 % of the population worldwide. In most people, NAFLD does not cause health problems. However, a small proportion (less than 10 %) of people with NAFLD will go on to develop a more serious condition called non-alcoholic steatohepatitis (NASH). IMI's LITMUS project focuses on NAFLD and predicting which patients are likely to progress to NASH and fibrosis by developing predictive and prognostic biomarkers.

Now the project has developed a patient reported outcome measure (PROM) tool which delivers accurate information on how a patient 'feels and functions' in their daily life. If approved by regulators, the tool could be used to assess symptoms and impacts on patients' quality of life in clinical trials and clinical practice. The project is in discussions with regulators to get this tool approved. Meanwhile it is available for licensing and project partners are using it in their own studies.

1.2.5 A vital contribution to rare diseases research

There are some 5 000 to 8 000 rare diseases and between them, they affect up to 36 million people in the EU alone. Yet despite ongoing research, fewer than 10 % of patients receive any treatment and just 1 % have a treatment specifically approved for their condition. IMI has a small but growing portfolio of projects addressing rare diseases. Meanwhile, projects working in cross-cutting areas are also delivering results that are relevant to the rare disease community.

IMI projects cited in new orphan drug development guidebook

Developing 'orphan drugs' (i.e. drugs for rare diseases) is highly challenging, and just 5 % of rare diseases have an approved treatment. The IRDiRC (International Rare Diseases Research Consortium) describes its Orphan Drug Development Guidebook as 'a patient focused guidebook that describes the available tools, incentives, resources and practices for developing traditional and innovative drugs/therapies for rare diseases and how to best use them.' It lists a range of resources from organisations around the world, including IMI projects c4c, EUPATI and PREFER.

c4c aims to generate a sustainable infrastructure that optimises the delivery of clinical trials in children, and the guidebook suggests this could be useful for those developing medicines for rare paediatric diseases.

On EUPATI, the guidebook describes its patient education resources as 'very relevant to rare disease medicines development and highly useful and appreciated by the rare disease patients that finished the academy and use the toolbox'.

On PREFER, the guide highlights how patient preference studies can be useful during regulatory benefit-risk assessment for certain drugs in several major ways.

The guidebook is presented in an article in Nature Reviews Drug Discovery. ‘By enhancing the use of available tools, delays in development timelines can be avoided, risks and costs reduced, and patient and regulatory acceptability improved,’ the authors conclude.

1.2.6 Cancer – contributing to a mission

The decision to make cancer one of the five missions under Horizon Europe reflects the serious and lasting impact cancer has on the lives of many Europeans. On the one hand, advances in research have delivered treatments that mean many people now survive cancer. However, the disease still kills almost 2 million people in Europe every year, and aggressive treatments mean that many survivors face long-term health problems. IMI projects are delivering tools and resources to advance cancer research and deliver safer treatments.

Long-awaited CAR-T project gets underway

Advanced therapy medicinal products (ATMPs) based on genes and cells have the potential to revolutionise treatments for certain diseases with a high unmet medical need, including some cancers. The ATMP field is evolving fast and is highly competitive, meaning that finding a space where companies are able to work together is far from easy. IMI provided the neutral platform for this collaboration to happen, and shared challenges in the complex ATMP field formed the focus for two new projects launched in 2020.

One, T2EVOLVE, focuses on ATMPs based on T cells. T cells are an important part of the immune system, and in recent years, scientists have succeeded in creating ‘engineered’ T cells designed specifically to seek out and destroy cancer cells. Scientists are working on a number of cancer treatments based on T cells, but their efforts are hampered by a number of challenges. Firstly, when developing a T cell therapy, it is very hard to predict if it will be safe and how well it will work. Secondly, their manufacture at scale is extremely complicated.

The aim of T2EVOLVE is to develop an innovation ecosystem that will accelerate the development of engineered T cell therapies in the EU.

Among other things, it will do this by delivering tools and markers that will improve our ability to predict the toxicity and efficacy of T cell therapies, as well as techniques to analyse the behaviour of T cells in the body. The team also plans to develop standardised methods for producing T cell therapies and monitoring them during treatment.

Another goal is to integrate patients more fully into all aspects of T cell research and development, and to deliver tools for education to improve communication between healthcare providers and patients.

ITCC-P4 delivers tools to advance research into childhood cancers

Today, 20% of childhood cancers remain incurable and cancer kills 6 000 young people in Europe every year, making it the leading cause of disease-related death in the under-19s. Moreover, two thirds of those who survive a cancer in childhood experience long-term side effects as a result of their treatment. The challenge for scientists seeking to develop new treatments is the lack of tools to study childhood cancers, which are quite different in nature to most cancers found in adults.

The ITCC-P4 project is creating a large-scale platform comprising 400 novel research tools based on cells and tissues from patients covering 10 common childhood cancers, including neuroblastoma, high grade glioma, and osteosarcoma. To date, the projects has over 200 models which are being characterised at the molecular level.

The project has also developed a method for matching known genetic mutations in childhood cancers (which could be the target of drugs) with proof-of concept papers on drugs targeting those mutations published in scientific journals. The team trialled this ‘target actionability review’ (TAR) approach on two mutations. Writing

in the European Journal of Cancer, they note that this approach identified potential treatments as well as gaps in our knowledge.

First batches of real-world data from prostate cancer studies added to big data platform

The first datasets have been added to the PIONEER big data platform, a major milestone for the IMI project. The researchers want to use real-world data from well-known prostate cancer studies to answer some vital questions about the disease. The first question they hope the data will help answer concerns the kind of variables that affect the prognosis for prostate cancer patients.

The first datasets will be followed by more; other partners are poised to add another 22 anonymised datasets to the platform, and PIONEER hopes that other data custodians, both private and public, will be encouraged to contribute. The ultimate aim is to improve the health and social care for all prostate cancer patients and their families.

1.2.7 Digital health, big data and artificial intelligence – bringing other industries into the fold

While most IMI projects focus on pharmaceuticals, a growing number are exploring how other sectors and technologies including big data, blockchain, artificial intelligence and digital technologies can advance health research and health care.

PharmaLedger selects use cases to advance adoption of blockchain in healthcare

The goal of IMI's PharmaLedger project is to deliver an open source, blockchain-based platform for the healthcare sector, using the supply chain, clinical trials, and health data as case studies. In 2020, it selected use cases in these areas to validate the blockchain platform architecture.

In the supply chain area, one of PharmaLedger's selected use cases will help to boost trust in medicines. A patient could simply scan a data matrix (QR) code on a packet of medicine to obtain (via a mobile app or website) a blockchain-anchored 'eLeaflet' on the medicine inside. The blockchain technology would guarantee the reliability of the information, and the solution could also be used to implement an anti-counterfeit feature where the user would be able to check product authenticity. Looking to the future, the eLeaflet could also be used to provide updates on the medicine, manage recalls, and offer advice on the safe (environmentally friendly) disposal of the drug.

In the health data field, PharmaLedger has selected a use case that will make it easier to match up patients with clinical trials (all while preserving patient privacy). In the clinical trials field, a use case on medical devices will integrate device data ('Internet of Things') with advanced analytics. This will support remote data capture during clinical trials, cutting down on the number of times patients would need to visit the clinic for tests.

In the health data and clinical trials fields, the project will also work on a use case that will strengthen patients' ownership of their data, giving them greater control over who can access their health data and when, with a view to enabling a health data marketplace.

PharmaLedger plans to open up the platform for external parties to connect their own use case solutions. The platform will work in a similar way to an app store which requires a minimum standard of compliance but which is open and flexible to the needs of different use cases.

Can computers learn to think like chemists? IMI's MELLODDY project thinks so

Machine learning promises to make drug discovery faster, better and cheaper, but it requires access to vast datasets of molecules and their properties. While every pharma company can apply machine learning algorithms to their own data, the true power of this technology comes from combining the (usually ultra-confidential) datasets of several companies to fuel the algorithms.

The MELLODDY project is working on using machine learning to make the most of the combined power of these highly valuable datasets without sharing them, exposing them, or even moving them from where they're housed.

Because companies' data is too valuable to risk sharing, MELLODDY is applying a technique called federated learning: this allows datasets to remain behind their firewall, stored independently from each other. With this method, algorithms go back and forth between subsets of each company's data and the central server, which prevents anyone from knowing which company's data adds to the central model. This exposes the algorithm to a much wider range of data than any one company has in-house. All this is done while keeping sensitive data safely ensconced within each company's own infrastructure.

In 2020, MELLODDY announced that it had managed to carry out the first successful federated learning run using this new predictive modelling platform – an enormous accomplishment.

One step closer: digital readouts of walking as a measure of health

Reduced walking speed is a sign of many health conditions. The MOBILISE-D project wants to make continuous digital measurements of the way a person walks, gathered using wearable sensor technology, accepted as valid indicators of their state of health, much in the same way as blood pressure readings or oxygen levels are. In 2020 the project received an early public nod of support for their working methods and plans from the European regulator, the European Medicines Agency (EMA).

MOBILISE-D's mission is to get these digital mobility outcomes, or DMOs, 'qualified' to be used as biomarkers in clinical trials. It's an ambitious goal and they are using five different diseases as test cases. The letter of support – an intermediary sign of encouragement from the EMA on the way to full qualification - is important because it demonstrates not only the promise of the innovation, but also how important it is to build a rapport with the regulating authorities early, something IMI encourages in all our funded research.

At the very start of MOBILISE-D, the consortium made a strategic plan on how to get regulatory acceptance for DMOs. They decided to interact with the EMA very early on by submitting a request for qualification advice, and to take an incremental approach, starting with qualification advice of monitoring biomarkers in Parkinson's disease.

1.2.8 Contributing to the 3Rs – addressing animal testing

EU legislation sets out strict rules on the use of animals in research and promotes the replacement, reduction and refinement of animal use whenever possible; this is known as the '3Rs'. IMI supports this policy via several projects which are developing alternatives to animal tests in fields as diverse as vaccine batch testing and pre-clinical toxicology research.

VAC2VAC vaccine test could cut tests involving animals

Before a batch of vaccines can be sent for distribution to the public, it must undergo a series of quality checks. These include a test for pyrogen content, which detects the presence of contaminants that could cause a fever in people who receive the vaccine. Currently, one of the approved tests for this is the rabbit pyrogen test (RPT), which as the name suggests, involves the use of rabbits. VAC2VAC has optimised a method called the 'monocyte activation test' (MAT) so that it could replace the RPT for pyrogenicity testing of a vaccine against tick-borne encephalitis. The optimised tests were validated by GSK, which manufactures the vaccine. The method was subsequently approved by the competent authorities and GSK is now using it. This is the first VAC2VAC method to reach regulatory acceptance and implementation, and so represents an important milestone in the project's efforts to develop and validate quality testing approaches for vaccines using non-animal methods. The optimised MAT is also described in the journal ALTEX - Alternatives to animal experimentation.

Could virtual animals replace real ones in toxicology testing?

Before medicines can be tested in humans, they must pass through a series of safety and efficacy tests in the lab, and some of these test involve animals. Over the years, pharmaceutical companies have amassed vast amounts of data from toxicity studies involving animals, and now IMI's eTRANSAFE project is exploring if and how this data could be used to create virtual control groups for future toxicity studies. One prerequisite for this is the availability of large, well-structured data sets, something that IMI's eTOX and eTRANSAFE projects have been working on. To establish the proof of principle for the virtual control groups, the companies participating in eTRANSAFE have started to collect and characterise control group data for specific studies. Presenting the concept in the journal ALTEX - Alternatives to animal experimentation, the project explains that once this is completed, the companies will share the control group data and investigate cross-company variability. Finally, a set of studies will assess whether the use of virtual control group data would have influenced the outcome of the study compared to the real control group. If successful, eTRANSAFE estimates that using virtual control groups instead of real control groups could cut animal use by 25 %.

1.2.9 Putting patients at the centre of medical research

It is widely acknowledged that patients can and should be involved in all stages of medical research and drug development. On the patient side, IMI projects have developed educational resources to ensure that patients are equipped with the knowledge and skills needed to contribute to research. At the same time, IMI projects have delivered a wealth of tools, resources and advice to help other researchers who want to involve patients in their work but are not sure how to go about it.

EUPATI platform achieves sustainability with launch of EUPATI Foundation

IMI patient education project EUPATI has set up an independent, non-profit foundation to build on the project's work. The creation of the EUPATI Foundation secures the project's legacy and paves the way for the further development of patient education resources in Europe and beyond.

EUPATI has pioneered patient education in medicines research and development. Close on 160 patient experts have completed the intensive, 14-month EUPATI course, and many graduates are actively applying their knowledge and skills in a wide array of organisations, projects and committees. The project's multilingual online toolbox is already packed with educational information and resources for patients and has attracted over 4 million individual users since its launch in 2016. And there are already over 20 EUPATI National Platforms (ENP) bringing together patient, academic and industry partners as well as other stakeholders and providing a forum for more local activities designed to raise awareness about the role of patients in research. Looking to the future, the new EUPATI Foundation plans build on these achievements.

PARADIGM releases patient engagement toolbox

In 2020, PARADIGM launched its Patient Engagement Toolbox that brings together in one place all the project's recommendations, tools and relevant background information to make patient engagement in medicines development easier for all. The toolbox is the result of a huge co-creation effort involving extensive research, surveys, focus groups, case studies, workshops, and multiple rounds of reviews.

The tools are divided into three groups: planning patient engagement; conducting patient engagement; and reporting and evaluation. Each tool comes with information detailing how the tool was produced and who contributed to its creation.

Although PARADIGM finished in 2020, the Patient Engagement Toolbox will be maintained and accessible via the EUPATI and PFMD (Patient Focused Medicines Development) platforms.

PREFER sets out 15 ways to listen to the patient voice

There is now broad recognition that patients can and should be involved in all stages of medical research and drug development, as understanding patients' preferences can improve decision-making. However, putting 'patient-centricity' into practice is not always easy. IMI's PREFER project has identified 15 critical decision

points in industry, regulatory and health technology assessment (HTA) decision-making where input on patient preferences can support the process.

Their findings are published in the journal Health Policy. ‘Currently, PP [patient preference] information is not considered as obligatory information to submit for any of the MPLC [medical product lifecycle] decision-points,’ the scientists write. ‘However, PP information is considered an important component by most stakeholders to inform future decision-making across the MPLC. The integration of PP information into 15 identified decision-points needs continued discussion and collaboration between stakeholders.’

1.2.10 Science meets art

While most research outputs are expressed in scientific language in scientific journals and conferences, some projects turn to the arts to showcase their results.

IMI’s RADAR-CNS project is investigating how wearable technologies and mobile phones can track and help prevent depression, epilepsy and multiple sclerosis. In 2020, Slovenian artist Sanela Jahić turned RADAR-CNS research into the impacts of depression on the way people speak into an art installation. She created PATAKA, a visual and auditory journey named after a vocal exercise used by speech pathologists – how someone says ‘PATAKA’ can offer clues as to their mental state. As part of the exhibition, parrots were trained to repeat the PATAKA sequence, and the cacophony was combined with data visualisations to make a point about what our own voices can tell machines about us.

Meanwhile, the project teamed up with dancers, musicians and technology experts to portray in dance symptoms which may be hard to express in words. The result is Feedback Loops, which was performed at Science in the City, Malta’s national science and arts festival. The performance responds to a quote from a member of the RADAR-CNS Patient Advisory Board: ‘A lot of my symptoms are invisible and people find it hard to understand what I’m going through.’

Both the art installation and the dance performance represent innovative ways of communicating the project’s work, results and impact to a wider public.

1.3 Project impacts and dissemination

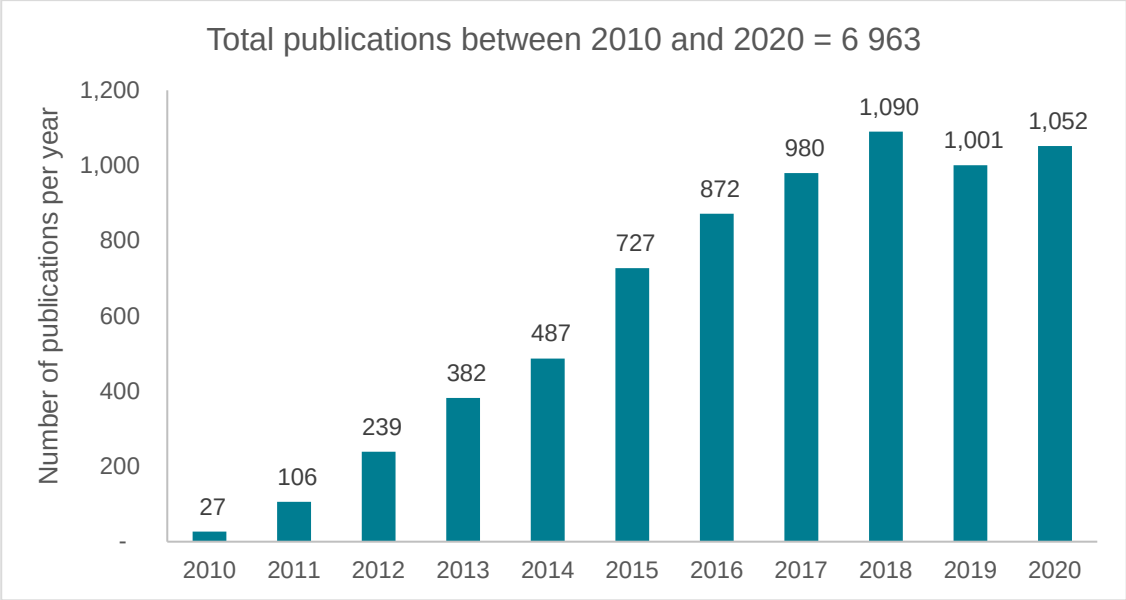
IMI projects are delivering diverse tools, resources and methodologies that are helping to change and improve the way new medicines are discovered and developed. This section describes how these resources, and information on them, are disseminated by both the project partners and IMI. IMI consistently reminds its projects of the importance of dissemination, and in 2016 issued a practical guide on this which remains valid to date.

1.3.1 Analysis of the published output of IMI-funded research projects

Scientific publications are the key communication and dissemination channel for scientific results. 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.

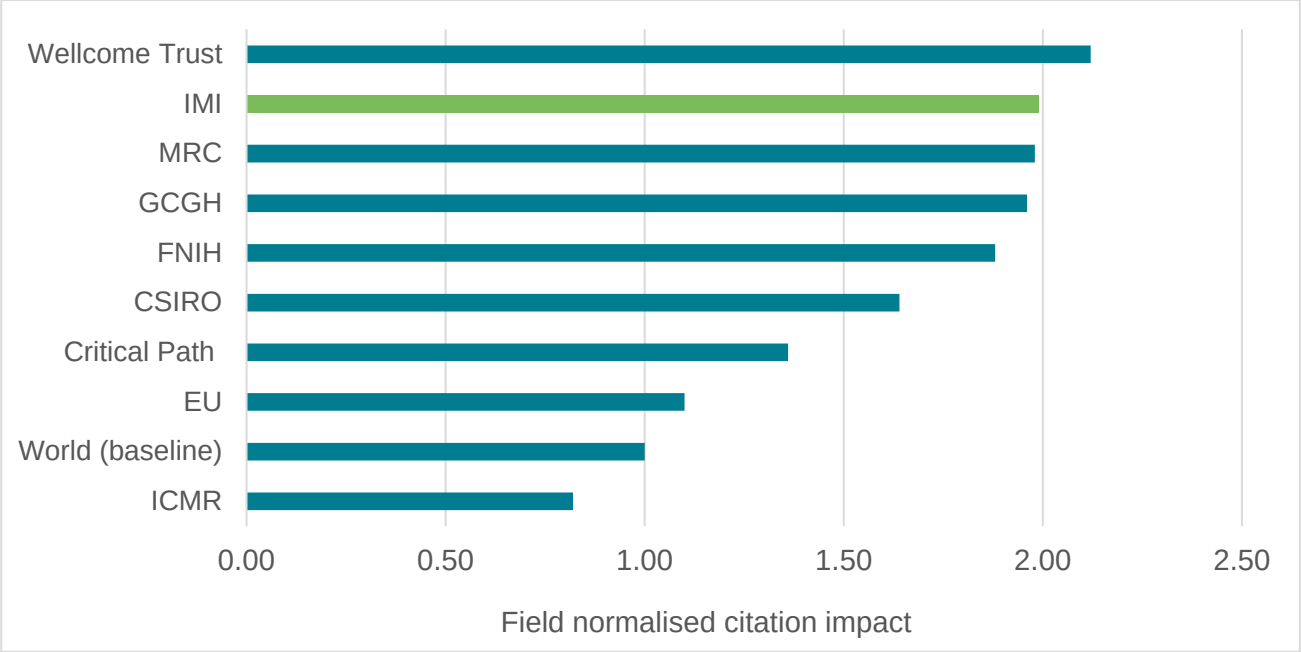
IMI projects are now producing an average of 1 000 publications per year

In 2020, IMI projects produced 1 052 publications, bringing the total number of publications produced by IMI projects between 2010 and 2020 to 6 963. As the graph below shows, between 2010 and 2018, the number of IMI research publications per year increased steadily and for the last 3 years (2018-2020) it has remained stable at just over 1 000 publications per year.



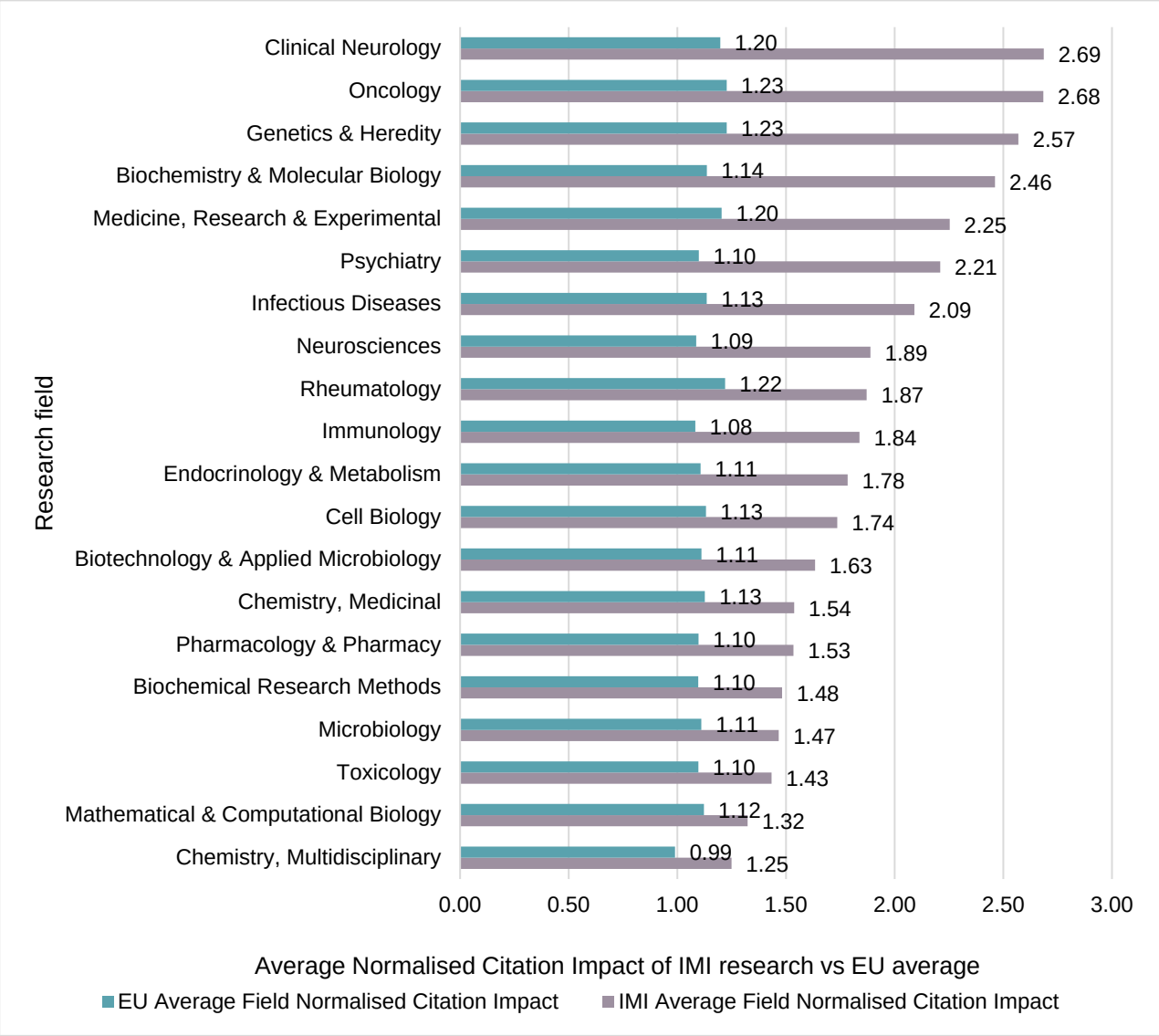
The citation impact of IMI research is higher than EU and world averages

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 Grand Challenges in Global Health (GCGH). 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 the case in the fields of oncology, genetics and heredity, clinical neurology, biochemistry & molecular biology where the IMI citation impact is between 2.4 and 3.



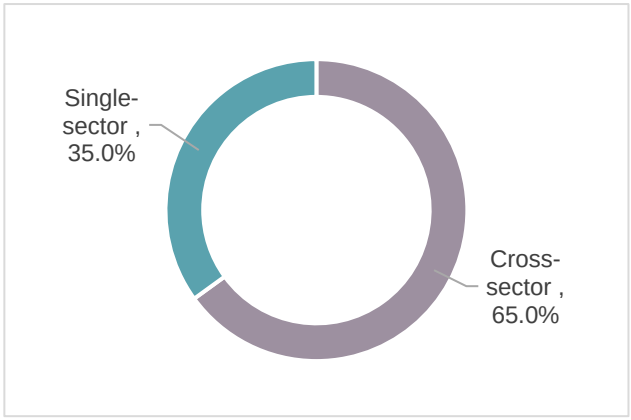
Other key facts and figures revealed by the latest analysis include the following.

- 25 % 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 1 278 journals to date, and the average journal impact factor for IMI research is 6.75.
- 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 Molecular Cell Biology, Nature Clinical Oncology, Nature Cancer), Science, Chemical Reviews, and the Journal of the American Medical Association (JAMA).
- The internationally collaborative nature of IMI is reflected in the authorship of the papers, with over half of papers recording authors from more than one country.

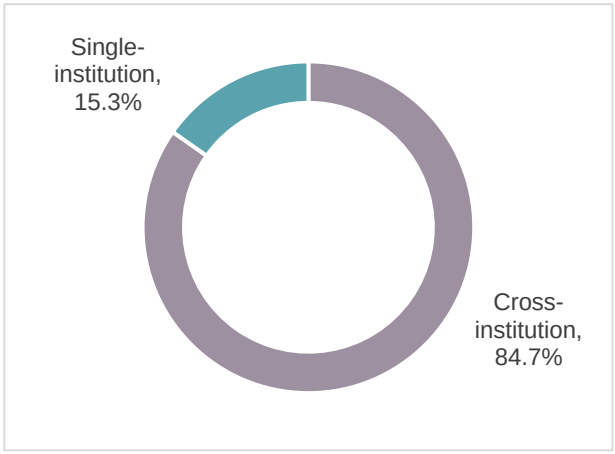
IMI research is highly collaborative

IMI research is highly collaborative; and collaborative IMI research produced a higher number of papers compared to non-collaborative research.

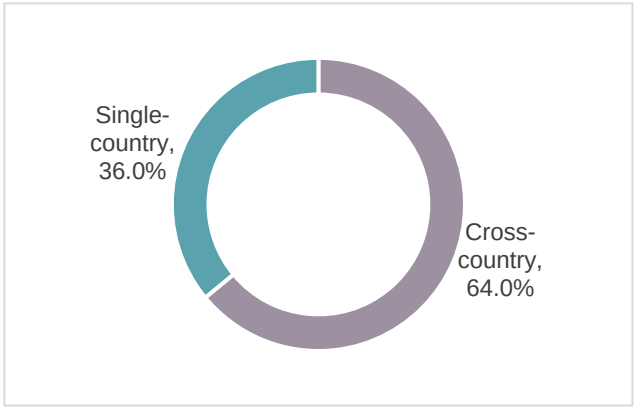
Nearly two-thirds of (65%) of all IMI project papers were published by co-authors working in different sectors.



More than three-quarters (84.7%) of IMI project papers involved collaboration between different institutions.



More than half (64%) of all IMI project papers involved international collaboration.



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 1.42 and 3.22.

Top 10 IMI projects producing the highest number of publications

Project	Total publications	Mean field normalised citation impact
BTCure	693	1.84
EU-AIMS	499	2.03
ULTRA-DD	366	1.69
EMIF	295	2.57
NEWMEDS	208	2.22
CANCER-ID	192	3.22
EUROPAIN	176	2.35
ORBITO	168	1.85
INNODIA	154	1.62
TRANSLOCATION	150	1.42

Between 2010 and 2020, IMI published papers in **1 278 different journals**.

Top 10 journals by number of IMI publications

Rank	Title	JIF	IMI papers
1	PLOS One	2.74	177
2	Scientific Reports	4.00	169
3	Annals Of The Rheumatic Diseases	16.10	119
4	Nature Communications	12.12	91
5	Diabetologia	7.52	70
6	Arthritis Research & Therapy	4.10	62
7	Frontiers In Immunology	5.09	60
8	Journal Of Alzheimer’s Disease	3.91	59
9	Journal Of Medicinal Chemistry	6.21	54
10	Pain	5.48	51

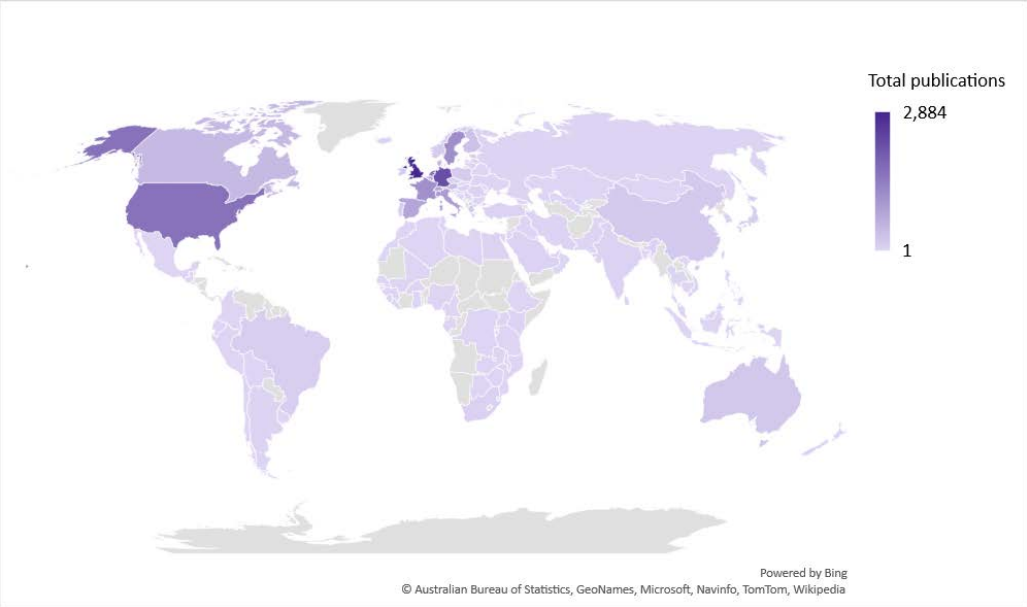
Top 10 journals by journal impact factor (JIF) in which IMI projects have published

Rank	Title	JIF	IMI papers
1	New England Journal Of Medicine	74.70	1
2	Nature Reviews Drug Discovery	64.80	6
3	Lancet	60.39	3
4	Nature Reviews Molecular Cell Biology	55.47	1
5	Nature Reviews Clinical Oncology	53.28	7

6	Nature Reviews Cancer	53.03	2
7	Chemical Reviews	52.76	2
8	JAMA-Journal Of The American Medical Association	45.54	6
9	Chemical Society Reviews	42.85	1
10	Nature	42.78	22

The analysis also reveals the global reach of IMI's research activities. In total, **117 countries** have at least one paper funded by IMI.

Countries with at least 1 paper funded by IMI



The scale shows countries having from 1 publication to 2 884 publications (UK being the top end with 2 884 publications).

1.3.2 Assessment of the socio-economic impact of the completed IMI1 projects

In 2020, IMI carried out an in-depth assessment of the socio-economic impacts of 44 IMI1 projects. The study was carried out by the Clarivate Analytics Centre for Innovation in Regulatory Science (CIRS). The team analysed the public summaries of the projects' final reports, applying the same methodology used in a previous study of 9 IMI1 projects carried out in 2016.

The scope of this report was to identify, summarise and quantify the project outcomes (if and when possible) and see if and how these outcomes have translated or could translate into impacts on citizens, patients, society.

The authors categorised project outcomes in four categories: innovation; infrastructure and resources for further research; structuring the European research area; and dissemination of information. The authors then analysed how these outcomes could contribute to six potential socio-economic impact types, and these are summarised in Table 1 below.

Table 1: Outcome measures used to evaluate socio-economic impact

Outcome	Activities involved (Measures)	Potential socio-economic impacts
Innovation	Development of new biomarkers, *in vitro*, *in vivo*, and computerised models and assays, identification of new drug targets, candidates, and delivery systems, and improvements in manufacturing processes	Increase robustness and reproducibility of research Reduce the time and cost of research Improve manufacturing processes
Infrastructure and resources for further research	Development of new biobanks, cohorts, preclinical and clinical networks and databases, platforms, tools, and technologies (e.g. assays, software tools), and guidance, recommendations, and standards	
Structuring the European research area	Collaborations and partnerships within and between the pharmaceutical industry and academia, creation of spin-off companies to commercialise findings, engagement with regulatory bodies on project findings	Support environmental sustainability Improve standards of care
Dissemination of information	Publication and accessibility of project outputs, and education and training of the future European workforce for the pharmaceutical sector and the next generation of (academic) researchers.	Consolidate and expand knowledge base

Analysis of the results

The report confirms that the 44 IMI1 projects analysed are delivering on IMI's goal of helping to make concrete improvements to the medicines development process, in terms of reduction of resources, time and sometimes costs. When reading the report, it is important to bear in mind that IMI projects were not designed to directly bring new medicines to market. Rather they are designed to impact on new product development by acting on the medicines development process itself, usually in particular disease areas, where safe, effective treatments are lacking, and/or where the impact on public health is greatest.

Innovation

The first highlight of the report is the fact that IMI1 projects did deliver several outcomes that will support the development of innovative new technologies and treatments, which eventually will benefit citizens, patients and society. Some examples are listed below:

- *Development of biomarkers:* Biomarkers have been developed, and some validated, as part of many IMI1 projects in areas including: neurodegenerative diseases (AETIONOMY, EMIF and PharmaCog), vaccines (BioVacSafe), rheumatoid arthritis (BTCure), autism disorders (EU-AIMS), diabetes and its complications (EMIF, IMIDIA, and SUMMIT), medicines safety (MARCAR and MIP-DILI), and cancer (OncoTrack and QUIC-CONCEPT). These biomarkers may be used to enhance understanding of disease processes and improve diagnosis, to identify drug targets and potential drug candidates, to better stratify patients, and to increase efficiency, thereby potentially reducing the duration and cost of clinical trials.

- *Development of in vitro, in vivo, and in silico/computerised models and assays:* models and assays have been developed, and some validated, as part of IMI1 projects investigating a wide range of diseases as well as cross-cutting issues. These models may improve prediction of the efficacy and safety of new drug candidates earlier in the development process. Once implemented, they will reduce animal testing requirements and human exposure to ineffective treatments, ultimately leading to time and resource savings.

- *Identification of new potential drug targets, candidates, and delivery systems:* New drug targets and candidates for the treatment of rheumatoid arthritis have been identified in BTCure and, with further research, may result in the availability of new innovative treatments. Novel drug delivery systems have also been developed in COMPACT and, if further testing is successful, may allow oral delivery of peptides (e.g. insulin), delivery across blood-brain barrier, delivery across air-lung barrier, and dermal delivery of proteins. These outcomes have the potential to provide new treatment options and improve standards of care across a range of disease areas.

- *Improvements in manufacturing processes to reduce their environment impact:* When implemented, innovations to manufacturing processes developed in CHEM21 will reduce the environmental impact of these processes, while also reducing costs and resource use. During the project, a number of new, cleaner catalysts were supplied to EFPIA members for use in their manufacturing processes.

Infrastructure and resources for further research

The second take-away of the analysis is the fact that the infrastructure and the resources generated as part of the IMI1 projects (such as biobanks, cohorts, and databases, platforms, tools, and technologies for further collaborative research and data sharing, along with guidance and recommendations on best practices in various areas) may facilitate and accelerate further innovation and potentially result in cost and resource savings as well as speeding up the medicine development process, ultimately to the benefit of citizens, patients and society:

- *The biobanks, cohorts, and databases:* examples of biobanks include those developed in the MARCAR and U-BIOPRED projects, in which samples from rodent studies and humans with severe asthma were included, respectively. Databases were also created in several projects. The creation of biobanks, cohorts, and databases facilitates the use of the data collected during the IMI1 projects for further research, potentially resulting in cost and resource savings and accelerating the medicine development process.

- *Development of platforms, assays, software tools and technologies:* Tools and technologies were developed by most of the IMI1 projects, in the form of software tools and platforms used for data analysis and sharing, tools and techniques used in pre-clinical and clinical research, tools aimed at improving trial design and drug candidate selection, and a mobile app for tracking adverse reactions to medicines (WEB-RADR). The infrastructure and resources developed during some of these projects are already being used in further research or data collection.

- *Guidance, recommendations, and standards:* many projects have generated guidance, recommendations, and standards on topics as diverse as the development, description, and storing of models (DDMoRe), incentivisation of antibiotic development (DRIVE-AB), routine banking, characterisation, and distribution of induced pluripotent stem cell (iPSC) cell lines (EBiSC), use of health data for research (EHR4CR), terminology used in pre-clinical studies (eTOX), use of real-world evidence in drug development (GetReal), standard operating procedures for precision-cut tumour slicing (PREDECT), assessment of activity monitoring in trials for COPD (chronic obstructive pulmonary disease) (PROactive), methods used in pharmacovigilance and pharmacoepidemiology (PROTECT), working with pluripotent stem cells (StemBANCC), diagnostic criteria for severe asthma (U-BIOPRED), and use of mobile applications and social media data for pharmacovigilance (WEB-RADR). The guidance, recommendations, and standards

developed may help to improve and standardise the drug development process, potentially accelerating the development of and reducing the cost of developing innovative new drugs.

Structuring the European Research Area

The third impact assessed reaffirms the success of the IMI1 model (public-private partnership) as a platform that builds long-lasting collaborative networks across industry, academia, small and medium-sized enterprises (SMEs) as well as patient groups, and regulators, and in leveraging funding amongst different stakeholders able to drive innovation in life science. Effective collaborations can minimise duplication of work at different organisations and bring together the resources needed for innovation. In addition, engagement with regulatory bodies can help to generate the evidence to support development of regulatory guidance and standards for use in the medicine development process, potentially improving efficiency and ultimately being beneficial to the patients, the citizens and the society. Some examples include:

- *Collaborations and partnerships:* the IMI1 projects have provided a platform for effective collaboration within the pharmaceutical industry, between industry and academia, and extending to healthcare payers, patient groups, and regulators. The projects have enabled collaborators to establish and use standards as part of the drug development process, in areas such as vaccine development (BioVacSafe), rheumatoid arthritis (BTCure), and autism disorders (EU-AIMS). Collaboration has continued, both formally and informally, following completion of the IMI1 projects, and not-for-profit foundations have been established by the industrial and academic partners of some projects (DDMoRe and Open PHACTS) in order to maintain the frameworks and infrastructure developed. Effective collaborations can minimise duplication of work at different organisations and bring together the resources needed for innovation.

- *Spin-off companies:* spin-off companies have been created to commercialise the output of some of the IMI1 projects, including ELF, eTOX, K4DD, OncoTrack, Open PHACTS, and SUMMIT. The establishment of new companies ensures continuation of the development and implementation of innovative technologies, supporting and enhancing scientific research in Europe through the provision of novel R&D services. In addition, the creation of SMEs has wider societal benefits, providing employment and promoting European competitiveness in the pharmaceutical industry.

- *Engagement with regulatory bodies:* IMI1 projects have involved engagement with regulatory bodies on issues including biomarkers/outcomes suitable for use in drug development (EUROPAIN, PreDiCT-TB, PROactive, and SAFE-T), improvement of pre-clinical carcinogenicity testing strategies for new drug candidates (MARCAR), patient involvement across the drug development process (EUPATI), environmental issues associated with medicine manufacturing processes (CHEM21), and good practices for the use of new technologies to gather pharmacovigilance information (WEB-RADR). In some cases, this has already resulted in regulatory acceptability on the use of the tools developed as part of projects (e.g. qualification of PROactive tools) or letters of support for those tools shown to be promising based on preliminary data (e.g. EU-AIMS).

Dissemination of information

The fourth take-away of the report is about **the knowledge-sharing and dissemination opportunities** generated by the IMI1 projects as well as the ability to contribute to the development of a skilled workforce to put Europe at the forefront of scientific R&D. Dissemination of the findings from IMI1 projects is critical to ensuring that their outputs can be used for further research. Education and training activities are also important, both to ensure dissemination of findings, and to develop a skilled workforce to put Europe at the forefront of scientific R&D. A skilled work-force will add value to the society and to the citizens. Examples of information-sharing tools and activities are:

- Catalogue of project tools: Platforms, tools, and technologies have been developed for collaborative research and data sharing as part of many of the IMI1 projects. The IMI website provides links to accessible project tools from IMI projects[2], including 67 tools from IMI projects object of this report.

- Publications: The IMI1 projects delivered approximately 4 000 high-quality scientific research publications with an average citation impact of 1.83, which is nearly twice the world average of 1.00 and approximately

[2] www.imi.europa.eu/projects-results/catalogue-project-tools

60% higher than the EU average of 1.10. Although open-access publication was not a requirement for EU funding and was often not budgeted for in IMI1 projects, on average 56 % of publications per project were printed in open access journals. The publication of findings from the IMI1 projects facilitates the application of learnings from these projects to further research.

- Education and training: Five of the IMI1 projects (EMTRAIN, EU2P, EUPATI, PHARMATRAIN, and SafeSciMET) focused specifically on education and training, providing training platforms, supporting lifelong learning for those already working in the pharmaceutical sector, supporting patient representatives to engage with the medicine development process, and offering training courses and qualifications. While it was not their primary focus, many of the other IMI1 projects provided education and training for young researchers across public-private institutions and funding or enabling academic qualifications. Through these activities, the IMI1 projects have helped to reduce the cost and resource burden associated with re-training professionals moving between institutions, and to develop highly-skilled and mobile current and future workforces, thereby positioning Europe as a hub for scientific research in the longer term.

Overall, the report highlights how IMI1 projects are changing the manner in which new medicines are developed, improving the R&D infrastructure and streamlining R&D processes, involving collaborative networks, but also disseminating findings to develop a skilled workforce to put Europe at the forefront of scientific R&D.

The analysis shows that IMI project outcomes provide a significant contribution in addressing 'bottle-necks' during the drug discovery and development process to ultimately create value for patients, citizens and society. IMI has demonstrated its role as a key actor within a complex process where other elements also play a key role, such as strategies, investments and actions of the industry as well as the decisions of regulators, the healthcare system and policy makers.

Based on the information available today, the report affirms that IMI1 projects have produced key outcomes that have the potential to result in several socio-economic impacts. In some cases, the potential socio-economic benefits generated by the projects are more concrete and visible while, in other projects, the potential benefits are perceivable but not yet tangible. Such a dynamic is in line with the nature of IMI projects, which involve research in the healthcare space, multi-stakeholder partnerships and cross-sector collaboration. The scale of the investment required, the stepwise approach, very long development timelines and the successful involvement of relevant stakeholder are concrete challenges. It requires time to produce innovative solutions, often happening in the later phases of the project lifecycle and very often even beyond the end date (after projects have been completed). As a result, as experience shows that the greatest impacts often come in the months and years after the final project report has been submitted, it is likely that in the long-term, these projects will have an even greater impact than what is reported today.

The full text of the Socio-Economic Impact Report on IMI1 projects is available on the IMI website.

1.4 Stakeholder engagement

1.4.1 Small and medium-sized enterprises (SMEs)

The IMI 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 2020, the review of all Call texts to ensure expected SME participation is highlighted was continued. In addition, the importance of SME participation in Call proposals was emphasised to applicants and evaluation experts by emphasising the updated evaluation criteria.
- **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 Calls launched in 2020, attracting a total of 194 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 in a limited form due to the COVID-19 restrictions. SME impact was emphasised in project kick-offs and general assembly meetings. In addition, opportunities for SME participation in IMI projects were promoted via the IMI States Representatives Group and Scientific Committee.

Research activities of SMEs that have joined IMI projects as partners have been advanced. For example, the ENABLE project continued to support SME Juvabis in the evaluation of EBL-1003 (a purified form of apramycin) as a new antibiotic against a variety of WHO priority pathogens. The results of a first-in-human Phase I clinical study in healthy volunteers showed that EBL-1003 is both safe and well tolerated. Juvabis is now planning to pursue further Phase I trial in patients with complicated urinary tract infections.

Several IMI projects support SMEs outside of the project. For instance, through the collaboration with ELF/ESCulab, the SME Metabomed has discovered a series of potent and selective inhibitors of ACSS2 (the AcetylCoA Short chain Synthase 2 enzyme) for the treatment of cancers dependent on acetate metabolism, thus advancing cancer metabolism research. Metabomed have mobilised significant additional investments based on this result.

In addition, the EHDEN project offers training and certification to SMEs so that they can harmonise data to the OMOP (Observational Medical Outcomes Partnership) common data model. In 2020, the project ran its second data harmonisation service providers call which attracted 36 applications, out of which 15 SMEs receiving training and certification. Including the SMEs certified in 2019, a total of 28 SMEs are now eligible to harmonise the data of the data partners and are included in the EHDEN business directory. Additional SME calls will be held in 2021 and future years. Furthermore, in 2020, 16 contracts to perform data harmonisation activities were made between the EHDEN data partners and the certified SMEs.

In January 2020, FAIRplus ran an Innovation and SME Forum which brought together nearly 100 researchers and data management experts from academia, SMEs and industry working with life science data. The project has additional SME-focused activities planned for 2021.

Finally, a collaboration between the IMI2 Trials@Home project and ECSEL JU led to the launch of a call to develop novel technologies to support remote decentralised clinical trials, which should appeal to SMEs in particular.

For the IMI2 programme, SMEs account for 16.1 % of EU funded beneficiaries (by participations), 24.3 % of EU funded beneficiaries (by participants), and receive 11.9 % of EU funding so far.

In October 2020, IMI focused on SMEs in its communication activities, publishing news items, an opinion piece and a video highlighting the many ways SMEs contribute to and benefit from IMI's projects.

1.4.2 Patients

Since the beginning, IMI has been committed to promoting patient involvement in its projects and activities. Over the years, patients have been actively involved in a wide range of IMI activities – as project partners, as members of the IMI Scientific Committee, and as speakers in events. As of the end 2020, 60 % of IMI2 projects have patient organisations as consortium partners, members of advisory boards, ethics boards or members of stakeholder groups.

In 2020 the Programme Office laid the foundation for a more systematic involvement of patients and carers at both strategic and operational levels. This was mainly achieved by engaging regularly with patients and carers from the IMI pool of patient experts, an initiative introduced for this purpose in late 2019.

Drawing from the IMI pool of patient experts, in 2020 the Programme Office invited patients and carers with the most suitable profile to perform a variety of roles and tasks aiming to provide in a rigorous and systematic way, patients' perspectives, needs and priorities within IMI activities and subsequently, to improve the relevance, quality and validity of its projects.

Panels evaluating applicant proposals submitted following IMI Calls for proposals

Call	Number of expert panels (Stage 1 and 2)	Number of expert panels with patient participation (Stage 1 and 2)
Call 20	12	4 (Topics 1 and 6)
Call 23	12	6 (Topics 1, 5 and 6)
Total	**24**	**10**

Panels reviewing ongoing projects: Patients and carers were invited to participate in panels of independent experts to carry out the monitoring of the following projects: INNODIA (2); RESCEU (1); AIMS2TRIALS (1); Hypo-RESOLVE (1); and RADAR –AD (1). Total: 7 participations.

In order to deploy the full potential of the IMI pool of patient experts, the Programme Office provided tailor-made support to patient experts with one-to-one training and follow-up meetings after the conclusion of the evaluation and review process.

In an effort to promote patient participation in the whole cycle of its activities, in 2020 the Programme Office invited patients and carers to the PRISM, WEB-RADR2, Do-IT, ROADMAP, MOPEAD, NGN-PET, and iPiE project close out meetings. Patients had the opportunity to get an overview of how an IMI consortium works, get valuable insights of the different tasks undertaken by an IMI project and learn first-hand about the project outcomes.

Patients and carers were also involved in different types of activities organised by IMI projects in 2020, such as: the c4c workshop dedicated to patients' training, the Patient Engagement Open Forum organised by PARADIGM and EUPATI, the Stakeholder Workshop organized by EU-PEARL, webinars on real world data / evidence organised by EHDEN, and the Hypo-RESOLVE Patient Advisory Committee.

In September 2020, IMI organised together with the PARADIGM project an online session with the IMI pool of patient experts dedicated to patient engagement in R&D. The purpose of the meeting was to share the outcomes of the PARADIGM project fostering the use of the Patient Engagement Toolbox (PE Toolbox), the tools developed by PARADIGM, as well as to give patients the opportunity to provide input on their implementation in research.

Creating and developing communication channels with patients is instrumental in keeping them engaged and informed about the latest developments in IMI. Throughout 2020, IMI provided to all the members of the patient pool detailed updates on its activities with IMI news and highlights from projects, with a particular focus on IMI's response to the COVID-19 pandemic.

As part of IMI's efforts to share best practices and experiences on patient engagement, IMI attended the BIOTECH Conference, which took place virtually in September 2020. An IMI staff member participated as a speaker in a workshop where patient advocates and chief patient officers discussed the many different aspects of patient centricity in research and innovation and shared best practices in patient engagement.

Patients also formed the focus of IMI's communication efforts in January, with a series of articles and a video highlighting patients' involvement in IMI activities.

1.4.3 Regulators

As the scientific knowledge derived from IMI projects has the potential to support the evolution of the regulatory environment, IMI continued to maintain in 2020 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, interaction with the EMA and other national regulatory agencies in the EU occurred also through the Scientific Committee. To further strengthen the interactions of IMI with other national regulatory agencies, the IMI Programme Office presented to the EU-Innovation Network (EU-IN), a working group of the Head of Medicines Agencies, the IMI Scientific Committee recommendations on the involvement of regulators and regulatory science.

IMI continued to encourage consortia to take advantage of possible ways to engage in early dialogue with regulators and raised awareness among consortia of existing services offered by 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.

Finally, the IMI Programme Office launched a tender on 'supporting regulatory acceptance of IMI results'. The overall objective of this tender is to provide a central support system which will capitalise on project results generated such as novel biomarkers, by increasing or securing their impact and sustainability through adoption into regulatory agency guidelines or standard practice. The framework contract service was awarded to the Critical Path Institute, Limited. The set-up phase of the contract has started and aims at identifying and prioritising the relevant project results that would be suitable for regulatory endorsement.

1.5 Calls for proposals and new projects

1.5.1 Launch and management of Calls in 2020

In 2020, four Calls for proposals were launched (IMI2 - Calls 20, 21, 22 and 23) and three Calls were at various stages of the evaluation and granting process (IMI2 - Calls 17, 18 and 19). The evaluations for IMI2 - Calls 17 and 19 were completed in 2019 but Grant preparation and Grant Agreement signature were completed in 2020.

Each single stage and stage 2 evaluation encompasses ethics screening of the full proposals performed by a separate ethics expert panel. In 2020, the following evaluations were concerned: IMI2 - Call 18 (stage 2), IMI2 - Call 20 (stage 2), IMI2 - Call 21 (single stage) and IMI2 - Call 22 (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 AWP 2020 were addressed through Calls launched in 2020.

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

- Cx Topics Text GB DEC – Call x topics text Governing Board decision
- Cx – Call Launch
- SP SUBM – Short proposal submission deadline
- SP Evaluation – Short proposal evaluation
- SP GB DEC – Short proposal Governing Board decision
- FP SUBM – Full proposal submission deadline
- FP Evaluation – Full proposal evaluation
- FP GB DEC – Full proposal Governing Board decision
- GAP – Grant Agreement preparation
- GA – Grant Agreement

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

IMI2 – Call 21 on coronavirus treatments and diagnostics

On 30 January 2020, the WHO declared the outbreak of the then novel coronavirus (COVID-19) a public health emergency. In response, and in line with the European Commission's wider response to COVID-19, IMI decided to reallocate EUR 45 million of IMI's 2020 budget to a fast-track, single stage Call for proposals on the subject. Due to the emergency nature of the situation, the Call was prepared and approved extremely rapidly, and was launched on 3 March. The Call focused on two things:

- the development of treatments to rapidly respond to the current COVID-19 outbreak and/or future coronavirus outbreaks – this could include potential drugs that are already at a very advanced stage of development, or an existing, approved drug that could be 'repurposed' to treat COVID-19. It could also include drugs that are in the earlier stages of development, as well as strategies to address drug resistance;
- the development of diagnostic tests to rapidly and reliably identify people infected with the coronavirus that causes COVID-19, and for use in clinical trials of new drugs.

Preventive vaccines were not included in the Call, as IMI did not want to duplicate the work of other organisations in this area.

Applicants had just 4 weeks to submit a proposal. Nevertheless, thanks to a strong communication campaign by IMI as well as the European Commission and EFPIA, the Call attracted 144 proposals. These were evaluated remotely, as the pandemic made travelling and holding in-person meetings impossible.

A review of the strongest proposals prompted the IMI Governing Board to increase the IMI funding pot from EUR 45 million to EUR 72 million. This allowed IMI to fund eight projects under the Call – three on treatments,

and five on diagnostics. EFPIA companies, IMI2 Associated Partners and other organisations are contributing over EUR 45 million to the projects.

IMI subsequently worked hard to inform the applicants of the outcome of the evaluation as quickly as possible (time to inform was just 41 days), and start working on the Grant Agreements to allow the projects to get underway.

Ethics evaluation process

In addition to the scientific evaluations, the IMI Programme Office organises ethics for stage 2 and single stage proposals recommended for funding. Within the H2020 ethics appraisal framework, the IMI Office independently operates the ethics screenings with external ethics experts. In 2020, IMI ran three ethics screenings for four IMI2 Calls for proposals:

- IMI2 - Call 18 (stage 2): 6 proposals
- IMI2 - Call 18 Call 21 (single stage): 8 proposals (of which 1 ethics assessment performed by RTD ethics sector due to involvement of human embryonic stem cells)
- IMI2 - Call 20 (stage 2) & IMI2 - Call 22 (single stage) merged into one evaluation with 6 and 3 proposals respectively.

All 23 proposals were conditionally cleared by the expert panels with a set of requirements to be addressed by the consortium during the granting phase and/or as specific ethics deliverables over the project implementation phase.

Redress procedures

There were 9 redress cases following the evaluation of Calls in 2020. The review committee evaluated the complaints and found that for 7 of the complaints, there were no grounds for a re-evaluation. However, in 2 cases the redress committee recommended re-evaluation:

- One proposal from IMI2 - Call 21 was wrongly declared ineligible due to a technical problem during the transfer from the H2020 submission environment to the evaluation system, which resulted in the full list of participants not being imported for that proposal. The proposal was re-evaluated against the award criteria set out in the Call for proposals and taking into account the results of the evaluation review.

- One proposal in IMI2 - Call 23, stage 1 was partially re-evaluated as the complaint was considered to be founded regarding the evaluation of one of the award criteria.

In both cases the re-evaluation of the proposals did not impact the overall outcome of the Calls. Although the number of redress procedures was higher than in previous years, 2020 was marked by an increase in Call activity and a large increase in the number of proposals submitted in response to the Calls[3]. In accordance with H2020 rules to ensure a high quality evaluation and that the Programme Office maintains these standards, an Independent Observer is appointed to follow all of IMI evaluation sessions. Their reports are publicly available via the IMI website. It is noteworthy that none of the reports identified issues that would call into question the fairness, transparency and integrity of the IMI2 Call evaluations held in 2020.

[3] 144 proposals received under IMI2 - Call 21 is the highest number that IMI2 JU has ever received.

Chart showing overview of Call processes in 2020

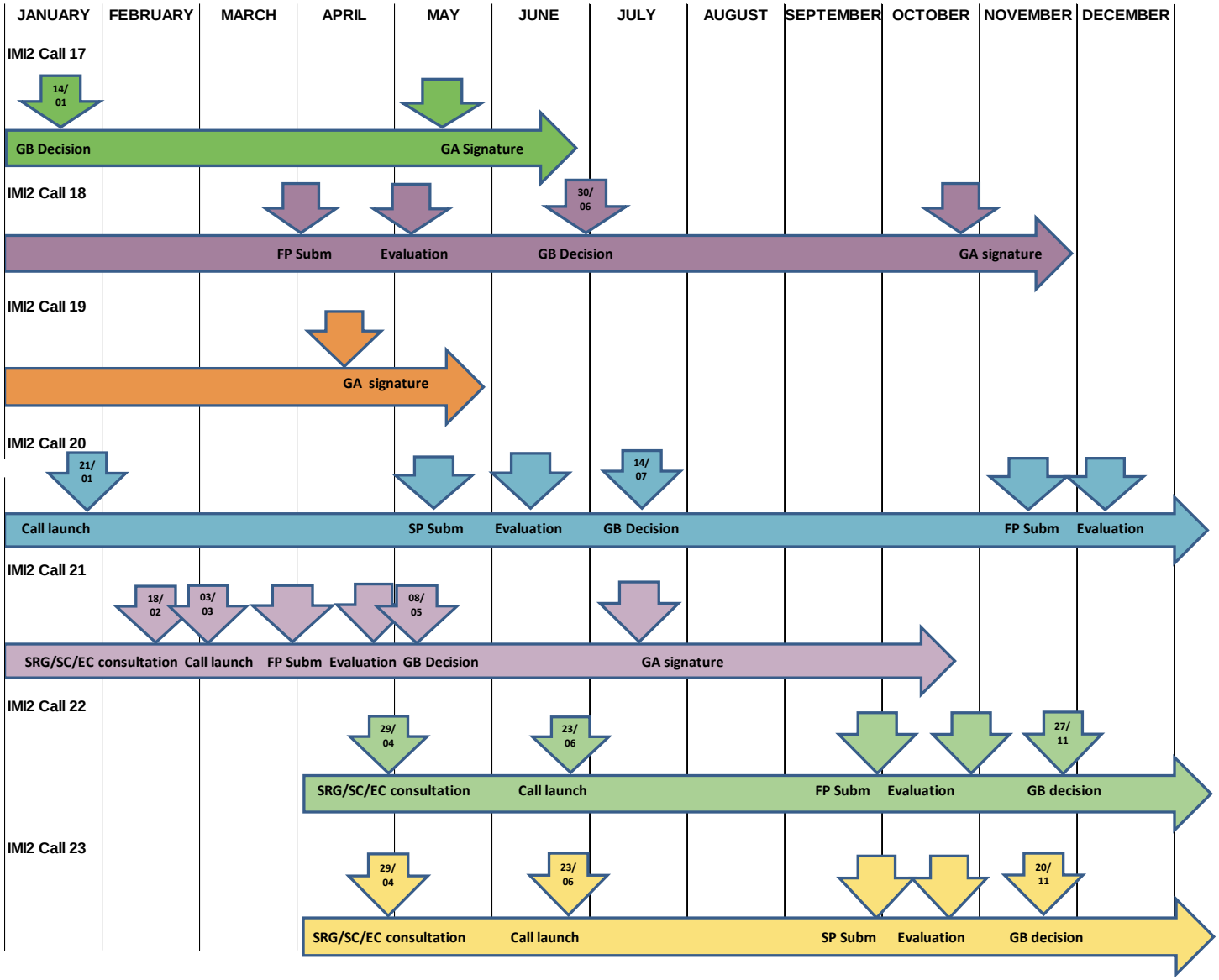


Table summarising key information related to IMI Call launches, submission deadlines and Grant Agreements signed in 2020

IMI2 Call	Topics	Call process	Launch date	Deadline for submission of SPs	SPs received (FPs in single stage Calls)	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2020
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	3
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	6	6
19	Restricted Call to maximise impact of IMI2 JU objectives and specific priorities	Single stage	26/06/2019	26/09/2019	5	128	N/A	2	2

IMI2 Call	Topics	Call process	Launch date	Deadline for submission of SPs	SPs received (FPs in single stage Calls)	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2020
20	Early diagnosis, prediction of radiographic outcomes and development of rational, personalised treatment strategies to improve long-term outcomes in psoriatic arthritis Innovations to accelerate vaccine development and manufacture Academia and industry united innovation and treatment for tuberculosis (UNITE4TB) Tumour plasticity Proton versus photon therapy for oesophageal cancer – a trimodality strategy Handling of protein drug products and stability concerns	Two stage	21/01/2020	12/05/2020	27	330	6	open	open
21	Development of therapeutics and diagnostics combatting coronavirus infections	Single stage	03/03/2020	31/03/2020	144	1121	N/A	8	8
22	Restricted Call to maximise impact of IMI2 JU objectives and specific priorities	Single stage	23/06/2020	29/09/2020	8	153	N/A	3	open
23	Returning clinical trial data to study participants within a GDPR compliant and approved framework Modelling the impact of monoclonal antibodies and vaccines on the reduction of antimicrobial resistance A platform for accelerating biomarker discovery and validation to support therapeutics development for neurodegenerative diseases	Two stage	23/06/2020	29/09/2020	56	826	6	open	open

IMI2 Call	Topics	Call process	Launch date	Deadline for submission of SPs	SPs received (FPs in single stage Calls)	Participants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2020
	Optimal treatment for patients with solid tumours in Europe through artificial intelligence Shortening the path to rare disease diagnosis by using new born genetic screening and digital technologies Behavioural model of factors affecting patient adherence								

Table summarising IMI2 Calls for proposals launched in 2020, highlighting the priorities of the Annual Work Plan 2020 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 20	Two stage	6	Infection control including vaccines Oncology Immunology Handling of protein drug products and stability concerns	21/01/2020	133 009 000	110 209 500	30 000 000
IMI2 - Call 21	Single stage	1	Development of therapeutics and diagnostics combatting coronavirus infections	03/03/2020	72 000 000	See note	See note
IMI2 - Call 22	Single stage	1	Restricted Call	23/06/2020	11 427 098	See note	See note
IMI2 - Call 23	Two stage	6	Neurodegeneration Infection control including vaccines Big data, digital health, clinical trials and regulatory research Oncology Facilitating rare disease therapies (including advanced therapy medical products) reaching patients in Europe Behavioural model of factors affecting patient adherence	23/06/2020	47 790 000	47 110 000	250 000

Note re IMI2 – Calls 21 & 22: As these were single-stage Calls for proposals, no EFPIA / Associated Partner contributions were indicated at Call launch as these contributions depend on the selected proposals. Information on the EFPIA / Associated Partner contributions to IMI2 – Call 21 projects can be found in the table of Grants signed in 2020, later on in this section.

Evaluation experts

In 2020, IMI2 JU used 235 experts from 29 countries in the evaluation of IMI2 - Calls 18, 20, 21, 22 and 23. Most of the experts (96.7 %) came from EU, UK and Horizon 2020 associated countries. More than half of the 199 experts appointed for the scientific evaluations came from academia and research organisations (38.6 % and 16.2 %, respectively). Other experts came from private for-profit entities (16.2 %), public bodies (14.8 %) and other type of organisations (14.3 %).

IMI2 Call	Total no. experts	Scientific evaluation	Rapporteurs in science evaluation	Ethics screening	Observers	Gender female	Gender male
Call 21 single stage	60	43	12	4	1	18	42
Call 18 stage 2	37	32	n/a	4	1	16	21
Call 20 stage 1	43	41	n/a	n/a	2	19	24
Call 23 stage 1	42	41	n/a	n/a	1	24	18
Call 22 single stage	13	8	n/a	4	1	10	3
Call 20 stage 2	40	34	n/a	4	2	18	22
TOTAL	235	199	12	16	8	105	130

Progress / activities by Call in 2020

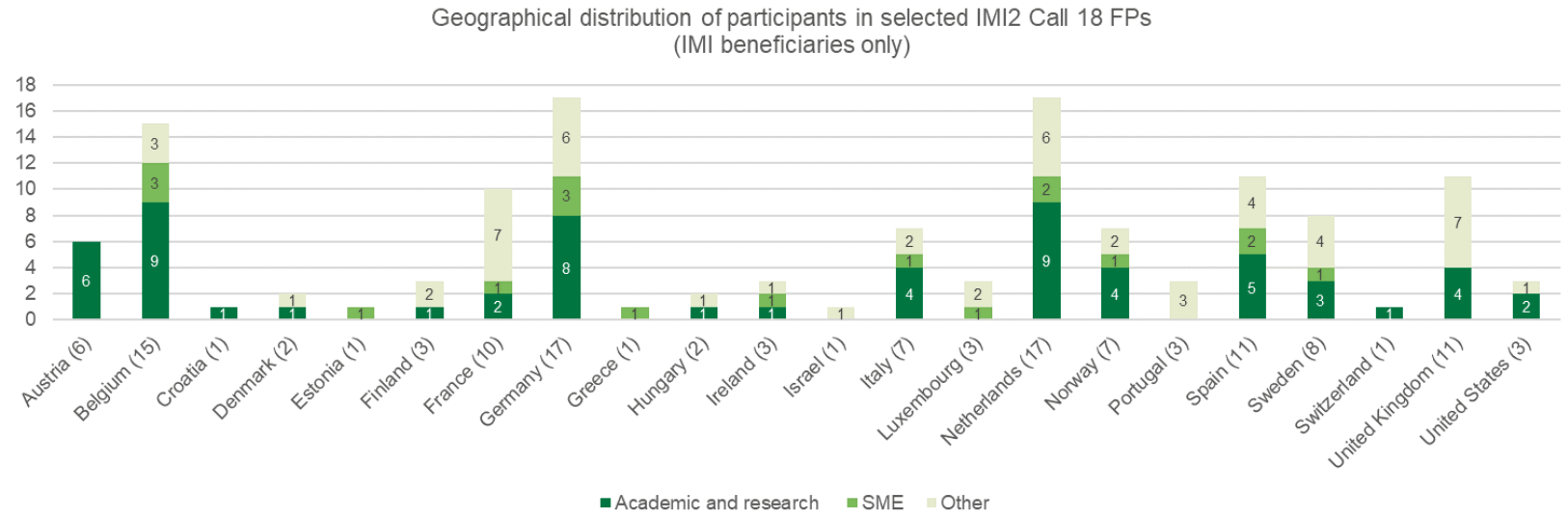
In 2020, IMI organised 6 evaluation sessions – 5 sessions for the 4 Calls launched in 2020: IMI2 - Call 20 (stages 1 and 2), IMI2 - Call 21 (single stage), and IMI2 - Call 22 (single stage), plus 1 session for Calls launched in 2019: IMI2 - Call 18 (stage 2). The 6 evaluation sessions were completed successfully, according to the IMI rules and procedures.

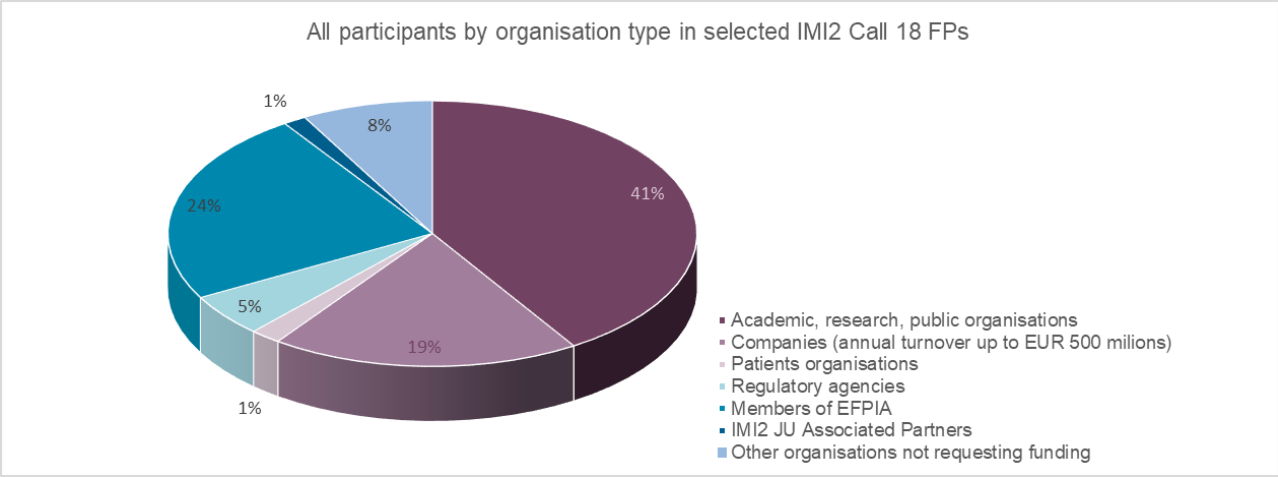
The table below presents the Calls in different stages of the process in 2020, from the Call launch until sending the letters to start GAP.

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 18	Two stage	6	26/06/2019	26/09/2019	03/12/2019	06/12/2019	02/04/2020	30/06/2020	01/07/2020
Call 20	Two stage	6	21/01/2020	12/05/2020	14/07/2020	16/07/2020	19/11/2020	open	open
Call 21	Single stage	1	03/03/2020	31/03/2020	08/05/2020	N/A	N/A	N/A	11/05/2020
Call 22	Single stage	1	23/06/2020	29/09/2020	27/11/2020	N/A	N/A	N/A	01/12/2020
Call 23	Two stage	6	23/06/2020	29/09/2020	20/11/2020	30/11/2020	17/03/2021	open	open

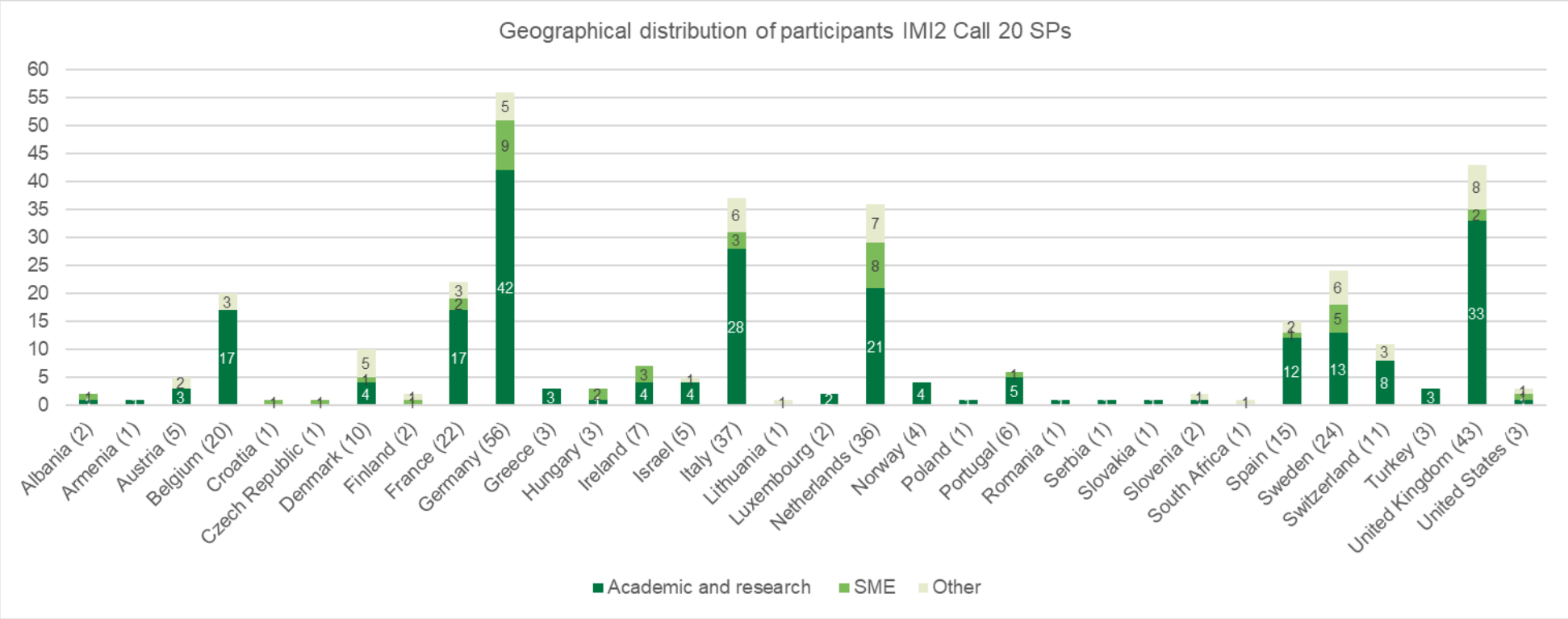
Participant details

IMI2 – Call 18: Full proposal participant details

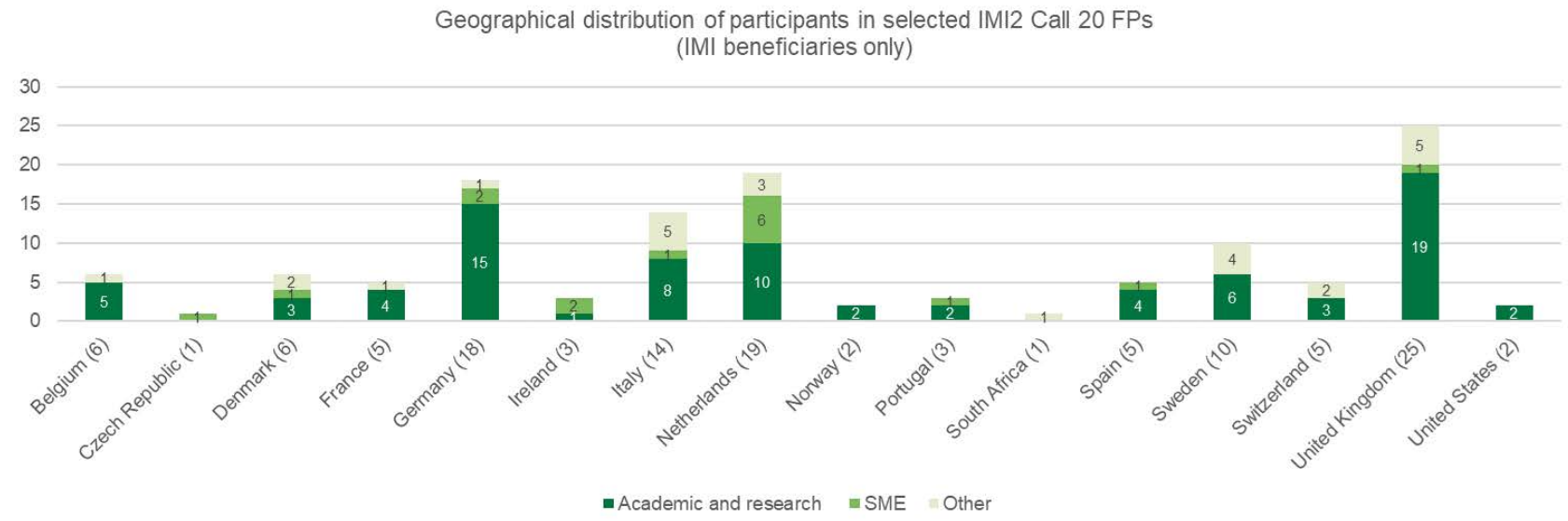


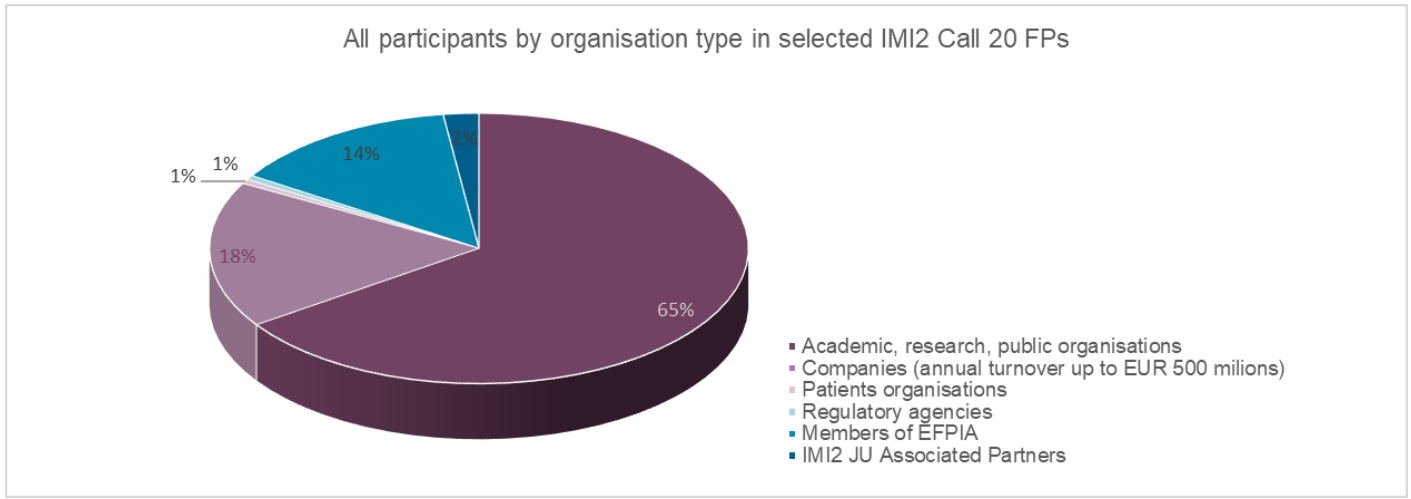


IMI2 – Call 20: Short proposal participant details

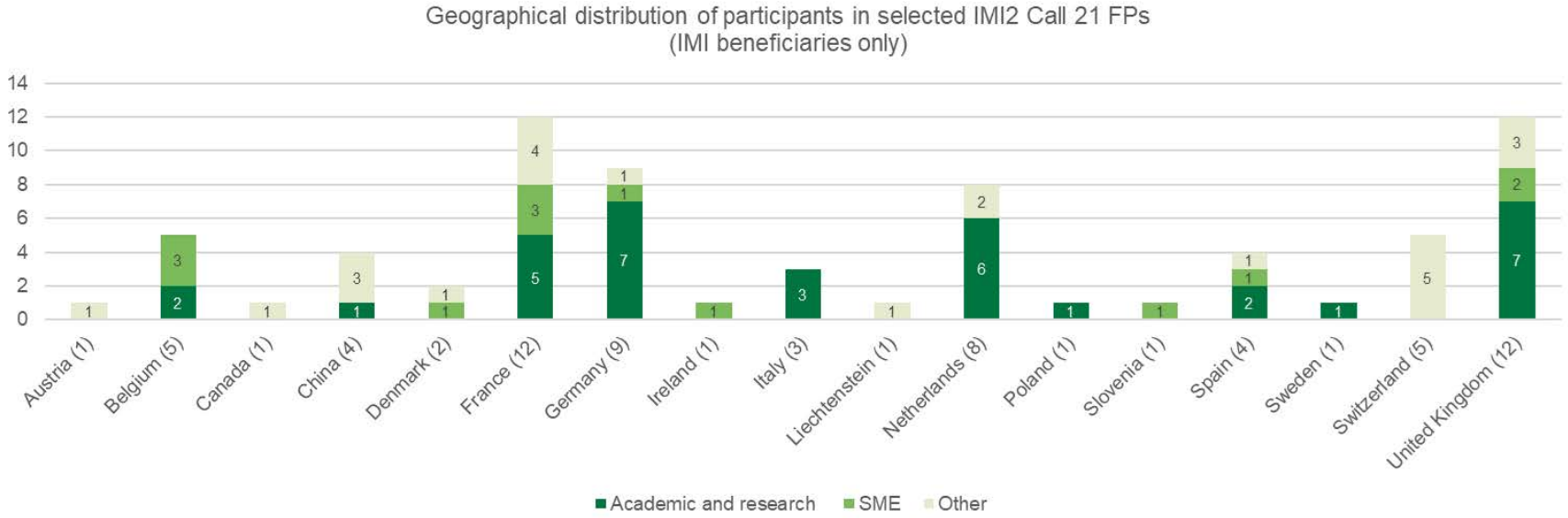


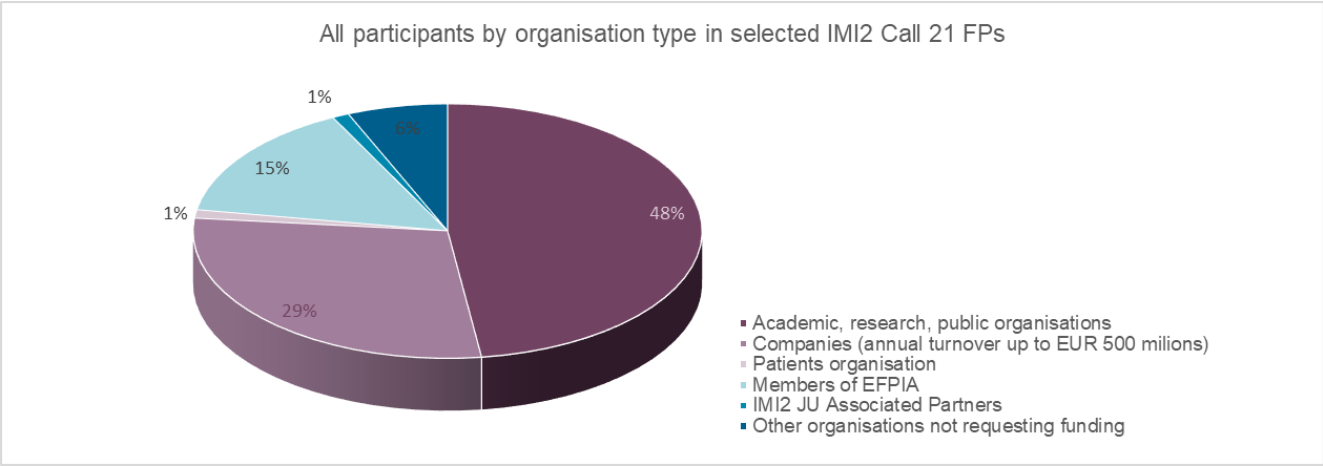
IMI2 – Call 20: Full proposal participant details



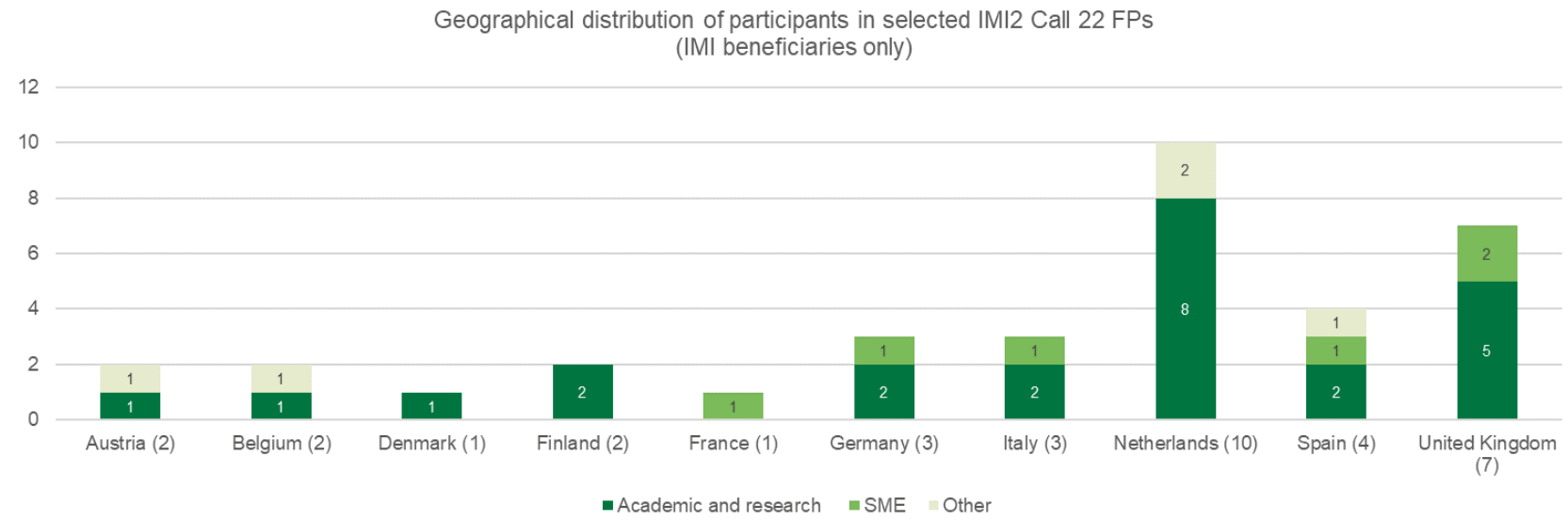


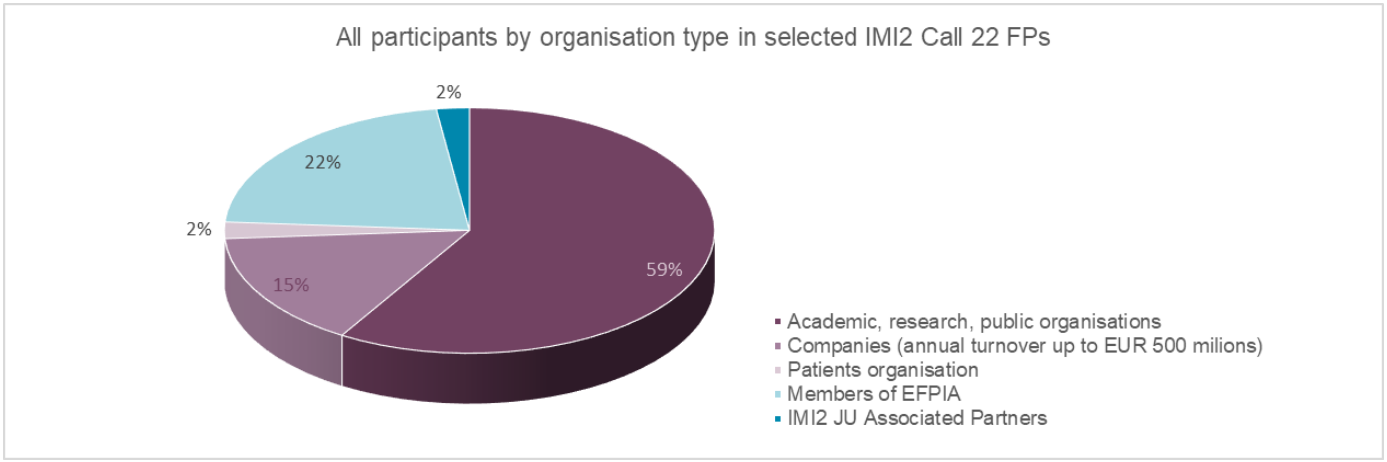
IMI2 – Call 21: Full proposal participant details for selected proposals





IMI2 – Call 22: Selected full proposal participant details





IMI2 – Call 23: Short proposal participant details

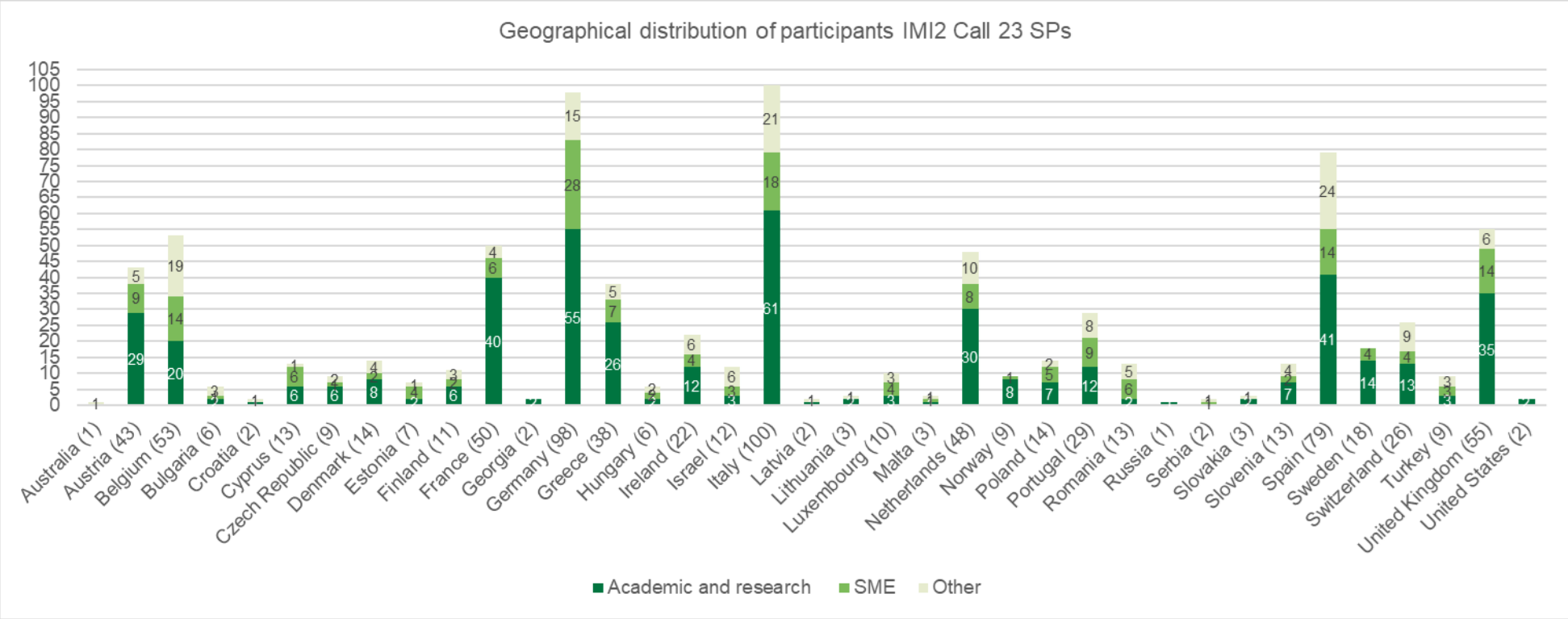


Table summarising the number of beneficiaries and budgets for projects with GAs signed in 2020

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)	EFPIA in-kind contribution (EUR)	Associated Partners' contribution (EUR)	Total budget (EUR)
17	EUbOPEN	14	5	4	27 935 000.00				27 935 000.00	23 777 950.00	6 445 380.00	65 773 473.00
17	PREMIER	15	10	0	3 226 313.90	1 276 685.75		47 000.00	4 549 999.65	5 218 030.00		9 768 029.05
17	SOPHIA	24	4	3	7 276 000.00	1 000 000.00		25 000.00	8 301 000.00	6 466 250.00	1 201 139.00	15 977 544.50
18	ARDAT	23	11	0	8 996 269.75	2 776 730.00			11 772 999.75	13 717 492.00		25 490 491.75
18	BIGPICTURE	38	10	0	20 528 887.50	5 674 750.00		6 116 187.50	32 319 825.00	37 762 082.00		69 641 907.00
18	Gravitate-Health	30	10	1	5 250 787.50	2 266 460.00	297 725.00	1 465 027.50	9 280 000.00	9 150 000.00	25 000.00	18 561 750.00
18	H2O	13	8	2	7 418 329.70	1 130 312.50		1 928 045.25	10 476 687.45	9 903 000.00	168 000.00	20 618 937.50
18	SISAQOL-IMI	28	5	0	2 203 083.75			78 756.25	2 281 840.00	2 935 000.00		5 944 754.75
18	T2EVOLVE	22	6	1	6 138 175.00	1 042 250.00	240 000.00	1 307 760.00	8 728 185.00	7 771 500.00	2 575 000.00	19 074 685.00
19	HARMONY PLUS	36	5	0	4 165 750.00	1 080 000.00	280 875.00	1 189 000.00	6 715 625.00	5 167 044.00		11 882 669.00
19	INNODIA HARVEST	32	6	2	5 508 055.00	38 750.00		452 250.00	5 999 055.00	2 758 000.00	3 685 389.00	12 442 444.00
21	CARE	28	11	3	26 374 835.35	2 728 953.49		7 455 397.25	36 559 186.09	33 897 299.00	5 382 915.00	75 839 401.07
21	COVID-RED	8	2	0	3 080 356.25	3 774 250.00		2 737 422.50	9 592 028.75	737 225.00		10 329 253.75
21	DECISION	4	0	0	406 350.00	2 603 500.00		425 250.00	3 435 100.00			3 435 100.00
21	DRAGON	17	1	0	5 225 120.34	5 214 349.66	478 750.00	463 750.00	11 381 970.00	160 672.00		11 542 642.00
21	Impentri	5	0	0	1 875 072.50	974 976.75		812 913.75	3 662 963.00			3 985 732.00
21	KRONO	5	0	0	568 000.00	28 750.00		187 720.00	784 470.00			1 819 963.75
21	MAD-CoV 2	5	4	0	2 399 793.75			1 349 875.00	3 749 668.75	2 655 500.00		6 405 168.75
21	RAPID-COVID	5	0	0	855 062.50	1 977 522.50			2 832 585.00			2 832 585.00

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

1.5.2 Interim reviews for IMI projects

In 2020, IMI conducted 14 interim reviews of ongoing IMI2 projects. 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.

Project acronym	IMI2 Call	Full project name	Date
MACUSTAR	7	Intermediate AMD: development of novel clinical endpoints for clinical trials in patients with a regulatory and patient access intention	03/02/2020
INNODIA	1	Translational approaches to disease modifying therapy of type 1 diabetes: an innovative approach towards understanding and arresting type 1 diabetes.	07/02/2020
RESCEU	6	Respiratory syncytial virus consortium in Europe	19/02/2020
eTRANSAFE	9	Enhancing translational safety assessment through Integrative Knowledge Management	03/03/2020
NEURONET	13	Efficiently networking European neurodegeneration research	25/06/2020
RespiriTB	16	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	09/09/2020
FAIRplus	12	FAIRplus	09/10/2020
MOBILISE-D	13	Connecting digital mobility assessment to clinical outcomes for regulatory and clinical endorsement	26/10/2020
Hypo-RESOLVE	10	Hypoglycaemia - redefining solutions for better lives	29/10/2020
IMI-PainCare	10	Improving the care of patients suffering from acute or chronic pain	11-12/11/2020
IMMUcan	3	Integrated immunoprofiling of large adaptive cancer patients cohorts	16-17/11/2020
VITAL	12	Vaccines and infectious diseases in the ageing population	17/11/2020
LITMUS	9	Liver investigation: testing marker utility in steatohepatitis	24/11/2020
STOPFOP	13	Saracatinib trial to prevent FOP	14/12/2020

MACUSTAR

MACUSTAR looks at developing and validating appropriate and acceptable clinical endpoints in intermediate age-related macular degeneration (iAMD) to support the clinical development of novel treatments in this condition, which is a leading cause of blindness in industrialised countries and for which there is currently no treatment available. The panel appreciated the excellent work the consortium has done so far despite the time delay in activities. The consortium set up timely and effective mitigation measures to overcome the delay in the recruitment of the clinical study patients, mainly due to GDPR implementation and delays in supplying all the equipment to sites, accompanied by late site staff certification on that equipment. However, this has generated delays in the subsequent activities that depend on the collected baseline data and on the completed cross-sectional study data.

The panel considered that the project will likely generate results that will have a strong impact on future clinical studies aiming at better understanding iAMD disease and at developing new endpoints (and eventually new treatments) for iAMD patients, which may be relevant for other retinal diseases. The panel made a number of recommendations to the consortium with the view to further maximise the impact of the project results, including enhancing dissemination and communication beyond the ophthalmology field on ethics, regulatory, operational, methodological and educational aspects as well as other relevant findings from the project. The panel recommended also a follow-up review to assess the progress of the project, including the implementation of the panel's recommendations.

INNODIA

INNODIA aims to advance the way we predict, evaluate and prevent the onset and progression of type 1 diabetes (T1D), by creating novel tools, such as biomarkers, disease models and clinical trial paradigms. These tools will make it possible to distinguish and understand at the cellular and molecular level distinctive paths of ontogeny and progression in this heterogeneous disease, thus impacting on the future management of T1D patients and at risk individuals. The review panel praised the excellent work and progress and recognised that INNODIA has to date demonstrated true potential to bring about a step change in how T1D research is carried out.

The reviewers were particularly impressed with the following key results: establishment of a unique data source for a detailed understanding of the natural history of disease development; development of novel approaches for *in vivo* imaging of beta cell mass; establishment of a clinical research infrastructure for newly diagnosed T1D with a master protocol, a network of accredited sites and innovative adaptive trial design that lower the hurdles for conducting interventional trials now and in the future; discovery and pre-clinical validation of novel biomarkers of beta cell mass, dysfunction and death in human T1D; novel clinical trial designs for the mechanistic trials that will be determined based on the novel biomarker signatures coming from other WPs; and impressive outreach and communication efforts with best-practice patient involvement. Since the project is very much on track, the panel's recommendations focused mainly on ensuring sustainability and continuation of the key activities and resources generated by the project, such as the clinical network and unique data collection. The consortium was also encouraged to expand their network within the southern Europe.

RESCEU

The project aims to better understand the impact of respiratory syncytial virus (RSV) on European health systems and to actively engage stakeholders in order to improve strategic planning and decision-making. It also seeks to create a powerful RSV bio-repository for future research which includes clinically annotated biological specimens from already existing prospective studies and new clinical studies run by the project.

The reviewers were satisfied with the good progress that the project has made so far, which is going well and is in line with its objectives.

The project has delivered several high-quality scientific reviews on the burden of RSV based on extensive processing of the available literature and unpublished data-sets made available by the partners. On the other side, the recruitment of patients for three of the planned clinical studies turned out to be slightly behind the schedule, even if the feasibility of reaching full recruitment with limited delay was acknowledged by the reviewers by extending it by one RSV season.

The consortium has made a lot of effort to make research results publicly available and to increase RSV awareness by reaching out to a variety of stakeholders. The reviewers however encouraged the consortium to more actively involve the Patient Advisory Board in the project's activities and also emphasised the importance of considering EMA-HTA advice early on.

eTRANSAFE

The expert panel reported good progress in data modelling and prediction tools, methodologies and workflows which build on work from previous projects, and the addition of model training with confidential data. Increased awareness of requirements, design and development of data sharing policies and interaction with stakeholders was also noted. The panel found the project guidelines and

reports to be sound. The experts reported the project to have a high innovative potential. In particular, they highlighted the following innovations:

- advanced *in silico* modelling to predict toxicity;
- pre-clinical text mining solution for treatment response;
- the Rosetta Stone – Bridging the gap between pre-clinics and clinics.

The expert panel recommended that the project should be more comprehensively presented to the greater community and emphasised the importance of sustainability measures such as business model(s), market access, long-term data access, regulatory issues and end-user acceptance.

NEURONET

This project is a coordination and support action for the portfolio of neurodegeneration projects and the reviewers appreciated that NEURONET had demonstrated good progress both in providing cross-project support to the portfolio of neurodegeneration project via different tools, and in creating a genuine interest for cross-learning and collaboration among the projects.

The reviewers recognised that in the short term, the next reporting period will be critical to determine how projects can collaborate in the context of the project aims and whether the objectives can be achieved, especially given the challenging times associated with the COVID-19 pandemic. For the longer term, the key area to be addressed is the sustainability of NEURONET which is critical for the benefit of the target projects and the whole neurodegeneration portfolio.

RespiriTB

The aim of RespiriTB is to find new drug candidates as potential components of a new, more efficient combination drug regimen against TB that is less prone to resistance and allows the shortening of treatment duration for TB and multidrug-resistant TB. Such a drug combination will synergistically target the energy metabolism of *Mycobacterium tuberculosis* or complementary targets.

An early review of RespiriTB was requested by the panel of experts following the stage 2 evaluation of the full proposal. Following the early review in September 2020, the panel of reviewers considered that RespiriTB has achieved its objectives and milestones for the period for all work packages (WPs) except WP1, which experienced significant delays in the testing of an asset in a Phase I clinical trial. The panel made a number of recommendations to the consortium in order to timely monitor the progress of the clinical trial. The implementation of the recommendations will be closely monitored in the next reporting periods and the mid-term review.

FAIRplus

The expert panel reported that the project has achieved its objectives and milestones and has already delivered significant results for the research community. The panel highlighted the following innovations in particular:

- the FAIR Cookbook, a public repository of ‘ingredients’ and ‘recipes’ that can be used for processing data to a FAIRer state;
- FAIR capability maturity model (CMM) for assessing capability for making data assets FAIR;
- legal templates for cross consortia agreements, maximising value/impact of data generated by IMI projects;
- The innovation ecosystem for SMEs across multiple sectors interested in the FAIR domain.

The expert panel recommended that alternative business models for the sustainability of the project's assets be proposed and discussed in the SME events already planned, through collaboration with other FAIR initiatives, and with the pharmaceutical industry.

MOBILISE-D

MOBILISE-D aims to deliver a valid solution (consisting of sensor, algorithms, data analytics, outcomes) for real-world digital mobility assessment to predict clinical outcomes in conditions that affect mobility. Although the project is experiencing delays due notably to the COVID-19 pandemic,

the panel valued the excellent work completed to date and the commitment of the consortium to keep the critical work on track. Furthermore, the panel considered impressive that EMA was already ready to publish a letter of support on the use of wearable sensors in regulatory drug trials.

The panel made a number of recommendations to the consortium with the view to further maximising the impact of the project results, including enhancing dissemination, data sharing and communication also to the tech innovation community. The panel recommended also a follow-up review to assess the progress of the project, including the implementation of the panel's recommendations.

Hypo-RESOLVE

Hypo-RESOLVE aims to reduce the burden and consequences of hypoglycaemia among people living with diabetes by providing researchers and clinicians with more validated data about the condition by: creating a sustainable clinical database; conducting studies to better understand the underlying mechanisms of hypoglycaemia; defining predictors and consequences of hypoglycaemia; calculating the financial cost in European countries.

The reviewers were very positive about the project's progress and achievements so far despite some delays experienced by the project. The majority of the delays have been caused by the COVID-19 pandemic and the project was advised to come up with a concrete plan to mitigate them. The panel has stressed the importance of sustaining the Hypo-RESOLVE database and made other important recommendations to help maximise the project's impact.

IMI-PainCare

The reviewers recognised that the project once completed has the potential to positively impact pain research and management by providing better outcomes and more targeted treatments of chronic pain in specific patient groups. Areas of value are the core outcome set as an important resource for assessing pain outcomes in clinical research and practice, the development of new mechanical and electrical stimulation devices, the novel application of wearable technology to track patients' physical and sleep activity, and back translational activities of promise for future drug discovery programmes.

Unfortunately, the work completed at the time of the review was less than intended, primarily due to delays as a result of the COVID-19 pandemic, but is nonetheless promising and lays the foundation for the remaining stages of the project. The reviewers provided some recommendations for optimising the activities in the remaining time of the project and for a broader dissemination strategy towards non-academic stakeholders.

IMMUcan

The goal of IMMUcan is to understand how the immune system and tumours interact, and the impact of therapeutic interventions. Following the early review of the IMMUcan project, the reviewers reported that the project has made good progress and that efforts should be continued to reach the project objectives in the time frame of the IMMUcan project.

The reviewers recommended measures aiming at increasing the clinical sample collection since the COVID 19 crisis and other factors have negatively impacted collection and analysis of clinical samples in the different indications covered by the project.

VITAL

The objectives of the VITAL project are to map the burden of vaccine-preventable infectious diseases in the elderly, and investigate vaccinations and immunity to infections in the ageing population. VITAL is expected to provide estimates of the clinical and economic consequences of possible vaccination strategies in different age and risk groups, and develop educational materials for stakeholders such as healthcare providers.

Following the early review of the VITAL project, the panel of experts deemed that the consortium has made very good progress in accordance with the objectives set for the period covered by this report, despite the limitations of the current COVID-19 pandemic situation, to which they reacted

appropriately, showing flexibility and a good capacity to adapt. The reviewers highlighted that it is not clear whether the sources for the data on the burden of disease are sufficient and whether these diseases are diagnosed in the labs to a sufficient extent or whether there could be underreporting given the ongoing COVID-19 outbreaks. At this point most of the data has been retrieved from retrospective studies and that of prospective studies will provide more unbiased results. The panel recommended that attention needs to be paid to the comprehensiveness of the data and the applicability of results to other EU countries.

LITMUS

The goal of the LITMUS project is to develop and validate highly accurate biomarkers, both blood test based and imaging techniques, that will allow doctors and researchers to rapidly and easily diagnose the severity of patients' disease and monitor or even predict the progression of non-alcoholic fatty liver disease (NAFLD) to steatohepatitis (NASH).

The reviewers were very positive about the project's progress and achievements so far despite some COVID-19 related delays experienced by the project. Of particular impact already is development and validation of a new disease-specific patient reported outcome measure (PROM) called NASH-CHECK, which will be the first PRO developed for NASH F1-F3 and F4 patients, and with input from patients following FDA guidance. This instrument once qualified as a novel methodology (biomarker) has the potential to become a well-accepted measure to assess symptoms and health-related quality of life (HRQoL) in clinical drug development programmes and clinical practice.

STOPFOP

STOPFOP is a drug repurposing project focusing on a rare disease called fibrodysplasia ossificans progressiva (FOP). In FOP, muscle tissue and connective tissue are gradually replaced by bone, forming bone outside the skeleton. As the disease progresses, patients' mobility decreases and the disease can also result in difficulties eating, speaking and breathing. There is currently no treatment. The objective of the project is to run a proof-of-concept clinical trial that aims to investigate the efficacy and safety of the drug AZD0530 (Saracatinib) for treating patients with FOP.

The most significant results delivered by STOPFOP during the period under review were generated at the operational and management level of the project. The start of the clinical trial has been severely delayed, mainly due to the outbreak of COVID-19 pandemic and Brexit. The panel of reviewers concluded that the project has achieved some of its objectives for the reported period and made recommendations on implementation. While it is anticipated that the COVID-19 pandemic will continue to impact the healthcare sector and clinical trials in the coming months, the reviewers recommended that the consortium focus on deliverables that can be prepared or need to be improved (e.g. a clinical trial data management plan and exploitation plan, including communication and business plan). In addition, the reviewers, recommended to potentially extend the duration of the project to compensate for delays due to COVID-19.

1.6 Key performance indicators and statistics

The IMI2 objectives are far-reaching and ambitious. In order to track IMI's progress towards these objectives, IMI uses key performance indicators (KPIs) that track IMI's activities in the following strategic areas:

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

IMI gathers data on these points via a dedicated web platform through which project coordinators can submit their project's results. The platform also allows IMI to aggregate and analyse data, and build a picture of project achievements as they evolve over time. Although these KPIs are designed for IMI2, where relevant IMI also gathers the data for IMI1 projects, as this allows us to explore the impacts of IMI since the very beginning.

The analysis of the data collected up to 31 December 2020 shows that almost all the relevant priority areas in the IMI2 Strategic Research Agenda (SRA) are addressed by IMI2 projects (11 out of 12).

An examination of the data shows that IMI2 projects have generated 208 assets that completed a significant milestone during the project lifecycle (versus a target of 50), and if we look at both IMI1 and IMI2 programmes together, the analysis reveals that IMI projects have reached 362 assets that completed a significant milestone so far. The definitions of 'projects' asset and achievements' and 'significant milestone' were meticulously defined. Examples of assets are tools, methodologies, processes, services, training materials, etc.; and 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 13 completed procedures (versus a target of 10) and if we look at both IMI1 and IMI2 programmes together there are 31 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, SOPs, use of screening platforms, clinical trial networks, etc.). The data shows 176 implementation results in IMI2 (versus a target of 50) and 482 implementation results if we consider both IMI1 and IMI2 programmes together.

Additionally, more than half of the projects (60 %) involve patient organisations and healthcare professionals' associations as consortium partners, members of advisory boards, members of stakeholder groups etc., and this trend has remained stable during the course of the IMI2 programme.

This analysis reveals a dynamic in which IMI projects are getting on track and in some cases surpassing the established targets now that a number of IMI2 projects have finished and are reaching the end of IMI2 programme's cycle. It is clear that projects need time to generate innovation and impact that can be detected and reported, and 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.

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 H2020 objectives. This allows the assessment of the results and impacts of the specific objectives of the programme, as detailed in Annex I, II, and III of the Council Decision 2013/743/EU establishing Horizon 2020 - the Framework Programme for Research and Innovation.

2 Management

2.1 Governance

2.1.1 Governing Board

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

In 2020, the Governing Board held four meetings (28 January; 27 March; 19 June; and 11 December). The list of decisions taken by the Governing Board in 2020 is available on the Governing Board page of the IMI website.

The role of Chair of the Governing Board in 2020 was assumed as follows:

Dates	Chair
28 January – 6 July 2020	Ms Irene Norstedt (European Commission)
7 July – 31 December 2020	Mr Olivier Laureau (EFPIA)

2.1.2 Executive Director

Dr Pierre Meulien was Executive Director of IMI throughout 2020.

2.1.3 States Representatives Group

The SRG is composed of official delegates 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.

As the mandates of the previous SRG Chair and Vice-Chair were due to end on 3 February 2020, IMI launched the election process in 2019, allowing the election to take place during the SRG's February 2020 meeting. The position of Chair is now held by Marta Gómez Quintanilla (Spain) and the position of Vice-Chair by Jan Skriwanek (Germany) for a period of maximum two years, subject to IMI2 JU being wound up before this period ends, in which case their mandate would expire automatically.

In 2020, the SRG met in February in Brussels (Belgium), and, due to the COVID-19 pandemic, via teleconference in May and September. At the meetings, the IMI Programme Office provided detailed updates on its activities, including on SMEs and patient engagement as well as on closed and ongoing projects, budget execution and forecasts. The SRG members also had the opportunity to discuss the benefits for Associated Partners and other industry sectors of participating in IMI based on concrete experience and ongoing projects. During 2020, the SRG was consulted on the Call topics and documents and on the Annual Work Plan (including amendments).

In agreement with the SRG and the SC, and considering the COVID-19 pandemic, the IMI Programme Office did not organise the annual joint meeting between the two advisory bodies. However, the IMI Programme Office ensured the regular interactions between the SRG and the SC through the respective chairs on matters of joint interest for the two advisory bodies, notably on SC membership, proposed topics for 2020, and IMI measures in response to the COVID-19 pandemic.

2.1.4 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, chaired by Professor Isabelle Bekeredjian-Ding, met three times in 2020, with only one face to face meeting due to the COVID-19 pandemic. The agendas of the meetings are available on the IMI website. Two additional teleconferences were organised to progress the SC recommendations towards finalisation. As part of their role, the members provided 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 fast-track Call 21; Call 22 and Call 23 (launched in 2020).

This year, the Scientific Committee completed its work plan agreed in 2019 and provided recommendations to the IMI Governing Board on matters important to the IMI objectives. These recommendations, which are published on the Scientific Committee page of the IMI website, cover both topics related to IMI's governance and structures i.e. recommendations on data infrastructure and integration; the involvement of regulators and regulatory science; and equitable access; as well as topics related to the research programme i.e. recommendations on rare diseases, and drugs repurposing.

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 2020 (see section 1.5.2), as well as on close-out meetings on IMI projects that have ended. Further to a decision of the IMI Governing Board, the mandate of the committee members and additional experts was extended for an additional period of two years as from 1 October 2020. Professor Isabelle Bekeredjian-Ding was confirmed as Chair and Professor Alfonso Valencia was elected as Vice-Chair.

In 2020, the IMI Governing Board decided to terminate the mandate of Dolores Cahill as a member of the IMI Scientific Committee following her public statements on COVID-19.

2.1.5 Stakeholder Forum

The IMI Stakeholder Forum 2020 was held online on Tuesday 10 November. The event is described in more detail in the section 'Communication and events'.

2.1.6 Strategic Governing Groups

Cross-SGG coordination

Two cross-SGG coordination meetings were hold in 2020. These meetings focussed on discussing the role and activities of the SGGs in line with the SGG Charter and once the idea generation phase of IMI2 concluded with the last Call launch. The output of these discussions was advice for the IMI Governing Board.

In 2020, 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 2020, the EC representation in the SGGs encompassed DG RTD, DG CNECT and DG SANTE.

SGG Diabetes/metabolic disorders

No dedicated SGG meeting was held in 2020. However, members of the SGG contributed to the discussions in the cross-SGG group.

SGG Digital health and patient-centric evidence generation

This SGG builds on the achievements of the former SGG on data and knowledge management. The SGG met twice during 2020: both meetings took place via video conference. The digital health portfolio was reviewed and the SGG provided input to the IMI Governing Board regarding topics that were launched in IMI2 - Call 23.

SGG Immunology

No dedicated SGG meeting was held in 2020. However, members of the SGG contributed to the discussions in the cross-SGG group.

SGG Infections control

The SGG Infections control met three times via teleconference during the year, no face-to-face meetings were possible this year due to the COVID-19 pandemic. The SGG Infections control was active in providing input to the IMI Governing Board regarding the scientific priorities for 2020. Moreover, the SGG Infections control also contributed to the development of one topic published through IMI2 – Calls 23.

SGG Neurodegeneration

The SGG Neurodegeneration met once in plenary session at the beginning of 2020. The SGG developed one Call topic that was launched under the IMI2 - Call 23.

SGG Oncology

The SGG Oncology held two meetings via teleconferences in 2020. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2020 and developed two Call topics that were launched under IMI2 - Call 23.

SGG Translational safety

The SGG Translational safety met once in plenary session via videoconference. The meeting took place after the launch of the last IMI2 Call for proposals. It focused on the possible role of the SGG in the remaining IMI2 programme including progress monitoring of ongoing projects, ways to maximise synergies, sustainability of project results, as well as assessing uptake of project results by the industry.

2.1.7 Associated Partners

The scope of IMI2 covers all areas of life science research and innovation of public health interest. The research it supports should be undertaken in areas where the combination of societal, public health and biomedical industry competitiveness goals requires the pooling of resources between the public and private sectors, and foster collaboration between the key players involved in healthcare research. To help achieve these goals, IMI2 seeks to involve a broader range of partners from different industrial sectors, charitable foundations and philanthropic organisations. Therefore, IMI2 membership is open to any legal entities interesting in supporting the IMI2 objectives in their specific areas of research by offering the possibility to become an Associated Partner.

IMI has continued to develop Associated Partner methodologies including 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 38 Associated Partners, many of whom are participating in multiple topics.

Six new Associated Partners were accepted in 2020:

(1) DZIF (German Centre for Infection Research) is contributing to Call 20, topic 3 (Academia and industry united innovation and treatment for tuberculosis – UNITE4TB).
(2) Global Health Drug Discovery Institute is supporting the Call 21 Coronavirus Call.
(3) Ion Beam Applications S.A. is supporting Call 20, topic 5 (Proton versus photon therapy for oesophageal cancer – a trimodality strategy).
(4) Klinikum der Universtät München is contributing to Call 20, topic 3 (Academia and industry united innovation and treatment for tuberculosis - UNITE4TB).
(5) Link2Trials will contribute to Call 23 (Behavioural model of factors affecting patient adherence).
(6) Varian Medical Systems Particle Therapy is contributing to Call 20, topic 5 (Proton versus photon therapy for oesophageal cancer – a trimodality strategy).

Four existing Associated Partners expanded the scope of their association to support new topics:

(1) JDRF expanded their contribution to support Call 19 (INNODIA HARVEST).
(2) The Leona M. and Harry B. Helmsley Charitable Trust expanded their contribution to support Call 19 (INNODIA HARVEST).
(3) The Bill & Melinda Gates Foundation expanded their contribution to support the Call 21 coronavirus Call.
(4) The University of Dundee expanded their contribution to support the Call 21 coronavirus Call.

A full list of all IMI Associated Partners can be found on the Associated Partners page of the IMI website.

2.2 Communication and events

As in any other corporate area, the COVID-19 pandemic had a huge impact on the communication unit, and it did so at different levels. We reprioritised our content, reaching out to our stakeholders to inform them about the resources mobilised by IMI to tackle the spread of COVID-19; we reprioritised our activities and formats, in particular the events we had already planned; and we redoubled our efforts to share project success stories on all those other diseases that risked to be out of the limelight; above all, we continued to work very closely with our stakeholders to provide factual, rigorous information in times where misconceptions and false news can cost lives.

IMI's coronavirus response

A fast-tracked coronavirus Call for proposals – The urgency to publish this Call meant that the usual promotional activities were carried out extremely rapidly. The news article on the launch of the EUR 45 million Call for proposals had 11 933 unique views and the Call 21 topic page had 40 563 views, which proves the high levels of interest in the Call. In an unprecedented move, IMI also published high-level information on the projects that had been selected for funding before the Grant Agreements had been signed. Once the Grant Agreements were signed, we also published and promoted news items, which included interviews with the project leaders, on each project.

Expanding our reach by feeding into EC communications– since the beginning of the crisis, IMI has worked very closely with the European Commission to coordinate on the communication of the common European coronavirus response, by contributing information and materials about the IMI funded treatment and diagnostic projects.

Drawing attention to 'repurposed' IMI projects – In addition to IMI´s coronavirus Call, there are a number of past and ongoing IMI projects that have either contributed or are contributing to the collective effort to fight COVID-19. These projects were also highlighted in a speech that was delivered by the Executive Director, Pierre Meulien, during his appearance at the Budgetary Control (CONT) Committee hearing in the European Parliament.

Finding stories in research

IMI news articles – Building on the communication strategy implemented in 2019, each month the communication team takes an in-depth look at a particular topic, selected based on IMI´s project portfolio. IMI uses different formats to approach each topic: there are individual research project stories, interviews, Q&A articles, an editorial article from the perspective of the IMI Executive Director, videos that explain a research objective, and videos that explain IMI's funding approach. Over the course of 2020, IMI chose nine themes, ranging from SMEs to autoimmune diseases, featuring nine editorials by IMI's Executive Director, 26 project stories, 9 videos and 3 infographics. In addition, 25 further project stories and 11 articles on IMI internal news were also added to the Newsroom page.

Close-out meetings – Once a project's final report has been submitted, IMI convenes a close-out meeting. During a close-out meeting, one, two or sometimes even three different consortia present the achievements, challenges, sustainability plans and tangible results of their projects to assembled members of the IMI office and selected stakeholders such as members of the IMI pool of patients or the IMI Scientific Committee. Following each close-out meeting, the IMI communication team writes a factsheet that summarises the project's achievements and impacts. The factsheet is published on the IMI website and promoted through the IMI newsletter and social media channels. Depending on the project outputs, other communication materials such as news articles, testimonials or video interviews may be produced. The following material has been published following close-out meetings in 2020.

- WEB-RADR 2: summary of project achievements | Finally a reliable way to track drug side effects
- MOPEAD: summary of project achievements | Web search keywords can help spot early Alzheimer's patients
- EMIF: summary of project achievements | When data is FAIR, citizens ultimately reap the benefit
- BIOVACSAFE: summary of project achievements
- ADVANCE: summary of project achievements
- ROADMAP: summary of project achievements

- DOIT: summary of project achievements
- NGN-PET: summary of project achievements | IMI pain project creates new business for Italian SME Axxam

Amplifying the reach of IMI project results – Four articles were published in the Cordis 'Results in Brief' collection:

- ZAPI: Beyond COVID-19: Preparing for the next pandemic
- RESCEU: Pan-European study on RSV infection fuels future research and surveillance
- NGN-PET: Neuron-glia co-cultures, towards better treatment options for neuropathic pain. This project was further featured in an *Research*eu Magazine* special issue on New solutions to soothe chronic pain
- MOPEAD: Diagnosis of hidden Alzheimer's disease

In addition, PERISCOPE was added to the EC catalogue of research success stories: New tools and trials combat the resurgence of whooping cough,

Project results to counter misconceptions – Communicating widely and rigorously on IMI's activities and the results produced by our projects is crucial to ensuring a robust accountability vis-á-vis IMI´s founding members and the scientific community. We welcome informed criticism and are the first to acknowledge that constant improvement and new ideas are imperative to ensuring that IMI serves the interests of EU citizens. However, IMI sometimes faces criticism based on certain misunderstandings and inaccuracies. When this happens, IMI responds with clear facts, as demonstrated in our publication IMI - the full story: IMI responses to the GHA / CEO report "In the name of innovation" and the correspondence to the editor piece "Innovative Medicines Initiative plays the long game on research funding", authored by Pierre Meulien and published in *Nature Microbiology*.

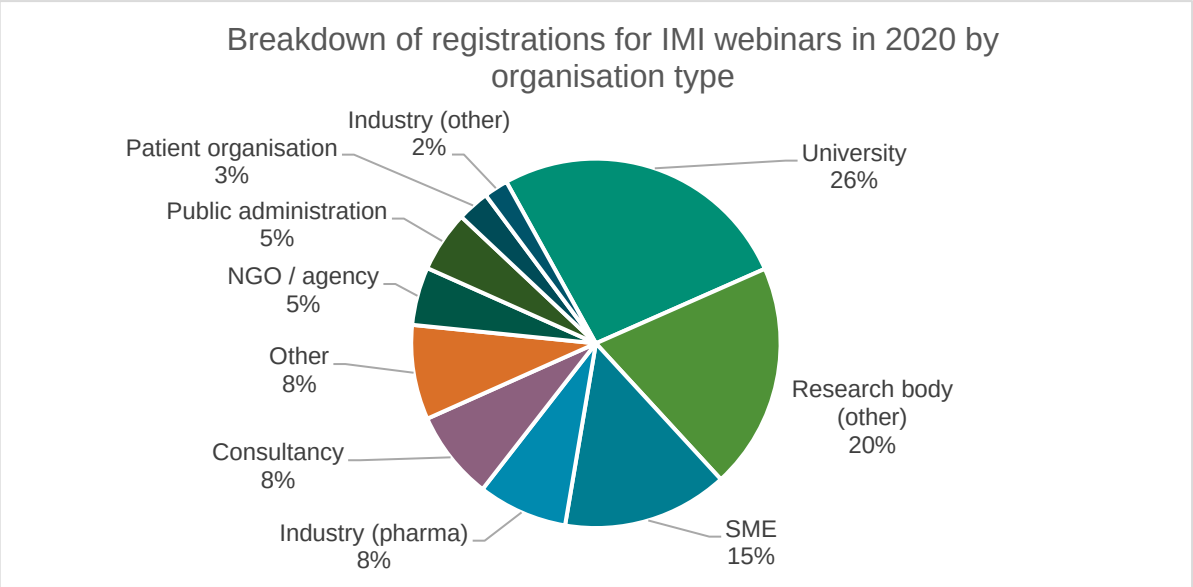
Call outreach activities

IMI launched four Calls for proposals in 2020: IMI2 – Call 20 (on 21 January); IMI2 – Call 21 (on 3 March); and IMI2 – Calls 22 and 23 (on 23 June). All Calls were actively promoted through IMI channels, namely the website, social media, videos (which were translated into 5 central and eastern European languages), press, mailshots, newsletters, flyers and multipliers (notably the SRG and National Contact Points).

As always, IMI published draft information on the topics and started promoting the Calls well in advance of the official launch, to give potential applicants a head start on preparing their proposals and forming a consortium.

This was particularly important for IMI2 – Call 21, which was a fast-track, single stage Call on coronavirus treatments and diagnostics with a deadline for submitting proposals just four weeks after the official launch. IMI alerted audiences to the fact that a Call in this area was under preparation on 11 February, and published the draft text on 17 February. Both the European Commission and EFPIA also promoted the Call through their channels, and this combined effort raised a lot of interest in the Call and resulted in a large number of proposals, despite the short timeframe.

IMI also ran 18 webinars on Calls for proposals in 2020, covering all Call topics, plus IMI's rules and procedures and opportunities for SMEs. In total, just over 2 000 people registered to attend the webinars. As the graph below shows, the majority of those registering come from universities, other research bodies, and SMEs, reflecting the main target audience for these events.



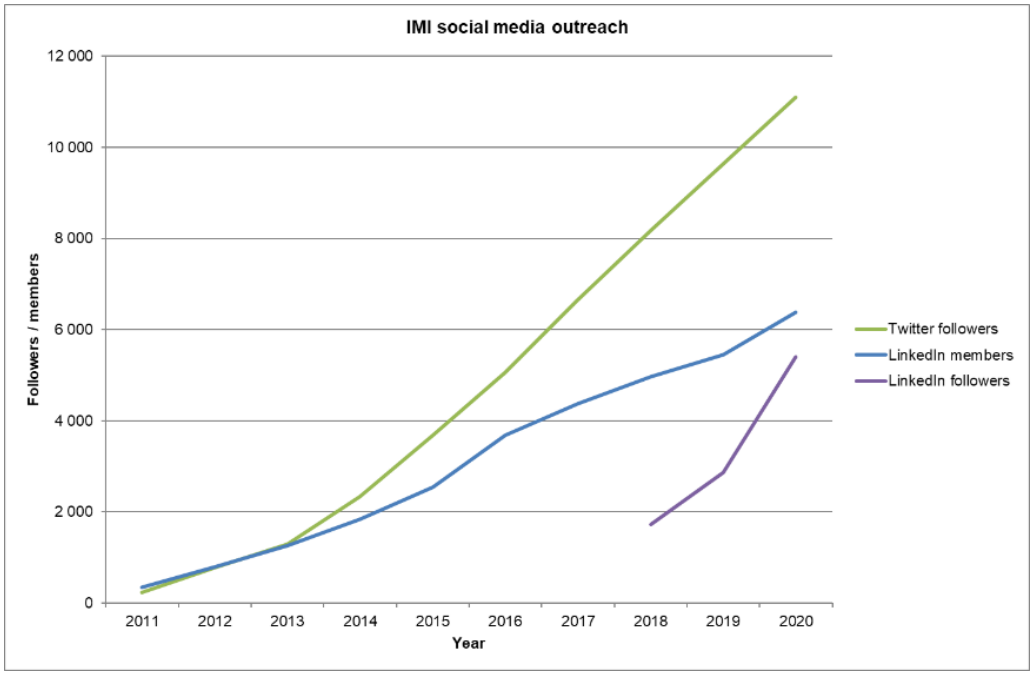
Social Media

Over the past few years, the IMI Twitter account has been one of the principal tools for distributing content to a wider audience. In 2020, @IMI_JU tweeted 510 original messages in addition to regular retweets, particularly from IMI projects, which resulted in 1.8 million impressions, 2 864 link clicks, 2 296 retweets and 3 706 likes. By the end of 2020, the IMI Twitter account had11 095 followers, up from 9 640 the year before.

IMI is also increasingly active on LinkedIn, using it to advertise Calls, project successes, and more. By the end of 2020, the number of IMI's followers had almost doubled, from 2 862 to 5 407. As on Twitter, IMI regularly shares posts by projects who tag IMI. In total, IMI's posts gained 207 557 impressions, 5 489 clicks, 2 929 reactions, 58 comments, and 811 shares. In general, engagement levels are much higher on LinkedIn than Twitter. A quarter of the followers are from the pharmaceutical industry, with other well-represented groups being research (14 %), biotechnology (10%) and hospitals and healthcare (7%).

IMI also has a LinkedIn group which has 6 379 members, but as engagement levels there are lower we plan to close this group in early 2021. Meanwhile we are encouraging members to follow the IMI LinkedIn profile.

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 urls were 'apply for funding' (63 701 unique page views), followed by 'news and events' (51 035 unique page views, which means and increase of 139% in relation to 2019) and the homepage.

According to Europe Analytics, the average number of visitors per month is 18 059. Geographically speaking, the United States, Belgium, the UK, Germany, Italy, Spain and France were the countries from where 47 % of visitors originated.

The figures below provide a snapshot of 2020 website visit-related indicators.

- **330,847** visits
- **2 min 18s** average visit duration
- **59.68%** visits have bounced (left the website after one page)
- **2.48** actions (page views, downloads, outlinks and internal site searches) per visit
- **0.2s** average generation time
- **697,814** pageviews, **579,303** unique pageviews
- **15** total searches on your website, **3** unique keywords
- **62,055** downloads, **56,870** unique downloads
- **58,634** outlinks, **53,159** unique outlinks
- **440** max actions in one visit

Newsletter

IMI publishes a monthly newsletter with corporate news and highlights from its projects. By the end of 2020, there were 3 825 subscribers (compared to 3 211 in 2019). The breakdown of subscribers' organisations is as follows: 47% research organisations, universities and hospitals; 14% SMEs; 14% large industry (424 pharma industry subscribers and 99 other large industry subscribers) and 2% non-profit organisations, largely comprised of patient organisations. It is worth noting that almost 14% of subscribers come from organisations that act as amplifiers of IMI such as EU, national and regional authorities (6%), consultancies (7%) and press/PR agencies (1%). The monthly tweet highlighting the newsletter stories features consistently among the most popular in IMI's Twitter feed.

Europe's research and innovation partnerships: Innovation in action!

Europe's research partnerships are delivering cutting-edge research and innovation and achieving great things together. These are the key messages of the week-long 'Innovation in Action' communications campaign run jointly by IMI and seven other joint undertakings, namely BBI JU (Bio-based Industries Joint Undertaking), Clean Sky 2, ECSEL JU (Electronic Components and Systems), F4E (Fusion for Energy), FCH JU (Fuel Cells and Hydrogen Joint Undertaking), SESAR (SESAR Joint Undertaking), and S2R JU (Shift2Rail Joint Undertaking). The campaign ran throughout the week of 30 November and targeted policy makers and opinion leaders in EU research and innovation. At the heart of the campaign was a brochure which highlights the mission-oriented nature of the JUs, as well as the ways in which they contribute to the EU's competitiveness and key European policies such as the European Green Deal and Digital Europe. Other campaign materials included two gifs showcasing some of the key facts and figures about JUs. On social media, the campaign hashtag #InnovationInAction was used. The campaign saw all JUs promote the shared messaging via all channels, including websites, newsletters and social media.

Publications

The publications delivered by the Communication team in 2020 prominently focus on IMI´s project results and include:

- Brochure: IMI - radical collaboration in action showcases some of IMI's recent project successes, which include an approved vaccine for Ebola, insights into the genetics of Alzheimer's disease, a new classification of diabetes, and advances on using liquid biopsies for cancer. In addition, many projects are making very practical contributions to the fight against COVID-19.
- IMI - the full story: IMI responses to the GHA / CEO report "In the name of innovation"
- Joint Undertakings: Innovation in Action (2020)
- Factsheet: How is IMI helping in the EU response to COVID-19?
- Factsheet: IMI preparing for pandemics
- Factsheet: IMI cancer research

Press

In 2020, IMI was mentioned in 7 233 articles in a range of magazines, industry press and online media worldwide (1 971 of them in the EU, including UK), which clearly indicates the international relevance of the PPP. Highlights for IMI include a wide coverage across Europe of the EC decision to grant marketing authorisations to Janssen for the IMI co-funded vaccine against Ebola and the COVID-19 funded projects. The IMI model was also featured in the discussions around the future partnership.

IMI was mentioned in the title or opening lines of some 10% of these articles. The tonality of the media coverage was predominantly neutral (94.5%), with 5.4% of articles registering a positive tone and the remaining 0.1% registering a negative tone.

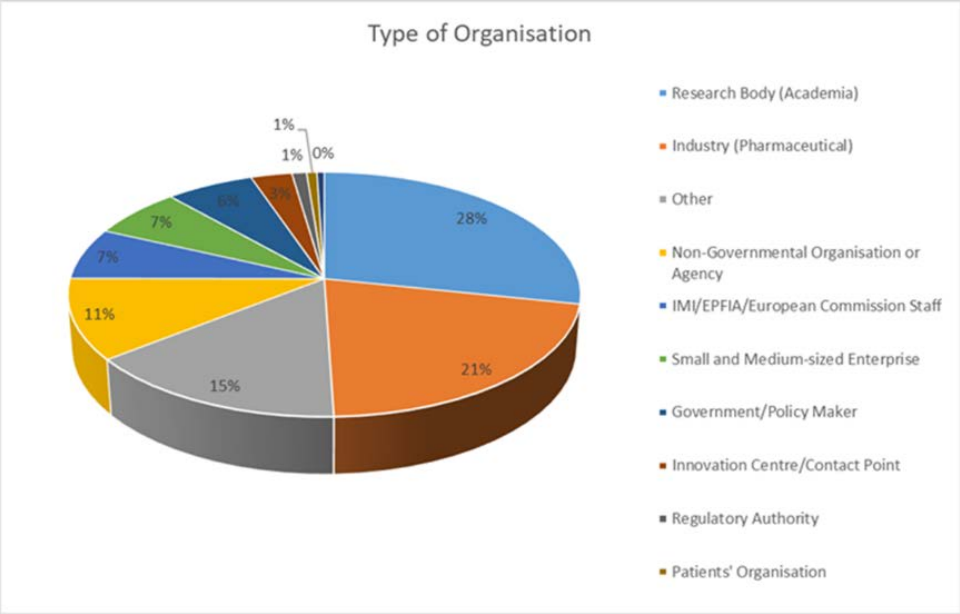
Events

At the start of 2020, IMI had a number of the events planned in Brussels and elsewhere. As COVID-19 spread and restrictions on travel and gatherings were introduced, these events were either cancelled or moved fully or partially online. We decided in the spring to move our annual Stakeholder Forum online, a decision which allowed us to plan for an online event from the start. Furthermore, this offered a measure of reassurance for speakers, attendees, contractors and ourselves that the planned activities would not be derailed by potential

travel restrictions. On the day of the event, a limited number of staff and contractors were present at the IMI offices to ensure the set-up and smooth running of the event. All followed the relevant safety protocols.

The IMI Stakeholder Forum 2020 took place on 10 November. The theme was 'Broader horizons: growing Europe's health partnership' which was addressed in two sessions and a keynote speech by MEP Maria da Graça Carvalho. A high-level panel representing the founders of the proposed new health partnership discussed the next phase of IMI, taking stock of what has been achieved. The second panel focussed on paediatric cancers to demonstrate how a new partnership would bring new stakeholders together, synergise with the European Commission's Cancer Mission and be more inclusive in the co-creation of ideas for the programme. A Science Business article published the following day captured the main discussion points around the next partnership.

Over 954 participants registered for the event. A total of 586 unique IP addresses in 48 countries worldwide participated in the Stakeholder Forum, with a peak of 494 participants connected at the same time. The audience remained stable during the whole event. As showed in the pie chart below, participation in the event was, once again, very balanced in terms of sectors, which makes the event a true stakeholder forum.



Regarding social media, a peak in engagement rate and views could be observed thanks to the increase of posts by IMI and their multiplier effect. @IMI_JU original messages got 31.8K impressions and 469 engagements. These figures show that the Stakeholder Forum remains a relevant tool to enhance IMI´s visibility.

For external events where IMI had planned to have a session and/or an exhibition stand in 2020, IMI decided on a case-by-case basis whether or not to go ahead with the online version of the event.

- IMI held an online session entitled 'Virtual patient cohorts: breaking the data deadlock' at ESOF (EuroScience Open Forum) 2020 on 4 September. Building on the research carried out by IMI´s EPAD and AETIONOMY projects, where scientists proved that it is possible to build a fully-functioning virtual patient cohort, panellist explored the scope for virtual patient applications.

- IMI sponsored a session on 'Preparing for the next pandemic. The role for PPPs in the health sector', which was part of the Science Business conference on *Industrial R&D: Europe First?* that took place on 9 September. The panellists from IMI, EFPIA and the European Commission discussed the essential contribution of the EU research and innovation funds to ensuring Europe is more prepared and more resilient for further pandemics and, in particular, the relevance of technology convergence in the next health PPP.

In addition, IMI staff members participated in the following events, raising IMI's visibility.

- 17 January: IMI2 Information Day at the EC Representation in Sofia (Bulgaria)
- 22 January: IMI info day in Milan 'Innovative Medicines Initiative 2020. Nuove call e prospettive future per la partnership europea'
- 18 February: European Alzheimer's Alliance & the European Parliament, lunch debate on 'The Innovative Medicines Initiative (IMI): Advancing Alzheimer's research through private-public partnerships', Brussels
- 18 February: I-com institute for competitiveness, conference on 'Innovative Europe - The way forward: Taking Stock and Thinking Ahead', Brussels
- 27-28 February: International Alliance for Biological Standardization (IABS) 65th Anniversary Scientific Conference on 'New paths for sustainable solutions to tackle global and emerging infectious threats', Lyon
- 20 May: European Parliament's Animal Welfare Intergroup, webinar on 'The role of non-animal approaches in COVID-19 related research'
- 14 May: IMI info day in France
- 2 June: 2020 International Brain Investigators Meeting IUCRC BRAIN - IUCRC CARTA - EU HBP
- 29 June: DIA Europe online conference, EMA session on 'Enabling the translation of Research and Innovation onto Regulatory Standards'
- 30 June: DIA Europe online conference, Roche session on 'Preparing health systems for Integrated and Personalised Care'
- 14 July: EAPM Global online conference: 'Forward Together - Where we are now and the necessary next steps for a resilient healthcare System – effective ways of investing in healthcare in a COVID 19 and Post COVID 19 World'
- 27 July: Turkey in Horizon 2020 Phase II (Call 23)
- 8 September: Science|Business public webcast conference 'Industrial R&D: Europe First?'
- 15 September: ERIC Forum policy seminar 'Funding mechanisms for access to ERIC translational services'
- 17 September: EUPATI Annual General Meeting
- 17 September: European Commission, DG RTD, EU-Japan webinar on COVID-19 & Research
- 17 September: 'The future of brain health in Europe' breakfast meeting with Frédéric Destrebecq, European Brain Council
- 17 September: Women's Brain Project 'Regulatory roundtable on advancing women's health and precision medicine'
- 24 September: BIOTECH Conference 'Patient engagement'
- 13 October: European Brain Council (EBC) event 'Disrupt and rewire: how brain innovation is changing Europe'
- 16 October: EurSci4Healtth, stakeholders workshop 'Science for Health: The Agenda for 2021-2027'
- 6 November: EBC Brain Talks
- 6 November: Sanofi Partnering Days
- 10 November: 8th International mRNA Health Conference
- 11 November: SCOPE Summit Europe and Clinical Trial Innovation Summit US
- 18 November: World Dementia Council High-level Workshop: 'RESEARCH progress towards the 2025 goals in the research space'
- 25 November: ISPOR Europe 2020
- 9 December: FAIRplus webinar 'What is the value of FAIR data'
- 10 December: BioFIT/MedFIT Digital 2020 Conference

2.3 Budgetary and financial management

2.3.1 2020 total budget

The total IMI budget for 2020 was **EUR 276 538 561** in commitment appropriations (CA) and **EUR 241 559 114** in payment appropriations (PA). The budget execution of the commitment appropriations and the payment appropriations reached **98.66 %** and **97.08 %** 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.

The IMI Governing Board approved the 2020 budget on 13 December 2019. The budget was subsequently amended during 2020, driven by revenue and expenditure updates as follows:

- to enter in the budget the carry overs of the preceding financial year;
- to update the forecast of revenue and expenditure on the basis of revised activities under the Horizon 2020 voted budget;
- to update the revised payments appropriations forecast, mainly driven by IMI2 - Call 21 pre-financing, related to coronavirus infections.

The Governing Board approved the first budget amendment on 28 February 2020 in order to include the carry over amounts (EUR 8 623 432 commitment appropriations (CA) and EUR 6 612 304 payment appropriations (PA)) from the previous year. The first budget amendment also included a reduction in the commitment appropriations of EUR 6 627 250 and in the payment appropriations of EUR 4 879 259, mainly due to prioritisation of and redeployment to climate-related activities under Horizon 2020 in the voted 2020 budget.

The Governing Board approved the second budget amendment on 8 May 2020 in order to reflect the adjustments of budget allocated per Call. It included the increase of the IMI2 JU financial contribution allocated to IMI2 - Call 21 (actions related to the development of therapeutics and diagnostics combating coronavirus infections). The total budget remained unchanged.

The Governing Board approved the third budget amendment on 19 June 2020 in order to include the latest figures of the operational commitment appropriations and a change in administrative expenditure. The administrative budget was reduced by EUR 29 400 on commitment appropriations and by EUR 14 700 on payment appropriations, due to the transfer from the EC Health programme.

The Governing Board approved the fourth budget amendment on 6 October 2020 in order to include the increase of operational payment appropriations by EUR 30 000 000, for IMI2 - Call 21 pre-financing. The total budget remained unchanged.

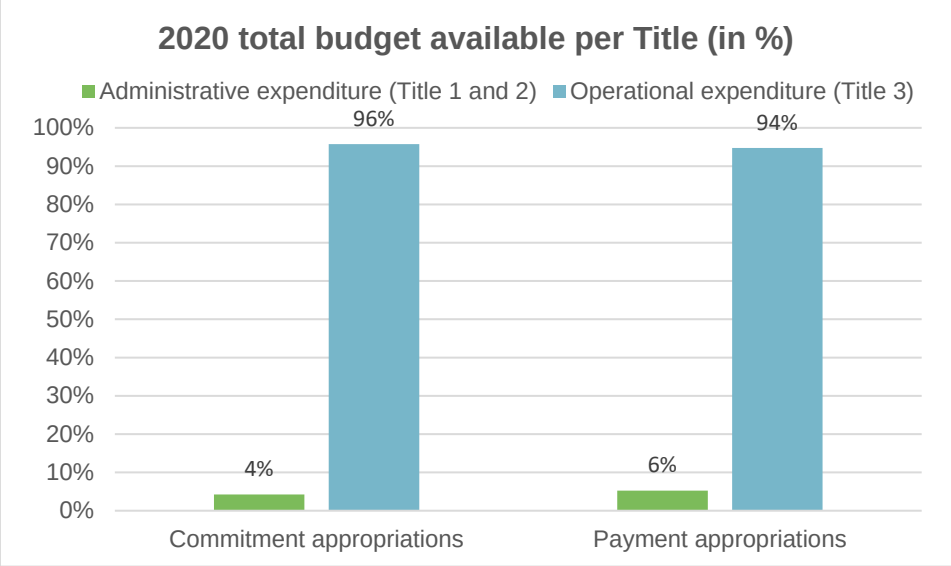
Overview of the total budget 2020 in EUR

	Revenue	Adopted Budget 2020.0		Budget 2020 Amendment 1		Budget 2020 Amendment 3		Budget 2020 Amendment 4		Assigned revenue*	Assigned revenue*	Final Budget 2020	
Title Chapter		CA	PA	CA	PA	CA	PA	CA	PA	CA	PA	CA	PA
10	European Commission contribution (including EFTA contribution)	261 547 957	200 631 535	-6 641 950	-4 893 959	-14 700			30 000 000			254 891 307	225 737 576
C2	Appropriations carried over	6 314 588		8 623 432	6 612 304							14 938 020	6 612 304
EC contribution		267 862 545	200 631 535	1 981 482	1 718 345	-14 700	0	0	30 000 000			269 829 327	232 349 880
20	EFPIA contribution	5 576 241	5 576 241	14 700	14 700	-14 700	-14 700					5 576 241	5 576 241
21	Subsidy from other Members other than the Union and the Associated Partners or their constituent entities or their affiliated entities		1 000 000									0	1 000 000
EFPIA and other Members' contributions		5 576 241	6 576 241	14 700	14 700	-14 700	-14 700					5 576 241	6 576 241
30	Associated Partner contributions		1 500 000									0	1 500 000
Associated Partner contributions			1 500 000	0	0							0	1 500 000
C4	Assigned revenue									1 132 993	1 132 993	1 132 993	1 132 993
	Total revenue	273 438 786	208 707 776	1 996 182	1 733 045	-29 400	-14 700	0	30 000 000	1 132 993	1 132 993	276 538 561	241 559 114
	Expenditure												
Title 1	Staff expenditure	6 579 673	6 579 673	-	131 463					595	595	6 580 268	6 711 731
Title 2	Infrastructure expenditure	4 572 809	4 572 809	29 400	1 972 835	(29 400)	(14 700)			52 325	52 325	4 625 134	6 583 269
Title 3	Operational expenditure	262 286 304	197 555 294	1 966 782	(371 253)				30 000 000	1 080 072	1 080 072	265 333 158	228 264 113
	Total expenditure	273 438 786	208 707 776	1 996 182	1 733 045	-29 400	-14 700	0	30 000 000	1 132 993	1 132 993	276 538 561	241 559 114

Notes on the budget table:

- The assigned revenue shows the amounts recovered during the year from suppliers and projects.
- The second budget amendment reflected the adjustments of budget allocated per Calls, within Title 3. The total budget remained unchanged.

The graph below shows the total 2020 budget available per Title in %.

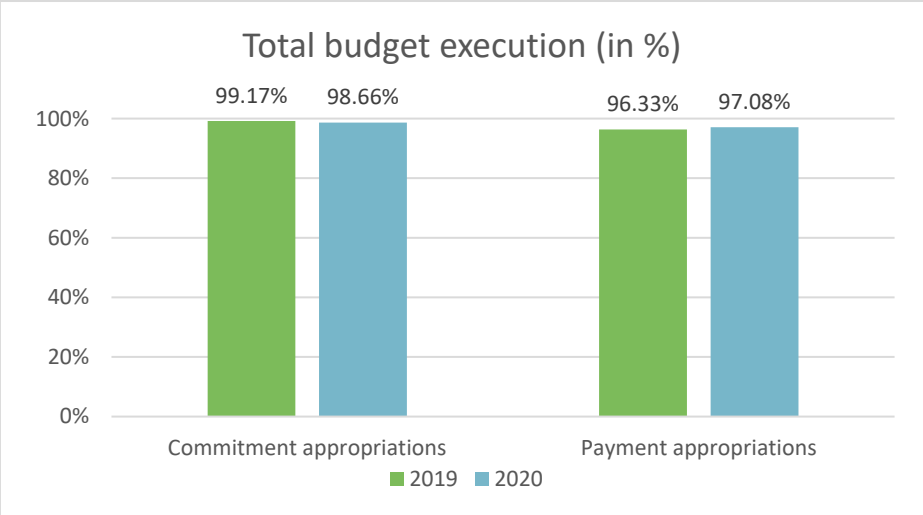


2.3.2 Total budget execution

The table below shows the execution of the 2020 budget per Title in absolute amounts.

Title	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	6 580 268	5 397 963	82.03%	6 711 731	5 416 371	80.70%
Title 2	4 625 134	3 210 436	69.41%	6 583 269	3 368 952	51.17%
Subtotal administrative expenditure	*11 205 403*	*8 608 399*	*76.82%*	*13 295 000*	*8 785 322*	*66.08%*
Title 3	265 333 158	264 231 583	99.58%	228 264 113	225 726 192	98.89%
Total (Title1, 2 and 3)	276 538 561	272 839 982	98.66%	241 559 114	234 511 515	97.08%

The following graph shows the 2020 total budget execution compared with 2019.



2.3.3 Budget transfers

In 2020, there were no budget transfers between titles. Budget transfers between chapters were authorised in 2020, which led to the following changes in commitment appropriations (CA):

Chapter		Budget adopted and assigned revenue (EUR)	Budget transfer (EUR)	Budget after transfers (EUR)
		CA	CA	CA
11	Staff in active employment	5 972 049	-20 700	5 951 349
12	Staff recruitments – misc. expenditure	19 538	-	19 538
13	Missions expenses	186 203	-	186 203
14	Socio-medical structure	207 100	20 700	227 800
15	External staff services	175 840	-	175 840
17	Representation	19 538	-	19 538
20	Office building and associated costs	776 625	-10 000	766 625
21	IT (hardware and software)	796 582	226 400	1 022 982
22	Office equipment	154 348	-149 348	5 000
23	Current administrative expenditure	164 116	26 000	190 116
24	Telecommunication & postal expenses	78 283	-	78 283
25	Formal meetings	156 302	-26 652	129 650
26	Administrative expenditure in connection with operational activities	388 801	-16 000	372 801
27	External communication, information and publicity	610 555	-	610 555
28	Service contracts	522 635	-50 400	472 235
29	Expert contracts & cost of evaluations	976 887	-	976 887
	Total	**11 205 403**	**-**	**11 205 403**

2.3.4 Overview of total commitments outstanding

The table below shows the summary of commitments outstanding at the end of 2020, for administrative and operational expenditure.

	EUR
Commitments carried from previous year	871 011 118
De-commitments (-)	-8 240 244
Payments made during 2020 related to commitments carried forward (-)	-197 009 653
Commitments made during 2020	272 839 982
Payments made during 2020 related to commitments made during 2020 (-)	-37 501 861
Total commitments outstanding at the end of 2020	**901 099 341**

2.3.5 Operational budget

IMI's operational budget in 2020

The total operational budget for 2020 was EUR 265 333 158 in commitment appropriations (CA) and EUR 228 264 113 in payment appropriations (PA). In 2020, the operational commitment and payment appropriations reached a level of 99.58 % and 98.89 % respectively.

The year 2020 was the last year of the H2020 program. The commitment appropriations related to H2020 were consumed by launching last IMI2 Calls for proposals: 20, 21, 22, and 23, and by Grant Agreements implementing IMI2 - Calls 17, 18 and 19.

The payment appropriations related to H2020 were mainly used by pre-financing for projects of IMI2 - Calls 15, 17, 18, 19, 21, and by interim and final payments for projects of IMI2 – Calls 1-16.

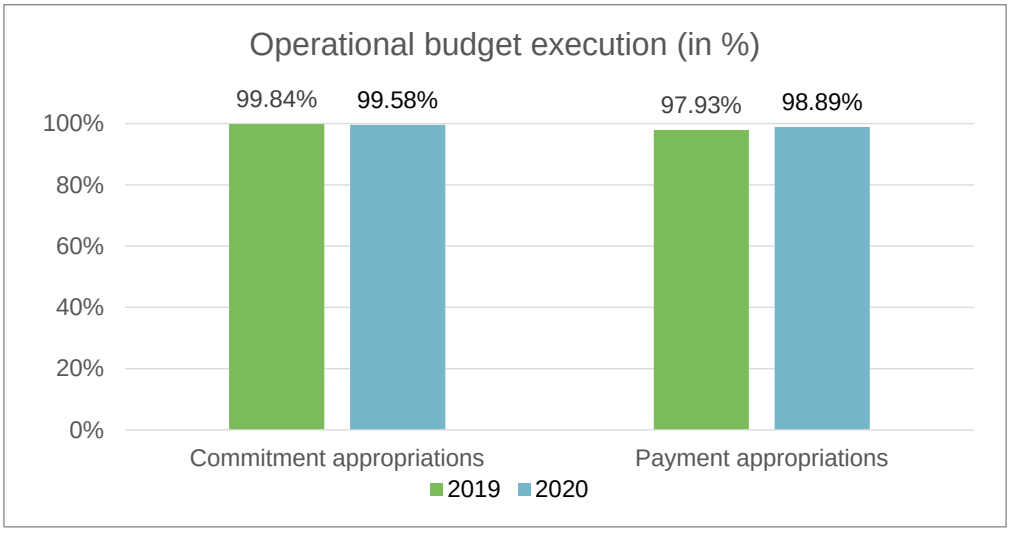
The payment appropriations related to FP7 were mainly used by payments for periodic or final reports for projects of IMI1 – Calls 3-11.

The significant achievement of both commitments and payments execution rates shows a continuation of the trend start in previous years in the absorption of operational appropriations, as a result of continuous actions taken in the budgetary planning and monitoring processes. In the context of 2020, despite the exceptional circumstances created worldwide by the COVID-19 pandemic, IMI has managed to achieve remarkable results.

More specifically, regarding operational commitment appropriations, in 2020 four competitive Calls for proposals implementing the 2020 scientific priorities were launched. In particular, IMI2 - Call 21 responded to the public health emergency regarding the novel coronavirus outbreak (COVID-19). It was initially launched with a budget of EUR 45 million, which was later increased to EUR 72 million.

In terms of operational payments appropriations, during 2020, the operational payment appropriations were increased by 30 million EUR, through a budget amendment, for IMI2 Call 21 in connection with actions related to the development of therapeutics and diagnostics combatting coronavirus infections. As eight new projects were added to IMI 2020 portfolio, there was also a need to pay pre-financing not foreseen in the original 2020 budget adopted in December 2019.

The graph below shows the 2020 operational budget execution compared with 2019.



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

Execution of commitment appropriations in EUR.

	Totals		%
	Appropriations	Execution	
*IMI1 (FP7) **	958 825	5 485	*0.57 %*
IMI2 (H2020)	264 374 334	264 226 098	*99.94 %*
Title 3 implementing the research agenda of IMI	**265 333 158**	**264 231 583**	**99.58 %**

**IMI1 (FP7) appropriations stemming mainly from amounts recovered during 2020 from projects (assigned revenue)*

Execution of payment appropriations in EUR

	Total		%
	Appropriations	Execution	
IMI1 (FP7)	53 366 988	51 333 903	96.19 %
IMI2 (H2020)	174 897 126	174 392 289	99.71 %
Title 3 implementing the research agenda of IMI	**228 264 113**	**225 726 192**	**98.89 %**

In the table below, the commitments carried forward from 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 (commitments level 1) are consumed by the commitments based on the Grant Agreements concluded (commitments level 2). 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 2020.

Commitments carried forward from previous year 2019	Commitment appropriations in EUR				
	Carry forward	Commitments made during 2020	De-commitments	Payments	Commitments outstanding at end 2020
IMI1 (FP7)	146 269 472	5 485	0	-51 333 903	94 941 054
IMI2 (H2020)	722 666 748	264 226 098	-7 651 571	-174 392 289	804 848 985
Total Title 3	**868 936 220**	**264 231 583**	**-7 651 571**	**-225 726 192**	**899 790 040**

At the end of 2020, the following level 1 commitments, related to Calls launched during 2020, were open and will be carried forward to 2021:

Description	EUR
IMI2 - Call 20	133 009 000
IMI2 - Call 22	11 427 098
IMI2 - Call 23	47 790 000
TOTAL	**192 226 098**

2.3.6 IMI's operational budget per programme

IMI's operational budget (Title 3) reflects expenses linked to the implementation of the IMI research agenda. 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)

  As initially set out in the 2014 Council Regulation, the EU has committed to contribute EUR 1.638 billion from H2020 to the IMI2 programme, comprising EUR 1.595 billion for operational activities and EUR 43 million for administrative activities.

  At the end of 2020, the total EU commitments available at programme level over the lifetime of IMI2 (2014-2020) amounted to EUR 1.4922 billion, comprising EUR 1.4492 billion for operational activities and EUR 43 million for administrative activities.

  This figure results from the initial EUR 1.638 billion (as initially foreseen in the 2014 Council Regulation), minus EUR 139.1 million (reduction in 2019), minus EUR 6.7 million (redeployment to climate related activities under Horizon 2020).

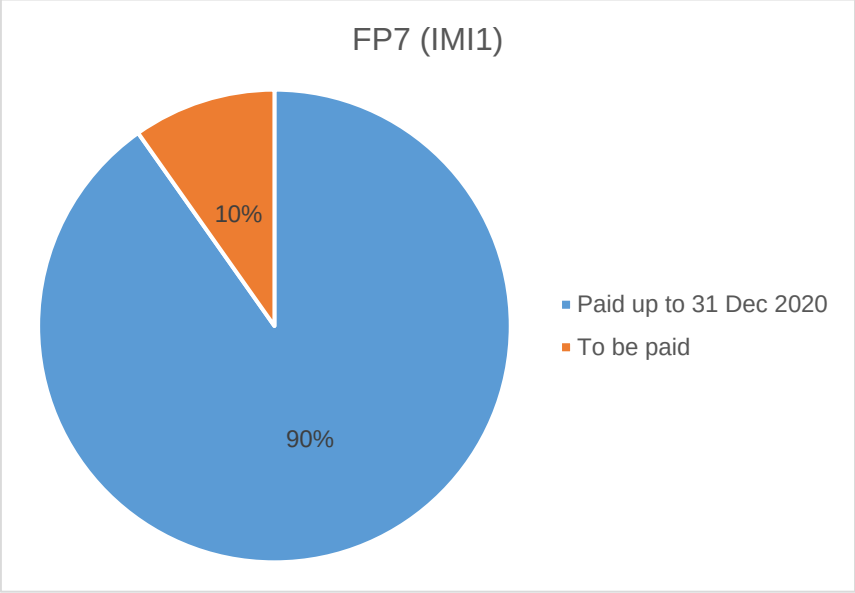
The table below outlines the breakdown per Call of EU committed funds for IMI1 (FP7).

			EUR '000
FP7 (IMI1)	Committed	Paid up to 31/12/2020	To be paid
Call 1	116 082	114 607	1 475
Call 2	85 765	85 216	549
Call 3	112 840	112 534	306
Call 4	97 944	97 168	776
Call 5	79 999	79 355	644
Call 6	125 417	100 311	25 106
Call 7	13 000	12 064	936
Call 8	98 733	82 847	15 886
Call 9	56 441	48 443	7 998
Call 10	6 100	5 496	604
Call 11	173 410	133 156	40 254
Total FP7 (IMI1)	**965 731**	**871 197**	**94 534**

In addition to the total amount to be paid, at the end of 2020, in ABAC there is the amount of EUR 401 675, representing the open amount of the ENSO (Exploring New Scientific Opportunities) Call.

At the end of 2020, 90 % of the commitment appropriations had been paid out.

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



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

				EUR '000
H2020 (IMI2)	Committed EU	Committed AP and other members	Paid up to 31/12/2020	To be paid
Call 1	17 630		15 334	2 296
Call 2	114 090		103 842	10 248
Call 3	49 060	7 000	53 363	2 697
Call 4	1 130		1 078	52
Call 5	47 477		35 616	11 861
Call 6	46 496	200	36 333	10 363
Call 7	46 429		34 230	12 199
Call 8	47 462		26 824	20 638
Call 9	53 606	4 000	38 482	19 124
Call 10	173 874		94 737	79 137
Call 11	3 284		2 839	445
Call 12	64 052		31 884	32 168
Call 13	114 152		45 927	68 225
Call 14	82 310		24 521	57 789
Call 15	165 608		43 657	121 951
Call 16	35 184		15 135	20 049
Call 17	40 786		10 407	30 379
Call 18	74 866		11 776	63 090
Call 19	12 715		6 809	5 906
Call 20	133 009		-	133 009
Call 21	72 000		30 093	41 907
Call 22	11 427		-	11 427
Call 23	47 790		-	47 790
Total H2020 (IMI2)	**1 454 437**	**11 200**	**662 889**	**802 748**

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

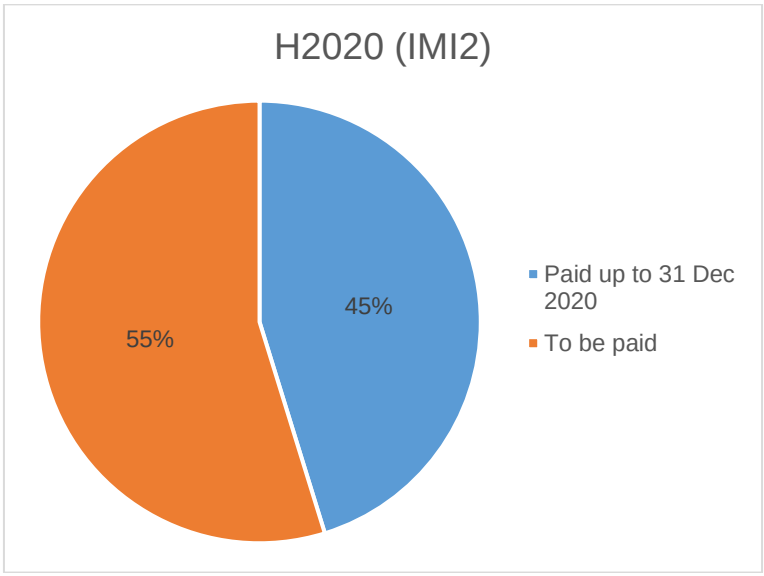
The committed amount for Call 7 comprises of total committed amount of EUR 46.795 million minus a de-committed amount during 2020 of EUR 366 251.

In addition to the total amount to be paid, at the end of 2020, in ABAC there is the amount of EUR 2.1 million representing the open amount of the PERISCOPE project.

At the end of 2020, the total EU commitments available at programme level for operational activities over the lifetime of IMI2 (2014-2020) amounts to EUR 1.455 billion. This figure results from the initial EUR 1.595 billion (as initially set out in the 2014 Council Regulation), minus EUR 139.1 million (reduction in 2019), minus EUR 6.7 million (contribution to European Green Deal), plus EUR 5.8 million (50 % of unused administrative commitments since 2014 transferred to the operational activities).

At the end of 2020, 45 % of the commitment appropriations had been paid out.

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

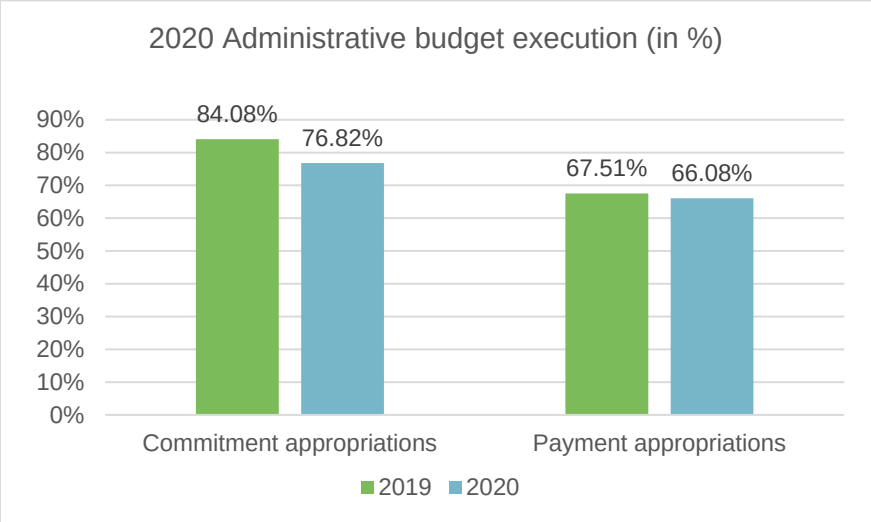


2.3.7 Administrative budget

The table below shows the execution of the 2020 administrative budget per Titles in absolute amounts.

Title	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	6 580 268	5 397 963	82.03%	6 711 731	5 416 371	80.70%
Title 2	4 625 134	3 210 436	69.41%	6 583 269	3 368 952	51.17%
Subtotal administrative expenditure	*11 205 403*	*8 608 399*	*76.82%*	*13 295 000*	*8 785 322*	*66.08%*

The graph below shows the 2020 budget execution for administrative costs (staff and infrastructure) compared with 2019.



The budget implementation of the commitment and payment appropriations in 2020 reached a level of 76.82 % and 66.08 % respectively.

The commitments and payments execution for administrative expenditure (Title 1 and 2) were significantly affected by the Covid-19 crisis. For example, the execution rate for expenditure planned for missions, meetings and events is lower than originally planned.

IMI continued to execute its budget applying principles of sound financial management, which resulted in a number of budget transfers between budget chapters, in line with operational needs (e.g. from meetings to office related expenditure). In 2020, there were no budget transfers between titles.

2.3.8 Overview of the carry over appropriations to 2021

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, IMI2 JU will re-enter into the 2021 budget the administrative payment appropriations corresponding to commitments carried forward from 2020, of EUR 1 309 301 and operational payment appropriations of EUR 2 537 921.

The year 2020 was the last year of the H2020 program when IMI2 JU launched Calls for proposals. At the end of 2020, the total unused commitment appropriations stood at EUR 3 060 665.

2.3.9 Procurement and contracts

The majority of IMI's contractual commitments in 2020 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 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 2020 outside existing FWCs with a value exceeding EUR 15 000.

Subject	Procedure	Contractor	Value (EUR)	Signature date
Personal face masks	Negotiated procedure, on behalf of 7 contracting authorities	Essential Embroidery Design Ltd	36 457	24 July 2020
Services supporting regulatory acceptance of IMI results	Open procedure	The Critical Path Institute Ltd	250 000	9 October 2020

The Call for tenders for face masks was launched rapidly in response to the COVID-19 outbreak and the urgent need to ensure the safety and wellbeing of staff on the rare occasions when they were required to work at the office (instead of at home, which was the default situation since the beginning of the first lockdown in Belgium). In order to exploit synergies, 7 joint undertakings launched a joint procedure, which IMI led.

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.

2.4 EFPIA and Associated Partner contributions

IMI is a public-private partnership between the EU (represented by the European Commission) and the pharmaceutical sector (represented by EFPIA). Some IMI2 projects also include Associated Partners.

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[4].

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[5], 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.

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

5 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 975.5 million as of 31 December 2020. The EU commitment remains 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	
TOTAL at 31/12/2020	965.7	975.5

IMI1 EU and EFPIA validated contributions - comparison by year

As of 31 December 2020, EFPIA contributions of EUR 737.5 million had been formally validated (checked by IMI staff and / or audited by external auditors). 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	62.5	55.2
2020	63.1	49.0
TOTAL	778.7	737.5

(*) excluding pre-financing

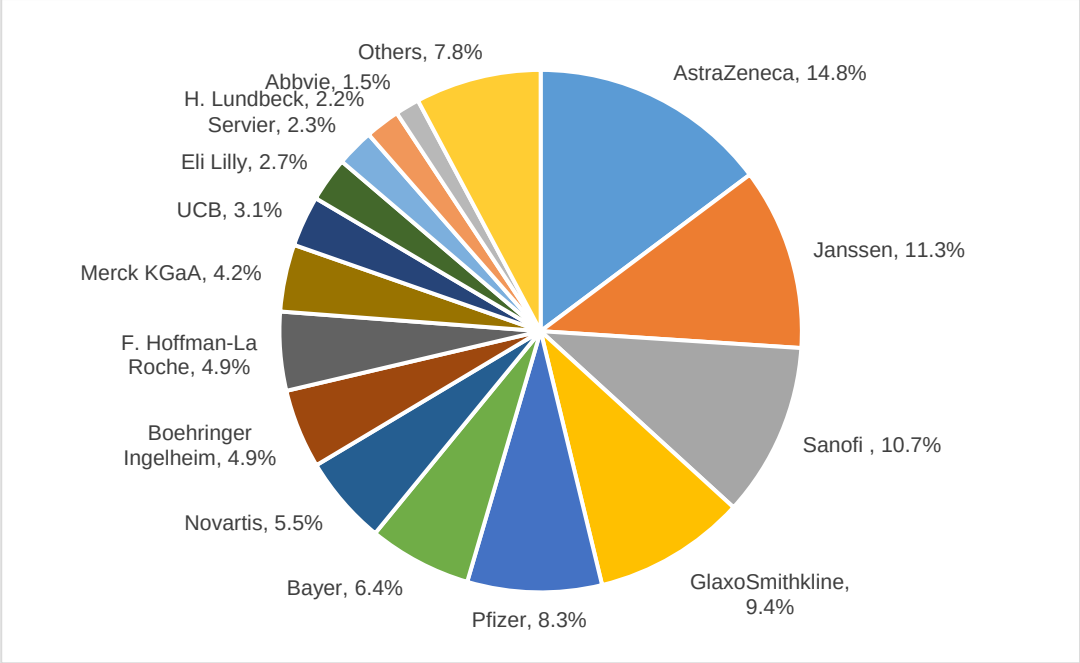
In terms of actual reporting however there is a difference between EU and EFPIA funding which results from the fact that, in some projects, tasks for the different consortium partners do not run in parallel but are often sequential.

Since 2016-2017, the number of IMI1 projects has started to decrease as the IMI1 programme winds down. Accordingly, the value of EU cost claims validated as well as EFPIA in kind reported per year has been decreasing steadily since 2018. At the end of 2020, there were 8 projects still running out of the initial 59 IMI1 projects.

In 2020, the IMI Programme Office continued to closely monitor the overall commitments of industry participants. The outstanding contributions will be made by the end of 2023 when the last IMI1 (FP7) projects will end.

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.



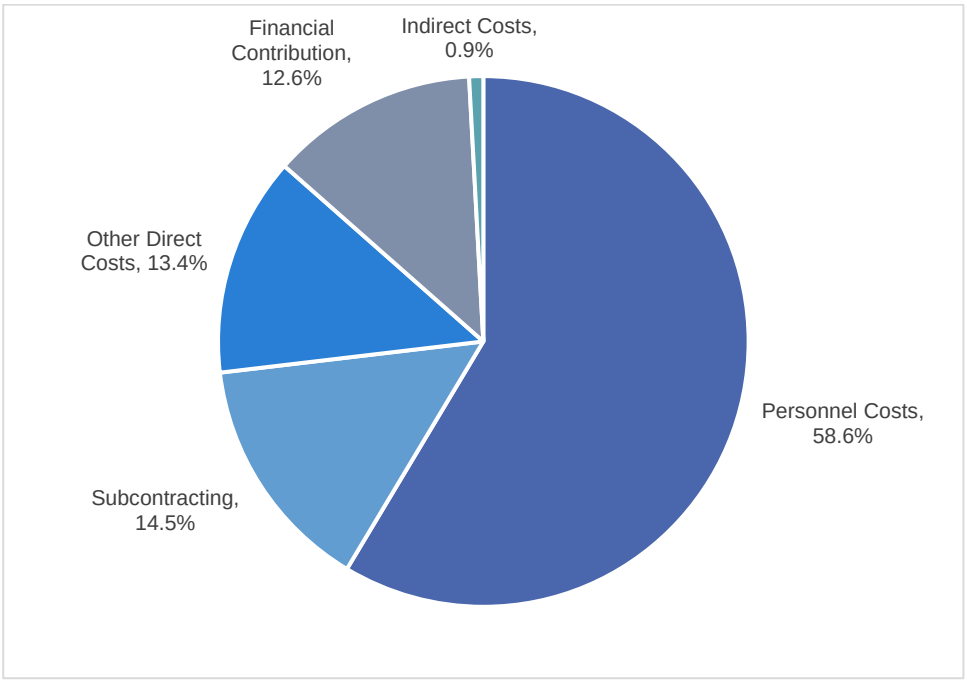
Companies listed under 'Others' are: Abbott, AC Immune, AiCuris, Alaxia, Almirall, Amgen (including Islensk Erfdagreining), Astellas, Basilea, Biogen, BMS Bristol Myers Squibb, Chiesi Farmaceutici, Da Volterra, Eisai, Esteve, Evotec, Farmaindustria, Grünenthal, INFARMA, Ipsen, Menarini, MSD Merck Sharp & Dohme, Novo Nordisk, Orion, Polyphor, Seqirus, Sigma-Tau, 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 2020, 19 Grant Agreements were signed, bringing the total number of IM2 projects to 108. At the end of 2020, the total commitments for signed Grant Agreements in IMI2 were:

- EUR 1 262.6 million in EU funding;
- EUR 1 279.6 million commitments from EFPIA companies (EUR 1 111.2 million) and Associated Partners (EUR 168.4 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 signed IMI2 projects:

IMI2 million EUR	EFPIA commitment	AP commitment	Total EFPIA + AP commitment	EU commitment
Up to 31.12.2019	939.6	157.7	1 097.3	1 062.2
2020	171.6	10.7	182.3	200.4
TOTAL on 31/12/2020	1 111.2	168.4	1 279.6	1 262.6

The increase of commitments in 2020 of EUR 200.4 million (EU funding) and EUR 182.3 million (EFPIA and Associated Partner commitment), results from the conclusions of 19 new signed Grant Agreements for IMI2 - Calls 17, 18, 19, 21, including 8 projects for the emergency coronavirus Call.

In addition, commitments were made in 2020 for selected proposals of ongoing Calls 20, 22 and 23 which were not yet signed on 31/12/2020, bringing the overall commitments for IMI2 programme at EUR 1 452.1 million (EU funding) and EUR 1 474.5 million (EFPIA and Associated Partner commitment).

Of the EUR 1 474.5 million committed by EFPIA and Associated Partners over the full IMI2 programme, EUR 1 022.3 million comes from the EU and H2020 associated countries; this represents 70.4 % of the EU's commitment (70 % of EUR 1 452.1 million is EUR 1 016.4 million). The remaining EFPIA and AP commitments come from outside the EU and H2020 associated countries.

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

On 31/12/2020, EFPIA companies and Associated Partners had contributed EUR 143.8 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 128.4 million. The following table shows the validated EFPIA and Associated Partner contributions as well as cost claims from beneficiaries receiving EU funding.

	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
2020	115.6	28.2	143.8	128.4
TOTAL	**321.4**	**42.1**	**363.5**	**298.8**

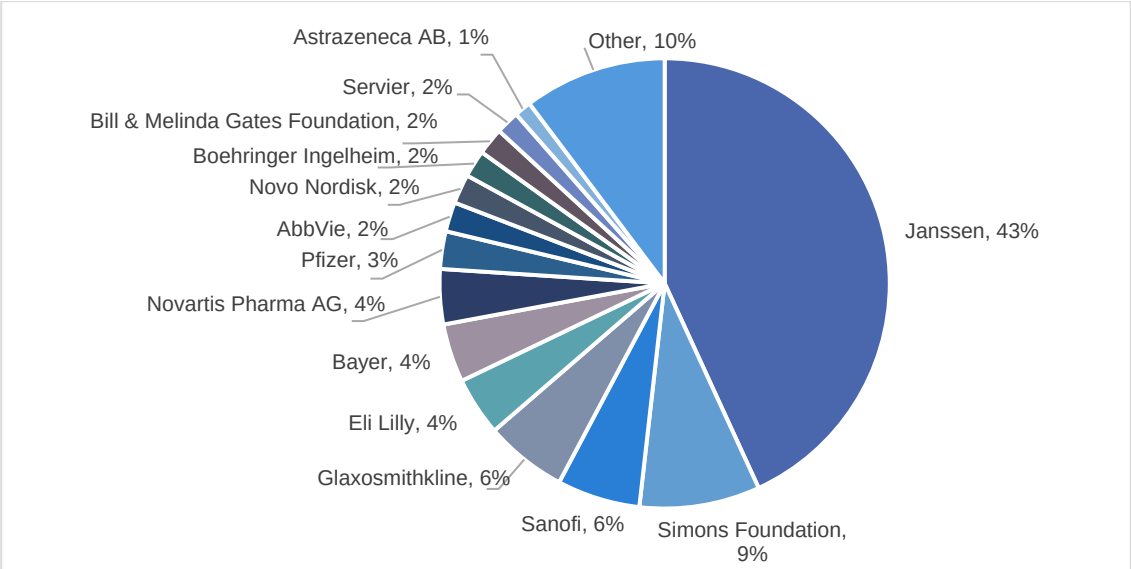
(*) excluding pre-financing

The significant increase of in kind contribution and costs claim in 2020 compared to 2019 is due to the fact that the number of IMI2 running projects has increased from 79 at the end of 2019 to 92 at the end of 2020. In addition, there are more projects which are now in a more advanced stage (third, fourth or fifth reporting years, where their spending pattern is higher).

IMI2 validated EFPIA and Associated Partner contributions by organisation up to the end of 2020

There are now more than 60 EFPIA companies and Associated Partners contributing to IMI2 projects. As the organisational breakdown below shows, 43 % of the total validated IMI2 contribution is provided by Janssen. This is due to the fact that Janssen has a high involvement in IMI2 projects (more than 50 projects). The remaining 57 % contribution comes from other EFPIA companies and Associated Partners (the Bill and Melinda Gates Foundation, JDRF, The Leona M. and Harry B. Helmsley Charitable Trust, the Simons Foundation, Coalition for Epidemic Preparedness Innovation).

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 363.5 million certified by external auditors and validated by IMI.



Organisations under 'other' include Abbott, Actelion, Amgen, Asociacion Nacional Empresarial de la Industria, Biogen, bioMérieux, BMS, Celgene, Charles River, Coalition for Epidemic Preparedness Innovation, Da Volterra, Ellegaard Gottingen, Esteve Pharmaceuticals, Evotec, EFPIA, GE Healthcare, Grünenthal, H. Lundbeck, Helmsley Charitable Trust, JDRF, Leo Pharma, Menarini, Merck, MSD, Merial, Orion, Pharmamar, Psychogenics, Rentschler, Seqirus, Takeda, Teva, ABPI, UCB, VFA, Zoetis.

IMI2 EFPIA and Associated Partner reported contributions by cost category

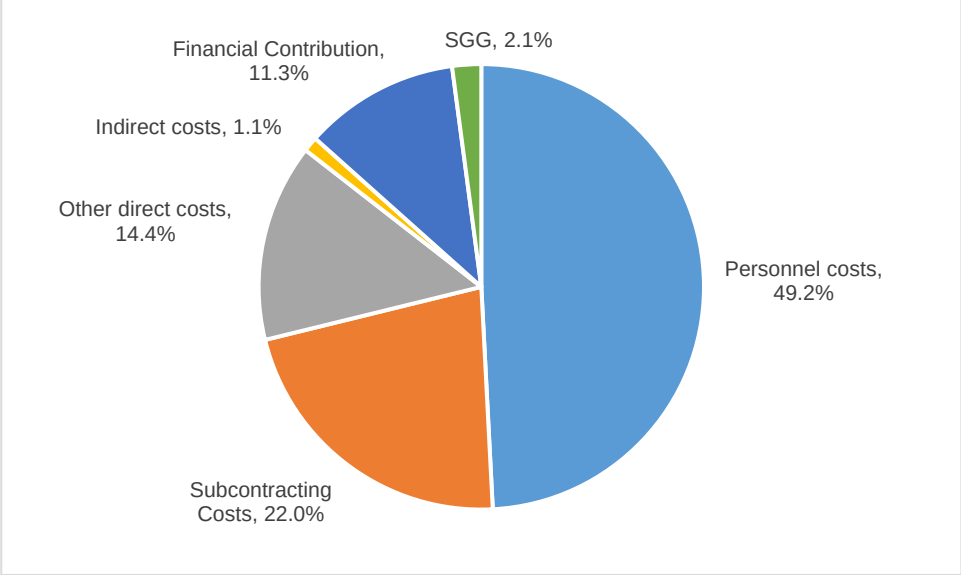
EFPIA companies' and Associated Partners' contributions can be broken down into in-kind and financial contributions.

- 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 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 higher 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 ERA4TB, AIMS-2-Trials, and Ebola projects), where significant tasks are subcontracted.

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

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

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

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

Ex-post review: This is a review of the in-kind methodology used by the EFPIA companies to declare in-kind contributions for all the IMI1 projects in which they participate, applying agreed-upon procedures to confirm the factual basis of the responses and descriptions provided in the submitted certificate on in-kind contribution methodology. On this basis, the auditors are able to conclude whether:

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

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

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

Audit coverage of the in-kind contribution

To date, IMI has completed ex-post audits of 21 EFPIA companies, covering a total of EUR 709.7 million in accepted contributions to IMI1 projects or 96 % of all EFPIA contributions. Two further audits will be finalised in 2021.

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 31/12/2020 (EUR million)
Total finalised audits	709.7
Total all EFPIA companies	737.5
Audit coverage	**96 %**

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 0.63 % of the total audited amounts.

Negative adjustments (EUR)	Positive adjustments (EUR)	Total absolute adjustments (EUR)	% of absolute adjustments
-2 293 847	2 200 131	4 493 979	0.63 %

2.5 Control systems

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 assurance on the achievement of the financial management and internal control objectives[6].

It includes additional information to support the conclusion that the available evidence is accurate and complete.

Financial procedures

In accordance with Art. 71 of the EU Financial Regulation 2018/1046 and Art. 60.2 of the Commission Delegated Regulation 2019/887, IMI adopted a set of financial rules[7] complemented by internal operating procedures. In particular, IMI internal financial management is based on the Manual of Financial Circuits (and related checklists and workflows) adopted by Executive Director Decision No 55/2018.

These documents outline the financial processes applied and describe the responsibilities of the financial actors as well as the internal control framework applied in order to:

- ensuring adequate management of the risks relating to the legality and regularity of the underlying transactions;
- safeguarding IMI's assets;
- checking the accuracy and reliability of recorded accounting data;
- promoting effectiveness and efficiency in financial operations.

For the management of the actions funded, IMI implements two different framework programmes - IMI1/FP7 and IMI2/H2020, with different obligations and modus operandi. In 2020, IMI continued the implementation of its programme in accordance with the two above-mentioned financial frameworks.

2.5.1 Ex-ante controls on operational and administrative expenditure

In order to support the assurance on the achievement of the internal control objectives, this section presents an assessment of expenditure (operational and administrative) with references to the budget execution and the indicators set out (while materiality criteria are outlined in Annex 5).

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)[8].

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 of Horizon 2020 ex-ante controls on interim & final payments[9], which allow a simplified and trust-based approach to beneficiary controls.

[6] Art 36.2 FR: a) effectiveness, efficiency and economy of operations; b) reliability of reporting; c) safeguarding of assets and information; d) prevention, detection, correction and follow-up of fraud and irregularities; and e) adequate management of risks relating to the legality and regularity of underlying transactions

[7] IMI2 JU Governing Board Decision 16/2020 of 27/05/2020.

[8] See above Section 2.3 'Budgetary and financial management'

[9] Version 2.2 of 20 May 2019.

	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 on the operational and financial 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 operational expenditure

The tables below show the balance between the actions implemented under the IMI1/FP7 and IMI2/H2020 programmes in terms of project portfolio and operational expenditure at the cut-off date of 31/12/2020.

IMI1 (FP7) project portfolio on 31/12/2020

Total projects funded			Pre-financing payments	Interim & final payments[10]
59	Running on 01/01/2020	11	0	51 333 903
	Ended[11] during 2020	(3)		
Total IMI1 projects running on 31/12/2020		**8**	**0**	**51 333 903**

10 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).

11 IMI1 projects which have ended their activities and presented, or are to present, their final report.

IMI2 (H2020) projects portfolio on 31/12/2020

Total projects funded			Pre-financing payments	Interim & final payments[12]	Total paid
108	Running on 01/01/2020	79	69 160 310	105 231 979	174,392,289
	Ended during 2020[13]	(6)			
	Signed in 2020	19			
Total IMI2 running on 31/12/2020		**92**	**69 160 310**	**105 231 979**	**174 392 289**

IMI1 and IMI2 full project portfolio on 31/12/2020

Total projects funded up to 31/12/2020			Pre-financing payments	Interim & final payments[14]	Total paid
167	**Running projects on 31/12/2020**	**100**	**69 160 310**	**156 565 882**	**225 726 192**
	Projects which ended during 2020	(9)	/	/	/

Control results on the operational budget implementation

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, 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 the IMI website, and the '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.

12 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).

13 IMI2 projects which have ended their activities and presented, or are to present, their final report.

14 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).

Indicator	Results 2020			Results 2019	Results 2018	Results 2017
% of annual coverage of Call topics identified in AWP 2020	Topics planned: **14** Topics launched: **14** Call 20: 6 topics Call 21: 1 topic Call 22: 1 topic Call 23: 6 topics		100%	100 %	100 %	100 %
No. redress procedures on the result of the evaluation	**9**	Cases per call: Call 20: 1 Call 21: 4 Call 22: 0 Call 23: 4		2	1	0

This year shows an increased number of redress applications (9) compared to the average of previous years (0.6 over the period 2015-2019), a circumstance that was attentively monitored by IMI Programme Office.

For re-evaluations, IMI follows the procedures described in the IMI2 vade mecum on proposals submission and evaluation and produces a re-evaluation report. The review committee evaluated all nine complaints and found grounds to re-evaluate two proposals[15]. The Independent Observer Reports on the evaluation process did not identify any issues that would call into question the fairness, transparency and integrity of the IMI2 Call evaluations held in 2020.

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.

During the GAP phase for selected proposals from Call 21 (the COVID-19 call), one proposal was found to have a work plan that depended on the completion of a study that was ongoing at the time of evaluation and the granting phase. Therefore, it was decided to split the pre-financing with the second tranche of pre-financing only being paid if the consortium reached the milestone. The IMI2 office was supported in this assessment by an independent external expert. The project Impentri has the aim to carry out clinical trials on the efficacy and safety of the generic drug Imatinib as a treatment for COVID-19 patients with a build-up of fluid on the lungs (both oral and IV administration). Based on a positive assessment of the outcome of the studies it was determined that the milestone had been achieved in December 2020. Therefore, it was confirmed that the project could continue its activities.

In 2020, 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 2020, the average TTI was 67 days against a legal target of 153 days, further improvement in comparison to previous years.

[15] For other details see also section 1.5 on Calls for proposals.

- **Time to Grant (TTG)** represents the maximum of eight months between the Call deadline and grant signature. In 2020, the average TTG improved again and is at 190 days, against the target of 245 days. This outcome demonstrates the close monitoring and the timely support provided by IMI Programme Office to beneficiaries during this phase.
- **Time to Pay (TTP)** represents the outcome of the process for the payment of pre-financing to newly signed Grant Agreements and costs claimed by beneficiaries. This year the average TTP of costs claims and final payments (considering IMI1 and IMI2 together) was 63 days, a few days longer than previous years due to the increased number of projects and transactions to be verified without any additional resources.

Indicators	Target	Results 2020	2019	2018
Total average Time to Inform (TTI)	**153 days**	**67**	73 days	75 days
Total average Time to Grant (TTG)	**245 days**	**190**	210 days	232 days
Total average Time to Pay (TTP) for pre-financing	**30 days**	**6**	9 days	9 days
Total average Time to Pay (TTP) for cost-claims and final payments	**90 days**	**63**	57 days	59 days

III - Grant Agreement implementation phase

In this phase, the IMI Programme Office plays a crucial role in forecasting, monitoring and checking the operational expenditure of both public funds and in-kind contributions related to the activities of IMI projects.

Scientific and financial officers check the project periodic reports to ensure that costs claimed by public beneficiaries are justified and that Grant Agreement rules are adhered to. 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 in-kind contribution) and Associated Partners. As nearly 95 % of the IMI budget is related to operational expenditure, a lot of effort goes into trying to get the closest estimate of our budget needs for the ongoing and coming years in order to reach the best budget execution rate.

In practice, the control of costs claimed by beneficiaries is triggered when IMI receives the periodic or final report. Before authorising any payment IMI verifies 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[16]. In addition, when necessary the IMI2 office can seek the support of independent experts to carry out more specific ad hoc reviews for particular requests submitted by the projects.

In 2020, two of the Ebola projects, EBOVAC3 and EBODAC, separately requested the addition of a beneficiary receiving funding which is not based in one of the EU Member States or H2020 associated countries. In both instances it was decided to seek the assistance of an independent expert in determining the merits of the request. In both cases the expert deemed that the addition of the beneficiary was essential for

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

carrying out the project action given the particular geographical environments. Therefore, based upon an internal assessment of the cases and supported by the recommendations of independent experts, it was decided to accept the requests to exceptionally fund the additional beneficiaries.

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[17]. In case of findings, they are also implemented as part of the project management cycle. This can result in the team working for many months on the file, even though the project has reached its official end date.

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

a) Volume of operational transactions

The total number of operational transactions performed during the year is one of the main indicators used by IMI to assess the efficiency of the Programme Office and the use of human resources to handle the workload related to project management. The tables below provide a multiannual overview of operational transactions, including both pre-financing payments (made to new projects) and interim and final transactions[18] made to ongoing projects funded within FP7 and H2020 programmes. Having in mind the complexity embedded in the concept of 'transactions', the trend shows that in 2020 the number of financial transactions related to IMI projects has further increased.

Number of operational transactions

	2020	2019	2018	2017	2016	2015	2014	2013	2012
Pre-financing payments	**25**[19]	29	20	16	16	16	18	14	12
Interim and final payments [20]	**76**[21]	62	70	66	59	30	32	33	26
Total	**101**	91	90	82	75	46	50	47	38

The number of transactions dealt with in 2020 is the highest ever managed so far by the Programme Office and this trend will continue in the coming years. That is due to the coexistence of some remaining IMI1 projects (FP7 programme), which continue phasing out (13 compared to 18 in 2019), and transactions related to IMI2 projects (H2020), which are steadily increasing (87 compared to 73 in 2019).

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 30.8 million with some projects having a budget higher than EUR 200 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 (8 out of 101 transactions in 2020). 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.

[17] See section below on ex-post controls.

[18] 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.

[19] In 2020, IMI processed 25 pre-financings: 18 pre-financings for new grants signed in 2020 and 7 complementary pre-financings for grants signed at the end of 2019. The pre-financing for the COVID project Impentri, which was split into two instalments, has been counted as one signed payment.

[20] Including the clearings of pre-financing.

[21] Of which, 13 on IMI1 projects, 75 on IMI2 projects and 1 additional payment related to an ex-post control finding.

The table below gives a picture of the modalities of the reporting process, where the number of interim payments made (75) during the year may not match with the number of reports received (77). 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.

Cost claims received with project reports against payments made

		2020	2019	2018	2017
1	**Cost claims received before 01/01/2020**	**14**	17	7	15
2	**Cost claims received during 2020**	**77**	57	80	58
3	**Cost claims not validated at the end of 2020 (to be paid the following year)**	**16**	14	17	7
4	**Cost claims processed during the year (1+ 2 - 3)**	**76**[22]	62	70	66
5	**Pre-financing new projects**[23]	**25**	29	20	16
6	**Total transactions (4 + 5)**	**101**	91	90	82

b) Value of operational transactions

The breakdown of the costs accepted and paid in 2020 by IMI based on the operational transactions described above is presented in the table below. In line with the increased volume of transactions, the value of payments also rose, reaching the value of EUR 260 650 109, of which EUR 225 726 192 was actually paid to beneficiaries as pre-financing and interim/final payments, while EUR 34 923 917 are the result of full and partial clearing made against pre-financing paid at the beginning of the project.

Overall, it is worth noting that continuous improvements in the project management workflow and the coordinated effort made by the staff overcame the difficulties linked to the COVID-19 pandemic period, ensuring business continuity and resulting in a considerable 98.9 % of operational budget execution in 2020.

This demonstrates that staff expertise and commitment, cautious planning and enhanced monitoring of payment appropriations absorption yielded a positive result.

[22] See above footnote 21.

[23] See above footnote 20.

		No of transactions		Value of payments	Value of clearings[24]	Value of all transactions
IMI1	Pre-financing payments	0		0		0
(FP7)	Interim payments	7	13	51 333 903	11,791,122	63 125 025
	Final payments	5				
	Full clearing	1				
IMI2	Pre-financing payments	25	87	69 160 310	N/A	69 160 310
(H2020)	Interim payments	57		105 231 979	23 132 795	128 364 774
	Final payments	3				
	Full clearing	2				
TOTAL			100	225 726 192	34 923 917	260 650 109
Annual approved budget 2020				227 184 041		
Annual budget after recoveries				228 264 113		
		Budget execution %		98.9 %		

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 2020, the financial impact of the systematic ex-ante controls on the cost claims resulted in the significant rejection of costs claimed by IMI1 projects. The reason was that project consortia reported eligible costs above the maximum grant amount. These costs were then capped at the maximum IMI contribution.

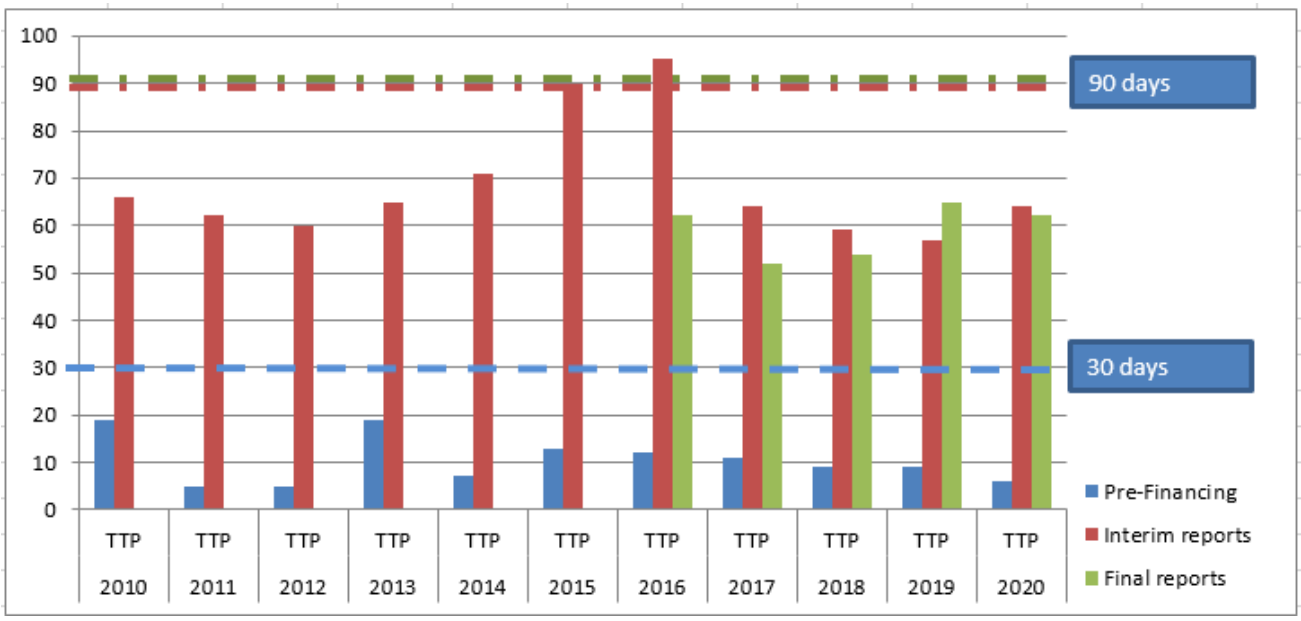
Total reported costs	**IMI1**	**69 621 684**	**198 929 124**
	IMI2	**129 307 440**	
Accepted costs	**IMI1**	**63 125 025**	**191 489 799**
	IMI2	**128 364 774**	
Rejection	**IMI1**	**6 496 659**	**9.3%**
	IMI2	**942 666**	**0.73%**

[24] Which includes both full and partial clearing.

d) Time to Pay (TTP)

Figures of 2020 confirm the positive trend undertaken by IMI. The TTP average remains at a positive level for pre-financing at 6 days (with a deadline of 30 days), while we reached 63 days (with a deadline of 90 days) for interim/final payments, which need considerable checks and exchanges with the consortia. Within this global average, interim payments have been managed in 64 days, while final payments required 62 days to be finalised.

The following chart summarises the average time to process payments against the deadlines set by the Financial Regulation and compare IMI performance throughout years of programme implementation.



Control results on administrative transactions

Regarding administrative expenditure, the TTP indicators presented further refer to all transactions (excluding budget Title 1 staff related costs).

The following table shows the number and amount of all administrative transactions in 2020 (including experts).

	No.	%	TTP Average	Amount paid (EUR)	%
Total no. payments (including experts)	678	100%	12 days	3 909 864	100%
No. payments on time (within 30 days)	647	95.4%		3 691 828	94.4%
No. late payments	31	4.6%		218 036	5.6%

The following table shows the number and amount of all payments made to experts (performing evaluations and project reviews) only in 2020.

No. payments	281	%
Average time to pay	8	/
No. late payments	1	0.36%
No. payments on time	280	99.64%
Total amount paid	EUR 909 215	+ 13 % (compared to 2019)

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

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

Since the legal bases and the budgetary frameworks are different, IMI reports separately on the IMI1 programme under FP7 and the IMI2 programme under Horizon 2020. Separate chapters below address the ex-post controls under IMI (FP7) and IMI2 (H2020). It should be noted that out of the cost claims paid out in 2020 for the total value of EUR 191 489 799[25], 67 % of the costs are paid under H2020 Grant Agreements, EUR 128 364 774, compared to EUR 63 125 025 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 5 – Materiality Criteria.

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

- 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 5 – 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.

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 (representative and risk based) 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	245	40 %
Projects	59	57	96.6 %
Contributions accepted by IMI (EUR, cumulative)	**643 417 715.01**[26]	**112 366 128.17**	**17.46 %**

The following table gives an overview of the status of individual audit assignments as of 31 December 2020.

	Total audits	Audits finalised[27]	Audits ongoing
Representative	262	255	7
Risk-based	19	17	2
Total	**281**	**272**	**9**

[26] Figure as of the cut-off date of 13 May 2020, corresponding to the last audit sample from which finalised audits were included in the current AAR.

[27] 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.

In 2020, 14 audits were finalised in total. One sample of representative audits was drawn in May 2020.

Representative and residual error rates as of 31 December 2020

At this point, the **cumulative Representative Error Rate** (RepER) resulting from all representative audits finalised by 31 December 2020 is 2.16 % in terms of IMI contribution.

The **cumulative Residual Error Rate** (ResER): error remaining in the population after corrections and recoveries) is 1.14 % in terms of IMI contribution. The residual error rate is thus below the 2 % materiality threshold established in Annex 5 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 2020.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
211	209	99 %	3 332 994

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	271
Pre-information letters / letters of conclusion sent	269
of which affected by systematic errors[28]	67
Extrapolation feedback received from beneficiary	65
of which implemented	65

Ex-post controls 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[29]. 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.

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

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

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

However, as the IMI2 Regulation[30] 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 2020

The error rates on the H2020 programme level on 31 December 2020 are:

- Representative detected error rate: 2.95 %[31,]
- Cumulative residual error rate for the R&I family of DGs: 2.16%

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 above-presented error rates 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. 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 2020

By 31 December 2020, IMI has launched six individual representative samples (one sample of representative audits was drawn in June 2020). Audits were finalised from the first five samples. A total of 52 representative audits sampled by IMI were finalised. In addition, 5 risk-based audits were finalised by the end of 2020.

The total IMI accepted contribution in the finalised audits is EUR 36 840 164 including both representative and risk-based audits. This represents 17.14 % of the total population of accepted contributions paid out, EUR 214 925 955[32].

The following table gives an overview of the status of individual audit assignments as of 31 December 2020.

	Total audits	Audits finalised	Audits ongoing
Representative	79	52	27
Risk-Based	10	5	5
Total	**89**	**57**	**32**

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

[31] Based on the 334 representative results out of the 467 expected in the three common representative samples.

[32] Figure as of the cut-off date of 4 June 2020, corresponding to the last audit sample drawn in 2020.

Representative and residual error rates specific to IMI's population as of 31 December 2020

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

- **Cumulative representative error rate** (RepER) resulting from the 52 finalised audits considered representative is 1.13 % in terms of IMI contribution.
- **Cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.74 % 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 2020.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
27	25	96 %	727 519

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	57
Pre-information letters / letters of conclusion sent	57
Of which affected by systematic errors[33]	5
Extrapolation feedback received from beneficiary	5
Of which implemented	5

Under H2020, 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 December 2020, IMI has implemented nine out of the eleven extensions of audit findings triggered by audits performed by other EU services on IMI beneficiaries.

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

2.5.3 Control efficiency and cost-effectiveness

The two sections below describe respectively the cost-effectiveness of IMI controls related to the ex-ante phase and to the overall control cycle (including Call management and evaluation, and ex-post controls).

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

The cost for ex-ante controls represent 0.98 % of the IMI operational expenditure in 2020 and can be quantified as EUR 22 277 per Grant Agreement, which corresponds to 0.01 % of the total operational expenditure.

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 validation of the in-kind contribution provided by industry.

The table below presents the cost-effectiveness ratio of all the controls.

Cost-effectiveness ratio	**Cost of controls / Total expenditure 2020 (Administrative and operational)**	**1.60 %**
	Cost of controls / Operational expenditure 2020	**1.66 %**
	Cost of controls / Total accepted cost 2020 (only beneficiaries' cost claims)	**1.96 %**
	Cost of controls / Total accepted cost 2020 (both beneficiaries' cost claims and validated EFPIA contribution)	**1.12 %**

The different indicators presented above provide an 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.

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 payments to beneficiaries, allowing them to conduct their research in line with the Grant Agreement.

Risk management

At IMI, risk management is a proactive process of identifying, assessing and managing the events that could threaten the implementation of activities planned for the achievement of the JU's objectives.

To that end, IMI implements a robust enterprise risk management (ERM) process based on the annual risk assessment exercise (RAE)[34]. The RAE is an important step in the definition of the IMI annual objectives and

[34] The annual RAE is performed in accordance with the methodology defined in the IMI guidance for risk identification and assessment version 2013, DORA Ref. IMI/INT/2013-03397, and Risk Management in the Commission, Implementation guide version October 2018.

priorities. It is also used as a key operational tool for day-to-day management. The RAE provides a comprehensive analysis of:

- the weaknesses and risks that might undermine the performance and capacity of IMI to achieve its objectives; and
- those risks that might be reduced and/or managed through mitigating measures.

Throughout the year, the Programme Office systematically monitored the evolution of the risks identified at corporate and operational levels in the annual RAE towards the AWP[35]. To that end, the Risk Management working group established by the Executive Director reviewed, discussed and updated the residual risks and corresponding mitigating actions where needed.

Even if no risks were initially considered as 'critical', this regular follow-up ensured that risk management was a continuous, dynamic and proactive process in view of evolving corporate priorities and considering that risks constantly develop, presenting new threats to the operations and strategy of the JU. In a nutshell:

- New research topics were developed, matching the IMI2 SRA priorities, ensuring the execution of the IMI programme and the budget (including in-kind contributions) within the conclusion of H2020 and guarantying the participation of a wide range of stakeholders and sectors.

- Fundamental misunderstandings on IMI's mission, objectives and results that fed the public debate, especially in light of the shaping of an IMI-like programme under Horizon Europe were constantly monitored and managed not to influence IMI's reputation at scientific and political levels.

- The ongoing and lasting COVID-19 pandemic impacted all IMI activities as well as working practices, communication methods and individual workloads, putting at risk the implementation of IMI's activities, staff wellbeing, and the annual declaration of assurance. The Programme Office continued to strive for operational excellence during this year, having ensured business continuity throughout 2020.

- More globally, the Programme Office planned an internal reorganisation to ensure that the capacity (enough resources and appropriate skills) and agility (flexibility of job profiles and re-allocation of tasks) of the organisation were aligned and supported the needs throughout 2020.

[35] RAE Report 2019/2020 of 16/10/2019 (ref. document: IMI2/INT/2019-01523; Ares: imi.admin(2019)6922591).

2.5.4 Fraud prevention and detection

In 2020 IMI adopted a revised anti-fraud strategy (AFS)[36], which aims at:

(1) updating and aligning anti-fraud actions with the Commission Anti-Fraud Strategy (CAFS 2019), while taking into account the harmonisation across research related activities through the Common Anti-Fraud Strategy for the Research family (RAFS 2019) set up by the Directorate-General for Research & Innovation (DG RTD)[37];

(2) to assess and develop additional anti-fraud actions to better cope with the specificities of IMI as a public private partnership. As part of the common antifraud strategy, IMI has also appointed an anti-fraud correspondent to support internal activities and to coordinate relations with the European Commission, other agencies and OLAF[38].

IMI implements the strategy in coordination with DG RTD and other R&I Commission services, executive agencies, and JUs through a multiannual action plan coordinated by the Fraud and Irregularity in Research (FAIR) Committee. In 2020, IMI's activities focused on:

- Cooperation with the FAIR Committee activities.
- Training all staff members on anti-fraud measures. A specific training course was organised in cooperation with OLAF. The training aimed to explain to, and familiarise staff members with, the concept of fraud, the anti-fraud cycle (with a focus on prevention, red flags, and detection), and the purpose of IMI's strategy including the related action plan.
- IMI staff had the opportunity to follow the OLAF Anti-Corruption Conference: 'Working together against corruption' on 9 December 2020.
- IMI internal guidance for staff on practical implementation of anti-fraud measures at IMI clarifying roles, responsibilities and workflows.
- Assessment of fraud related risks:
  - at programme management level where controls are embedded in the proposal evaluation, grant preparation and project management processes[39];
  - as part of the annual risk assessment exercise, where an in depth fraud risk assessment was conducted based on the introduction of the new AFS;
  - attention was also given to the risk of specific fraud in the context of COVID-19 pandemic.
- Adoption of the Commission Implementing Rules on whistleblowing.

In 2020 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.

Based on the above, IMI has reasonable assurance that the anti-fraud measures in place are effective.

[36] Adopted by the IMI2 JU Governing Board on 27/04/2020 (IMI2-GB-DEC-2020-12).

[37] This strategy has been adopted for all the Research family (DG RTD, DIGIT, REA, ERCEA, etc.) by the Executive Committee of the Common Implementation Centre on 21 March 2019 and updated on 26 June 2019.

[38] Office européen de lutte antifraude (the European Anti-Fraud Office).

[39] IMI applies the 'EU Grants: Guidance note' of 16.12.2019.

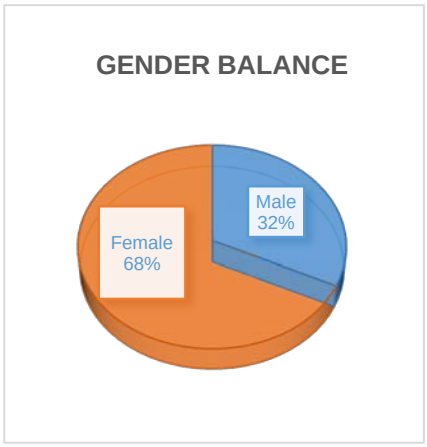
2.6 Human resources

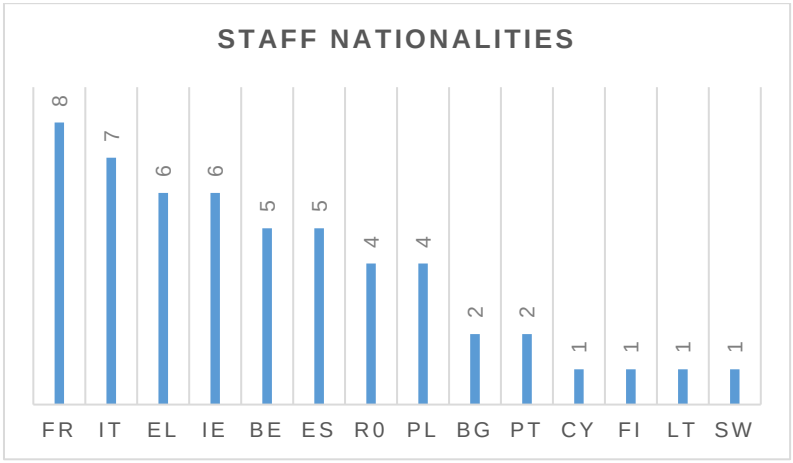
Staff and recruitment

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 31/12/2020 there were 53 positions occupied: 37 out of 39 temporary agents (94.87 %), 15 out of 15 contract agents (100 %) and 1 out of 2 seconded national experts (50 %)[40]. The table below provides a summary of the staff planning:

	Positions planned in SEP	Positions filled on 01/01/2020	Resignations / end of service in 2020	Recruitment / appointment in 2020	Positions filled on 31/12/2020
Temporary Agents	39	37	4	3	37
Contract Agents	15	14	1	2	15
SNEs	2	1	n/a	0	1
Total	56	52	5	5	53

The two graphs below show the gender and geographical balance (14 EU nationalities were represented) within IMI on 31/12/2020.





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 Audit Implementation Process (AURI), Risk management, EDES (Early Detection and Exclusion System) and reinforced monitoring; SAP coaching as well as ABAC invoices: hands-on training for FIAs (financial initiating agents).
- anti-fraud strategy: training and guidance for the Programme Office;

[40] Temporary Agents (TAs): the empty posts will be filled in 2021 as two selection procedures are on-going; Seconded National Experts (SNEs): the selection procedure was not successful / no successful candidate was found.

- in-house soft skills and well-being training courses such as giving and receiving feedback for all staff and appraisal exercise for managers;
- online 'soft' and 'hard' skills' courses, well-being lunchtime conferences and courses as well as language training courses organised by the European Commission and the European School of Administration (EUSA) were attended by IMI staff members. The European Commission's 'EU Learn' system helped IMI staff in the selection of their training needs, on both hard and soft skills;
- On- online individual coaching sessions for IMI managers;
- HR info sessions for staff and managers to provide IMI staff with a better understanding of HR procedures and processes for example on teleworking, appraisals and the reclassification exercise.

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 2020, in accordance with the Staff Regulations. As a result, 10 staff members (6 temporary agents and 4 contract agents) were reclassified to the immediate higher grade.

Staff regulations and implementing rules

During 2020, 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 eight implementing rules were adopted, including guidelines on whistleblowing; general provisions for implementing Article 87(1) of the CEOS of the European Union and implementing the first paragraph of Article 44 of the Staff Regulations; and general provisions for implementing Article 79(2) of the CEOS (Conditions of Employment of Other Servants) of the European Union, governing the conditions of employment of contract staff employed under the terms of Article 3a thereof.

COVID-19 - new ways of working

All throughout 2020, the well-being of IMI staff has been a high priority for IMI Programme Office and the HR team, especially under the challenging circumstances with the sudden change from office to remote working.

To support IMI staff during the pandemic, dedicated online coaching sessions on working in a time of COVID-19 for staff and managers were delivered in cooperation with other Joint Undertakings; weekly virtual staff check-ins were organised to ensure staff members' well-being and to keep IMI staff up-to-date on operational and HR matters. IMI staff were also provided with the equipment to support remote working based on their individual needs. New guidelines on teleworking were also adopted and updated accordingly to the evolution of the different pandemic phases, always bearing in mind the mental and physical health of the staff.

Several actions were taken to guarantee safe access to IMI premises for staff who needed to be in the office for critical tasks (e.g. personal protective equipment, extra cleaning of the offices and common areas, prior approval need to come to the office etc.). IMI took the lead to procure face masks for all the JUs. In addition, joint 'return to the office' guidelines were developed in cooperation with the other JUs. Following these measures none of the IMI staff got infected at the office.

Due to the COVID-19 pandemic, adjustments in IMI HR ways of working were necessary. For example, the travel restrictions imposed by Member States and the health emergency meant that as of March, 2020 IMI selection procedures (written and oral tests) were conducted remotely. Several learning and development activities also took place remotely. For example, to facilitate the on-boarding of IMI newcomers an online induction training course was organised, as well as bilateral meetings, mentoring sessions, and online social events such as virtual coffees with IMI staff members and the IMI Christmas lunch. The latter actions also contributed to uphold IMI's organisational culture.

2.7 IT and logistics

COVID-19

In the context of the COVID-19 pandemic and teleworking as a norm for IMI staff, IT activities in 2020 naturally focused on maintaining an appropriate and secure IT infrastructure and business support tools in order to provide remote access, smooth collaboration and business continuity.

One of the key points in this context was to raise awareness of cybersecurity threats and risks as the end users are generally considered the weakest point and the primary vulnerability within a corporate network. The collaboration with the inter-institutional Computer Emergency Response Team (CERT-EU) complemented regular internal communications on this topic, by giving updates on the cybersecurity threats landscape.

Another important subject was the use of web conferencing systems. The IMI IT team ran refresher Webex training sessions and produced detailed manuals for meeting organisers and external participants. In order to facilitate internal communication and collaboration, a pilot use of MS Teams was initiated.

To ensure a smooth experience working from home and during web conferences, the staff were provided with relevant IT equipment (laptops, headsets, web cameras etc.).

The reliable IT performance achieved was one of the key success factors for meeting the organisation's objectives in this challenging remote working environment.

Common IT infrastructure

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

The major common IT project, namely the renewal of the network infrastructure in the building, was successfully completed in 2020. The existing one (installed back in 2010, for a much smaller number of staff) reached the end of its life and could therefore no longer be technically supported. The risk of a significant postponing of the project due to the first COVID lockdown in spring was prevented, thanks to the joint efforts and the mitigation measures set in place.

Moving a secure TESTA line from the WA to the Infrastructure as a Service (IaaS) datacentre, completed in 2020, is another very important project, which proves the efficiency and economy of scale of the common IT approach. Newly established connection is shared between the six JUs and two other agencies. Thus eliminates the last dependency of the IT infrastructure on the WA building and ensures higher availability and business continuity even in case of emergency in the building.

Business support tools provided by European Commission

In line with the 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.

The migration to the EC missions management tool (MiPS) took place at the beginning of October 2020 with online trainings for staff.

The integration of electronic payslips and the PMO (Paymaster Office) payment systems (NAP) in SYSPER was another significant improvement made in 2020.

DPIA on Microsoft 365 online services

In order to ensure compliance with the recently adopted EU Regulation on the protection of personal data by EU institutions and bodies (Regulation (EU) 2018/1725), IMI performed a data protection impact analysis (DPIA) on Microsoft 365 online services, together with the other five joint undertakings.

The Regulation requires EU institutions to take appropriate technical and organisational measures to ensure the ongoing protection of the rights and freedoms of data subjects involved in the processing of their data.

Also, to embed 'privacy by design/by default' as from the very beginning of the design/configuration of an IT system/application. The project focused on the identification and mitigation of information security and data protection risks.

The approach followed for conducting the DPIA builds on the Regulation's requirement of Art. 39, as well as guidance and methodologies that have been developed to date by EU bodies, notably the European Data Protection Supervisor (EDPS) and the European Union Agency for Network and Information Security (ENISA), as well as best practices developed by the national data protection authorities (DPA). It also took into account other widely-recognised standards-setting risk assessment methodologies, such as ISO/IEC 27005 and ITSRM² Methodology (used by DIGIT for the conduct of information security risk assessments).

Based on the risk analysis outcome, a security implementation plan (SIP) was defined to ensure effective implementation of the M365 IT security plan. The SIP indicates details on the implementation of risk treatment plans where actions are defined to mitigate the risk to an acceptable level.

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)

- Major redesign and component updates following findings and recommendations from a vulnerability assessment requested by IMI and carried out by CERT-EU (Computer Emergency Response Team for the EU institutions, agencies and bodies).
- Improvements to the in-kind annual reporting module.

IMI specific cloud applications (KMP – knowledge management platforms):

- Preparation for migration to the latest Liferay version. User acceptance test is ongoing.

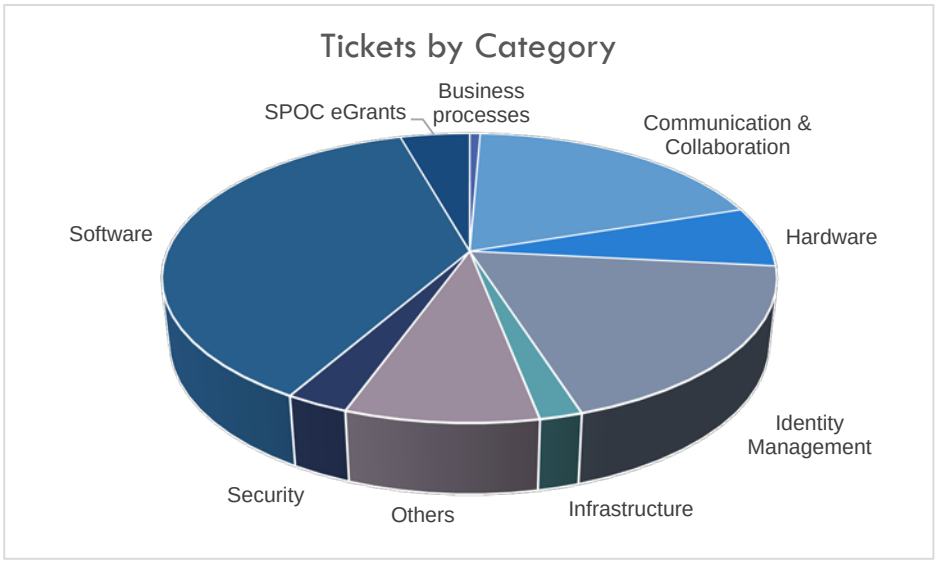
IMI data warehouse

The IMI data warehouse was further extended with a new data source - SEP Data Store (SEP DS) and it is combing data from:

- SOFIA - IMI1 projects and proposals, IMI2 proposals up to call 9;
- SEP DS – IMI2 proposals and evaluations after call 9 (including Stage 1 and Stage 2);
- CORDA – IMI2 projects (SyGMa/Compass) and reference data (PDM, countries, etc.);
- website content management system (tags assigned to projects) – e.g. tools, programs, disease areas, products, twitter etc.
- reference files (mainly data not available in our source systems) - e.g. Group of EFPIA companies, Partners in Research, ORG type grouping, SGG/SRA/WHO categories etc.

Service desk support

In 2020, a total of 1 216 requests for support were handled by the IMI IT Helpdesk. The following graph depicts the various categories assigned to the tickets.


Tickets by Category
Business processes
SPOC eGrants
Communication & Collaboration
Hardware
Identity Management
Infrastructure
Others
Security
Software

2.8 Data protection

In 2020, IMI pursued its efforts to render its website, processes and working methods fully compliant with 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 renewed the mandates of its data protection officer and deputy data protection officer, for an additional three-year period, and participated in various interinstitutional data protection activities, including events held by the European Data Protection Supervisor.

2.9 Access to documents

Regulation (EC) No 1049/2001 applies to IMI.

No requests for access to documents were lodged with IMI in 2020.

2.10 Assessment of audit and ex-post evaluation results during the reporting year

2.10.1 Internal Audit Service (IAS)

The Internal Audit Service (IAS) of the European Commission performs the internal audit function for IMI as specified in Article 28 of 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 Governing Board on annual basis.

In 2020 IAS performed an audit on Horizon 2020 grant implementation in IMI2 JU as originally foreseen in 2019-2021 Strategic Internal Audit Plan[41]. The objective of this audit was to assess the adequacy of the design and the efficiency and effectiveness of the internal control system in place in for the implementation of grant agreements under Horizon 2020. A preliminary survey and fieldwork phases of the audit were completed during 2020, and the final report was issued in 2021.

In November 2020, the IMI Executive Director informed the internal auditors on the latest IMI organisational and operational developments and the results of the latest risk assessment, and provided feedback on the potential audit topics in view of the IAS Strategic Plan.

2.10.2 European Court of Auditors (ECA)

Audit on IMI annual accounts for the financial year 2019

On 12 November 2020, the ECA published a specific *Annual report on the EU Joint Undertakings for the financial year 2019*[42] as well as the summary document '2019 audit of EU Joint Undertakings in brief'[43].

While the audit work for the financial year 2019 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.

The 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 2019 budget – the auditors noted that regarding 2019 budget available for FP7 projects, the implementation rate for payment appropriations was 97 %. Regarding the 2019 budget available for Horizon 2020 projects, the implementation rates for commitment and payment appropriations were 100 % and 98 % respectively. The also auditors acknowledged that 'the JU significantly improved in 2019, the planning and monitoring of its need for new payment appropriations'.
- Internal controls – the auditors confirmed that ex-ante control procedures based on financial and operational desk reviews are reliable; the new Internal Control Framework is implemented.
- The auditors have substantiated that audits of randomly selected IMI payments to H2020 beneficiaries showed no significant errors or control weaknesses.
- Other issues – the auditors acknowledged that in 2019, IMI significantly stabilised its staff situation.

[41] Ares(2019)4058461 - 26/06/2019.

[42] www.eca.europa.eu/en/Pages/DocItem.aspx?did=54396

[43] www.eca.europa.eu/en/Pages/DocItem.aspx?did=56383

Audit on IMI annual accounts for the financial year 2020

In accordance with Article 54 of the IMI2 Financial Rules, IMI's 2020 annual accounts are audited by the external audit company. In 2020 IMI office reopened the competition in the framework contract BUDG/19/PO/01 (audits and controls) and contracted Baker Tilly Belgium for a period of two financial years. The preparatory audit work started in November 2020.

The Court of Auditors will draw the final audit opinion on the 2020 accounts, revenue and transactions on the basis of the work by independent external auditors as well as the substantial audit work performed by the ECA dedicated team. The final report is due in November 2021.

2.11 Follow up of recommendations and action plans for audits and evaluations

There were no open recommendations in 2020.

There were no ex post evaluations on IMI2 JU in 2020. The action plan resulting from IMI2 JU interim evaluation has been completed in 2019 as confirmed by the Court of Auditors.

3 Assessment of the effectiveness of the internal control systems

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:

- operations are effective, efficient and aligned with the strategy;
- financial reporting is reliable; and
- the JU complies with the applicable laws and regulations.

The IMI internal control framework is based on 17 control principles aligned with the Commission control framework[44] and was adopted by the Governing Board in December 2017[45]. 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.

The original annual Internal Control Action Plan of IMI stated that during 2020 IMI would have continued '… *implementing the programme until 2024 as foreseen by the Council Regulation, to ensure the conclusion of the research projects funded …'*, which implied the following key internal control responsibilities for the management:

- coordination, supervision and monitoring of the 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.

However, from Q1 2020 IMI was forced to address the impact brought by the COVID-19 pandemic and, as a first action, to ensure business continuity and staff safety during lock-down phases.

To address this situation IMI management took immediate operational actions (staff teleworking, operations managed remotely, etc.) and revised the Internal Control Action Plan[46] to adapt to the new circumstances while maintaining the effectiveness and robustness of the overall system. To that purpose, a new overarching objective was added to the original annual IC Action Plan, while previous objectives and implementing actions were adapted or rescheduled where needed, as follows:

- Overarching objective: Prepare the Programme Office and its control environment for the short-term and long-term impacts of the COVID-19 pandemic, prioritising business continuity and staff health and safety.
- Objective 1: Taking into account the measures adopted in view of the overarching objective, ensure an effective and reliable internal control system giving the necessary guarantees concerning the legality and the regularity of policies and procedures as well as the underlying transactions.
- Objective 2: Ensure an effective and proportionate internal control system in line with sound financial management.

[44] 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.

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

[46] IMI2 JU Annual Internal Control Action Plan – Revision (Ares(2020)6801582).

- Objective 3: Maintain an effective risk management process, which allows IMI to identify, assess, and manage risks, i.e. potential problems (or changes) that could affect the achievement of the IMI2 JU objectives.
- Objective 4: Minimise the risk of fraud by implementing effective anti-fraud measures, integrated in all activities of the JU as well as by revising 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 2020 is 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 2020;
- 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 management's overview on progress made on the implementation of the corresponding action plans.

In order to ensure that all aspects of IMI operations and control (financial management, governance, administration and horizontal support, procurement and contracts, HR, IT, communication) were covered by the assessment, the 17 control principles were analysed both individually and as part of the corresponding control component[47]. The ranking of each principle, in terms of conformity, effectiveness and consistency is then summarised.

Annual evaluation of the IMI local financial systems by DG BUDGET

The annual evaluation 2020 (referring to financial year 2019) of the IMI local financial systems was performed by DG BUDGET[48] according to Article 49 (e) of the Financial Rules. The evaluation has not identified any internal control weaknesses, which would have a material impact on the accuracy, completeness and timeliness of the information required to draft the annual accounts and produce reliable reporting. On the basis of the available evidence, DG BUDGET concluded that the internal control systems are working as intended. DG BUDGET suggested a few improvements that overall do not impact the positive conclusions.

3.1 Conclusions of the assessment of the internal control systems

IMI2 JU uses the organisational structure and the internal control systems suited to achieving its policy and internal control objectives in accordance with the internal control principles and has due regard to the risks associated with the environment in which it operates.

The continuous efforts to improve quality management allowed the Programme Office to implement a number of specific actions (such as targeted presentations to staff, trainings on operating procedures adopted, etc.) that ensured the compliance of the overall control system and allowed the JU to improve its efficiency, and to better cope with the particular circumstances of 2020. In this context, risks that might pose a threat to the achievement of IMI objectives were systematically managed and controlled.

In conclusion, the IMI2 JU has assessed its internal control system during the reporting year and has concluded that it is effective and the components and principles are present and functioning well. Areas where further improvements can be made have been identified and will be prioritised in 2021.

[47] The new ICF consists of 5 internal control components: 'control environment', 'risk assessment', 'control activities', 'information and communication' and 'monitoring activities'.

[48] Note to IMI Ares(2020)7209196 – 30/11/2020.

4 Management assurance

4.1 Review of the 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[49];
  - reporting by the internal control 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 gathered from the sources of assurance covers both the operational budget related to the FP7 and H2020 programmes, as well as the administrative budget managed by IMI in 2020, 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. No significant weaknesses were identified or reported. 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 5. 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.

49 Head of Administration and Finance, Head of Scientific Operations, Head of Communications and Institutional Relations.

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

4.2 Reservations

There are no reasons for introducing any reservations.

4.3 Overall conclusion

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

4.4 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, 28 February 2021

signed

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, 28 February 2021

signed

Hugh Laverty, Head of Scientific Operations

5 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[50].

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

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

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

Brussels, 28 February 2021

signed

Pierre Meulien

50 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 – Key performance indicators

Table I - Horizon 2020 Key Performance Indicators common to all JTI JUs
Table II - Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs
Table III - KPIs specific to each single JU

Annex 2 – Project outputs

Annex 3 – Publications from projects

Annex 4 – Patents from projects

Annex 5 – Materiality criteria

Annex 6 – Organisational chart

Annex 7 – Staff establishment plan

Annex 8 – Final annual accounts

Annex 9 – List of IMI projects

Annex 10 – List of acronyms

Annex 11 – Analysis and assessment of the IMI2 JU Annual Activity Report 2020 (AAR 2020) by the IMI2 JU Governing Board

Annex 1 – Key performance indicators

Table I[51] - 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 2020
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	[On average, 20 publications per EUR 10 million funding (for all societal challenges)]	35.7 %

51 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. 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 2020
				(ranking) data to be collected by commercially available 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	9 patent applications 2 patents awarded
	16	Number of prototypes testing activities and clinical trials[52]	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: 59 Testing activities: 88 Clinical trials: 72
	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]	246 23.9 %
	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: 25 New processes: 16 New methods: 19

52 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 2020
EVALUATION	**NA**	Time to inform (TTI) all applicants of the outcome of the evaluation of their application from the final date for submission of completed proposals	To provide applicants with high quality and timely evaluation results and feedback after each evaluation step by implementing and monitoring a high scientific level peer reviewed process	Number and % of information letters sent to applicants within target Average TTI (calendar days) Maximum TTI (calendar days)	153 calendar days	No. of Short Proposal information letters: 83 (100 % on time) No. information letters for Full Proposals: 161 (100 % on time) Average TTI: 67 days Statistics refer to letters sent out in 2020 (SPs for IMI2 – Calls 20 & 23; FPs for IMI2 – Calls 17 & 18; and single stage proposals for IMI2 – Calls 21 & 22).
	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		There were 9 redress requests in 2020.[53] In 7 cases, the redress committee found no grounds for a re-evaluation. In 2 cases, the redress committee recommended re-evaluation. The re-evaluations did not affect the overall outcome of the Calls.
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)	19 out of 19 (100 %) were signed within the target Average TTG: 190 days. Maximum TTG: 243 days

[53] More information on the redress requests can be found in section 1.5.

	Correspondence to general Annex 1	Key Performance Indicator	Definition / responding to question	Type of data required	Target at the end of H2020	Results in 2020
	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	6 out of 19 (31.57 %) were signed within the target.[54] Average TTS: 122 days Maximum TTS: 164 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: 6 days (100 % on time) Interim payments: 63 days (100 % on time) Final payments: 72 days (100 % on time)
HR	**NA**	Vacancy rate (%)		% of post filled in, composition of the JU staff		Overall vacancy rate: 5.35 % TAs: 5.13 % CAs: 0 % 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	98.66 % CA to total budget 97.08 % PA to total budget

54 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 2020
	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)		678 payments of which 31 were late (4.6 %)

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.

Table II[55] - Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs

<table>
<tr><th>Correspondence in the general Annex 2</th><th>Cross-cutting issue</th><th>Definition / responding to question</th><th>Type of data required</th><th>Direct contribution to ERA</th><th>Results in 2020</th></tr>
<tr><td>2</td><td>Widening the participation</td><td>2.1 Total number of participations by EU-28 Member State</td><td>Nationality of H2020 applicants & beneficiaries (number of)</td><td>YES</td><td>Eligible proposals:
Applications: 7 019
Applicants: 2 495
Beneficiaries: 2 273
<table><tr><th>Country</th><th>Participations (Participants)</th></tr><tr><td>Austria</td><td>48 (21)</td></tr><tr><td>Belgium</td><td>228 (74)</td></tr><tr><td>Croatia</td><td>3 (3)</td></tr><tr><td>Czechia</td><td>10 (7)</td></tr><tr><td>Denmark</td><td>80 (27)</td></tr><tr><td>Estonia</td><td>5 (3)</td></tr><tr><td>Finland</td><td>41 (13)</td></tr><tr><td>France</td><td>277 (111)</td></tr><tr><td>Germany</td><td>363 (136)</td></tr><tr><td>Greece</td><td>10 (7)</td></tr><tr><td>Hungary</td><td>8 (5)</td></tr><tr><td>Ireland</td><td>27 (18)</td></tr><tr><td>Italy</td><td>148 (76)</td></tr><tr><td>Latvia</td><td>1 (1)</td></tr><tr><td>Luxembourg</td><td>30 (6)</td></tr></table></td></tr>
</table>

55 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. 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 2020
					Netherlands 247 (77) Poland 7 (6) Portugal 20 (19) Romania 2 (2) Slovenia 6 (5) Spain 144 (70) Sweden 95 (23) United Kingdom 473 (134) Total EU-28: 2 273 (844) (Cumulative figures as of 31/12/2020)
		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 / IMI contrib., M EUR (%) Austria 34.1 (2.9 %) Belgium 74.0 (6.3 %) Croatia 0.2 (0.0 %) Czechia 2.4 (0.2%) Denmark 18.8 (1.6 %) Estonia 2.3 (0.2 %) Finland 18.8 (1.6 %) France 129.3 (11.1 %) Germany 142.8 (12.2 %) Greece 3.2 (0.3 %) Hungary 3.6 (0.3 %) Ireland 20.7 (1.8 %) Italy 62.6 (5.4 %) Latvia 0.3 (0.0 %) Luxembourg 9.7 (0.8 %) Netherlands 184.8 (15.8 %) Poland 1.8 (0.2 %) Portugal 7 (0.6 %) Romania 1.5 (0.1 %)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2020
					Slovenia 1 (0.1 %) Spain 108.1 (9.3 %) Sweden 48.1 (4.1 %) United Kingdom 291.8 (25.0 %) Total EU-28 1 166.9 (Cumulative figures as of 31/12/2020)
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: - Applications: 530 - Applicants: 224 - Beneficiaries: 215 Country — Participations (Participants) Iceland 1 (1) Israel 17 (9) Norway 24 (13) Serbia 2 (2) Switzerland 169 (46) Turkey 2 (2) Total Assoc. countries 215 (73) (Cumulative figures as of 31/12/2020)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2020
NA		Total amount of EU financial contribution by Associated Country (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country / IMI contrib., M EUR (%) Iceland 0.1 (0.1 %) Israel 3.4 (4.8 %) Norway 8.6 (12.3 %) Serbia 0.8 (1.1 %) Switzerland 57.1 (81.3 %) Turkey 0.3 (0.4 %) Total Assoc. countries: 70.3 (Cumulative figures as of 31/12/2020)
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: 303 out of 1 887 (16.1 %) Participants: 207 out of 851 (24.3 %) EU funding: EUR 151.9 million (11.9 %) (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	52 % 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	29 %
		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 39 appointed nominees (61,5%) SC: 4 out of 10 full members (40 %)

<table>
<tr><th>Correspondence in the general Annex 2</th><th>Cross-cutting issue</th><th>Definition / responding to question</th><th>Type of data required</th><th>Direct contribution to ERA</th><th>Results in 2020</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Expert evaluators: 91 out of 211 experts (43 %)
Interim review experts: 22 out of 44 experts (50 %)</td></tr>
<tr><td>7</td><td>International cooperation</td><td>7.1 Share of third-country participants in Horizon 2020</td><td>Nationality of H2020 beneficiaries</td><td>YES</td><td>Eligible proposals:
- Applications: 231
- Applicants:158
- Beneficiaries: 117
<table><tr><th>Country</th><th>Participations (Participants)</th></tr><tr><td>Australia</td><td>2 (2)</td></tr><tr><td>Benin</td><td>1 (1)</td></tr><tr><td>Brazil</td><td>1 (1)</td></tr><tr><td>Burkina Faso</td><td>1 (1)</td></tr><tr><td>Canada</td><td>7 (7)</td></tr><tr><td>China</td><td>1 (1)</td></tr><tr><td>Congo</td><td>1 (1)</td></tr><tr><td>Gabon</td><td>2 (1)</td></tr><tr><td>Japan</td><td>2 (2)</td></tr><tr><td>Senegal</td><td>2 (1)</td></tr><tr><td>Sierra Leone</td><td>3 (2)</td></tr><tr><td>Singapore</td><td>1 (1)</td></tr><tr><td>South Africa</td><td>2 (2)</td></tr><tr><td>Tanzania</td><td>1 (1)</td></tr><tr><td>United States</td><td>90 (48)</td></tr><tr><td>Third countries:</td><td>117 (72)</td></tr></table>(Cumulative figures as of 31/12/2020)</td></tr>
</table>

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2020
		7.2 Percentage of EU financial contribution attributed to third country participants	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country / IMI contrib. M EUR (%) Australia 0.3 (0.8 %) Benin 0.6 (1.5 %) Brazil 0.3 (0.8 %) Burkina Faso 3.8 (10.1 %) Canada 0.4 (1.2 %) China 0 (0 %) Congo 3 (8 %) Gabon 0.8 (2.2 %) Japan 0 (0 %) Senegal 0.4 (1 %) Sierra Leone 20 (53.6 %) Singapore 0 (0 %) South Africa 0.6 (1.7 %) Tanzania 0.5 (1.3 %) United States 6.6 (17.8 %) Third countries: 37.4 (100 %) (Cumulative figures as of 31/12/2020)
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

56 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 2020
		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[57] between (4-6, 5-7)		2 projects TRL 4 2 projects TRL 5 5 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: 1 015 of 2 605 (38.9 %) Participants: 364 out of 989 (36.8 %) (Cumulative figures as of 31/12/2020)
		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 172.5 million out of EUR 1 247.6 million (11.9 %) (Cumulative figures as of 31/12/2020)
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 1 262.6 million (total cash contribution EC at the end of 2020)
		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 1 279.6 million) divided by EU contribution (EUR 1 262.6 million)

57 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 2020
			- additional activities (i.e. research expenditures/investment of industry in the sector, compared to previous year)		= leverage of 1.01.
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: 8 836 Total funding amounts: EUR 7 993 390
14	Participation patterns of independent experts	14.2 Proposal evaluators by country	Nationality of proposal evaluators		29 countries[58] (211 experts)
		14.3 Proposal evaluators by organisations' type of activity	Type of activity of evaluators' organisations	YES	81 – HES: higher or secondary education establishment 35 – REC: research organisations 34 – PUB: public bodies 31 – PRC: private for-profit entities 30 – OTH: other type of organisations

[58] Austria (5), Belgium (11), Bosnia and Herzegovina (1), Bulgaria (0), Cameroon (1), Colombia (1), Croatia (4), Denmark (7), Finland (5), France (17), Germany (21), Greece (14), Hungary (3), Ireland (7), Italy (15), Lithuania (2), Malta (1), Netherlands (11), Norway (4), Philippines (1), Poland (7), Portugal (13), Romania (4), Spain (16), Sweden (7), Switzerland (4), Turkey (3), United Kingdom (22), United States (4).

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2020
NA	Participation of RTOs and Universities	Participation of RTO[59]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: 461 (17.7 %) HES: 843 (32.4 %) % budget allocated: Res. org: EUR 309.5 million (24.3 %) HES: EUR 661.0 million (51.9 %) (Cumulative figures as of 31/12/2020)
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)[60]		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: 1.13 % Residual error rate: 0.74 %
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		Cases implemented 25 (96 %) Amount: EUR 727 519

59 RTO: Research and Technology Organisation.

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

Table III[61] - KPIs specific to each single JU

Reporting methodology: cumulatively reporting from the beginning of IMI2 until 31/12/2020

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 SRA priority areas are addressed by IMI2 projects. Number of projects: 72 Budget committed: EUR 1 937 426 519	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' b5: 'reduce the failure rate of vaccine candidates in phase III of clinical trials	50	208	362

61 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
			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)	13 completed procedures: CE mark: 2 Inclusion in regulatory guidelines: Regulatory letter of support: 1 Regulatory qualified opinion : 7 Submission for qualification opinion: 2 Number of projects: 7 Projects' budget: EUR 169 725 810	31 completed procedures: CE mark: 2 Inclusion in regulatory guidelines: 9 Regulatory letter of support: 7 Regulatory qualified opinion : 10 Submission for qualification opinion: 3 Number of projects: 20 Projects' budget: EUR 827 320 424

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	31 Number of projects: 10 Projects' budget: EUR 242 641 160	41 Number of projects: 14 Projects' budget: EUR 336 817 307
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 195.0 million (AP: EUR 161.4 million; Partners in Research: EUR 33.6 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%	40 % Number of projects: 30 Budget committed: EUR 769 843 442	54.62% Number of projects: 71 Budget committed: EUR 2 301 492 664

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	759	4 140
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	176 Number of projects: 30 Budget committed: EUR 703 763 249	482 Number of projects: 69 Budget committed: EUR 2 306 537 982
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 %	60.00 % Number of projects: 45 Budget committed: EUR 1 231 320 292	54.62 % Number of projects: 71 Budget committed: EUR 1 924 615 984

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: 16.1 % (303 out of 1887) (IMI2 cumulative figures until 31/12/2020, beneficiaries receiving EU funding only)[62]	SME participations: 16.0 % (501 out of 3 135) (IMI1 and IMI2 cumulative figures until 31/12/2020, beneficiaries receiving EU funding only)

62 Additional statistics on SME participation in IMI2 can be found in Annex 1 in table II 'Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs'.

Annex 2 – 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

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

Project title	Description of result(s)
SPRINTT geriatrics	The SPRINTT randomised controlled trial has been completed. 1 519 older people in 17 European sites were randomised to either a multicomponent intervention (MCI) programme (exercise intervention, nutritional counselling/dietary intervention, and information and communication technology intervention) or a Healthy Aging Lifestyle Education (HALE) programme in prevention of mobility impairment in initially non-disabled older people with physical frailty and sarcopaenia (PF&S). The final analyses are underway and the results that will be released soon are expected to provide new evidence of physical activity programme feasibility and efficacy to prevent mobility impairment among sarcopaenic and physically frail older adults.
SPRINTT geriatrics	A centralised biobank was populated with more than 4 200 biosamples. Biomarker studies are ongoing and will shortly provide validated biomarkers for physical frailty & sarcopaenia. Preliminary results from SPRINTT ancillary studies have shown that candidate biomarkers for PF&S exist pertaining to different biological processes, including inflammation, protein/amino acid metabolism perturbations, redox unbalance and stress responses.
SPRINTT geriatrics	Using baseline data from the SPRINTT study, the consortium analysed the association between physical frailty and care use in Europe. The results showed PF&S is associated with a significant increase in emergency admissions and hospitalisations, especially among low-income elders. These support the inclusion of frailty in the eligibility criteria of public long term care allowances and could contribute to decreasing the economic gradient in care use among the elderly community-dwelling European population.
ULTRA-DD drug development	The open access recombinant antibodies generated within the project to 14 targets in the tRNA-synthetase protein family hold specific future promise as biomarkers. The publication was featured on the front cover of the Journal of Biological Chemistry.
SPRINTT geriatrics	The SPRINTT randomised controlled trial has been completed. 1 519 older people in 17 European sites were randomised to either a multicomponent intervention (MCI) programme (exercise intervention, nutritional counselling/dietary intervention, and information and communication technology intervention) or a Healthy Aging Lifestyle Education (HALE) programme in prevention of mobility impairment in initially non-disabled older people with physical frailty and sarcopaenia (PF&S). The final analyses are underway and the results that will be released soon are expected to provide new evidence of physical activity programme feasibility and efficacy to prevent mobility impairment among sarcopaenic and physically frail older adults.

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

Project title	Description of result(s)
EMIF-AD Alzheimer's disease	Data clustering analysis of proteins in cerebrospinal fluid (CSF) from 127 control subjects and 425 individuals across the Alzheimer's disease (AD) clinical spectrum of the EMIF-AD Multimodal Biomarker Discovery study and of the Alzheimer's Disease Neuroimaging Initiative (ADNI) demonstrated that there are three distinct biological subtypes of Alzheimer's disease. Thus individuals with AD might require specific treatments depending on their subtype.

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

Project title	Description of result(s)
COMBACTE-CARE antimicrobial resistance	The REVISIT phase III trial has started recruiting patients (study number NCT03329092). This pivotal trial aims to assess the efficacy and safety of aztreonam-avibactam (ATM-AVI) for treating serious infections caused by Gram-negative bacteria, including metallo-beta-lactamase-producing multidrug resistance pathogens, for which there are limited or no treatment options. Despite the clinical, regulatory and logistical complexities the COVID-19 pandemic has introduced, more than 20 subjects have been already randomised. Out of the 40 sites already successfully activated globally, 23 are from the CLIN-NET network. This global part of this study sponsored by Pfizer is co-supported by the US Biomedical Advanced Research and Development Authority (BARDA).
COMBACTE-CARE antimicrobial resistance	The EURECA study had its final database, which contains comprehensive epidemiological, clinical and outcome data, locked. EURECA is a prospective observational study to assess the risk factors, clinical management and outcomes of hospitalised patients with serious infections caused by carbapenem-resistant Enterobacteriaceae (CRE) and *Acinetobacter baumannii* (CRAB) (study number NCT02709408). The study was conducted in 50 sites across 9 European countries, and more than 2 000 patients were prospectively recruited, including 770 patients with infections due to CRE, 266 control patients with carbapenem-susceptible *Enterobacterales*, 817 control patients without infection, and 244 patients with bloodstream infections due to CRAB. The database lock is an important step to enable the consortium to perform the analysis, with the first results expected to be available soon. Also, all the CRE and CRAB isolates that were collected are being microbiologically characterised. The results of the study will be important to inform the design of randomised trials and provide high-quality comparative historical cohorts.
COMBACTE-NET antimicrobial resistance	The final analysis of the ASPIRE-ICU study was completed and the results published. This observational study was conducted in intensive care units (ICUs) of 30 hospitals in 11 European countries, geographically spread across 4 regions (study number NCT02413242). The results showed that in this cohort study of 1 933 participants, the weighted incidence density of *Staphylococcus aureus* intensive care unit pneumonia (SAIP) was 4.9 events per 1 000 intensive care unit patient-days, and *S. aureus* colonisation was the only factor independently associated with SAIP. The team concluded that SAIP incidence may be higher than initially perceived, and future interventions to prevent SAIP should focus on patients colonised with *S. aureus* to achieve a higher efficacy.
COMBACTE-NET antimicrobial resistance	The ASPIRE-SSI study had its final database locked and all of the study samples shipped to the central lab. This is a major milestone for the teams to perform the data analysis and the analyses of the microbiological samples. ASPIRE-SSI is a prospective, observational, multicentre cohort study among adult surgical patients, which aims to determine the incidence of healthcare-associated *S. aureus* infections, particularly *S. aureus* surgical site infections (SSIs), across Europe and to assess the most important risk factors for this type of infection (study number NCT02935244). The knowledge obtained from this study will enable identification of the patients most at risk for developing *S. aureus* SSI. It should also indicate who would be likely to benefit the most from new prophylactic interventions.
COMBACTE-NET antimicrobial resistance	Extra-intestinal pathogenic *Escherichia coli* (ExPEC) is a leading and rising cause of bacterial invasive disease worldwide and there is no vaccine currently available to prevent *E. coli* infections. To collect more information to support the development of such a vaccine, two observational studies have started. General practitioners (GPs) in a maximum of 8 countries were asked to enrol adults aged 60 years or older in stable health, primarily with a history of urinary tract infections. The enrolment phase for EXPECT-1, a prospective observational pilot study to capture any hospitalisation, with a focus on hospitalisation due to invasive ExPEC disease (IED), and identification of the clinical and operational challenges that might occur during the Phase 3 vaccine

Project title	Description of result(s)
	efficacy study, was completed with 4 479 of the target of 6 000 participants (75%) enrolled. The participants are now being followed up. EXPECT-2, a prospective epidemiological study in the same hospitals participating in the EXPECT-1 study, aims to estimate the O-serotype distribution of ExPEC isolated from hospitalised patients with IED, and to evaluate the clinical case definition and risk factors for IED. Despite delays, more than 220 of the targeted 240 (92 %) patients with confirmed IED have already enrolled.
COMBACTE-NET antimicrobial resistance	The first patients have been enrolled in the HONEST-PREPS study after activation of sites in the Czech Republic, Serbia, Croatia and Romania despite challenges due to the COVID-19 pandemic. HONEST-PREPS is a prospective, observational, multicentre cohort study in patients at risks of hospital acquired and ventilator associated pneumonia (HAP/VAP). The results of this study will give valuable insight in the feasibility of a HAP/VAP platform study in Eastern Europe.
COMBACTE-NET antimicrobial resistance	The ARTHR-IS study has started recruiting patients. ARTHR-IS is a retrospective multi-centre study which aims to estimate the burden of *Staphylococcus aureus* prosthesis joint infection (SA-PJI) after a hip or knee arthroplasty and their risk factors through a case-control design. 15 hospitals have been activated (6 in Spain, 3 in France, 3 in the Netherlands, 2 in Italy, and 1 in Germany), of which 14 have started patient recruitment. 100 cases have already been included, which represents 89 % of the expected cases in the already activated centres and 66 % of cases in the whole project. In addition, 230 controls have also been recruited. The results of this study will provide critical information to develop strategies to prevent and treat SA-PJI and reduce treatment failures as well as helping in the design of future clinical trials to prevent SA-PJI prosthesis.
COMBACTE-NET antimicrobial resistance	Further to availability of the results from the observational study ANTICIPATE trial, that overall showed that that low gut microbiota diversity is a factor that favours the development of *Clostridioides difficile* infection (CDI); and the need to select another target population to perform the interventional study, the preparation of the Phase 3 trial is ongoing with the evaluation of site eligibility and the regulatory filings being submitted. This study (MICROCARE) aims to demonstrate the efficacy of DAV132, a microbiota-protective therapy developed by Da Volterra, in preventing the occurrence of CDI in patients with newly diagnosed acute myeloid leukaemia or high risk myelodysplastic syndrome treated with intensive chemotherapy.
COMBACTE-MAGNET antimicrobial resistance	A major step was reached for the EVADE study with the lock of the database in February 2020 and the start of the statistical analysis. EVADE is a Phase II, randomised, controlled safety and efficacy trial of MEDI3902, a bispecific monoclonal antibody against two *P. aeruginosa* proteins from AstraZeneca, for the prevention of ventilator-associated pneumonia in adult ICU patients (NCT02696902; EudraCT 2015-001706-34). The preliminary results presented at IDWeek 2020 showed that MEDI3902 may have a path forward in certain patient populations such as ICU patients with lower baseline inflammation.
ENABLE antimicrobial resistance	The project advanced Juvabis's EBL-1003 (a purified form of apramycin) to Phase I clinical study (first-in-human study to evaluate the safety, tolerability, and pharmacokinetics). The results showed that EBL-1003 is safe and well tolerated. A further Phase I trial in patients with complicated urinary tract infections is planned. If further trials confirm EBL-1003's antibiotic abilities, it may become a drug for treating bacterial infections resistant to existing antibiotics.
iABC antimicrobial resistance	The drug development of the compounds tested in the project has progressed: ▪ Pre-clinical toxicity testing of new formulation of Polyphor's Murepavadin (POL7080) in rodents and non-human primates has been successfully completed. Competent authority and ethics committee regulatory submissions have been

Project title	Description of result(s)
	made in the UK for a Phase I clinical study to investigate safety, tolerability, and pharmacokinetics of inhaled Murepavadin in healthy subjects. ▪ Regulatory approval (competent authority and ethics committee) has been obtained in France and the UK for the Phase I study of ALX-009 in cystic fibrosis and bronchiectasis patients. ALX-009 is a first-in-class candidate developed by Alaxia that consists in the combination of two endogenous substances, hypothiocyanite (OSCN-) and lactoferrin. Clinical sites have been initiated and recruitment is planned to begin in Q2 2021 Regulatory approval (competent authority and ethics committee) has been obtained in Germany, Spain and UK for the Phase IIa clinical study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of QBW251, a potentiator developed by Novartis for cystic fibrosis, in patients with n bronchiectasis. 17 clinical sites have been approved and recruitment is due to begin in February 2021.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
ULTRA-DD drug discovery	ULTRA-DD scientists continue to work with the IMI project FAIRplus to make all its open source data FAIR (findable, accessible, interoperable, and reusable). A total of 16 patient-derived cell assay datasets have been made available pre-publication.

Impact on regulatory framework

Project title	Description of result(s)
ZAPI infectious diseases	The EMA accepted the principle of platform technology as proposed by ZAPI in its platform master file (PfMF) for completing the annexes of the new regulation on veterinary medicinal products. This officially endorses the regulatory concept of the platform for the development and manufacturing of vaccines and opens the way for the accelerated registration of vaccines against zoonotic and animal emerging viral diseases.

Implementation of project results inside industry

Project title	Description of result(s)
ULTRA-DD drug discovery	Chemical probes, antibodies as well as chemical probe screening results from disease-relevant cell assays have been used by industry to guide drug discovery projects. The tissue platform collaboration focused on inflammatory bowel disease (IBD) (Takeda) continued until June 2020, focusing on development of new cell models (gut organoids) and compound validation. Anonymised datasets from patient-derived cell assays were shared with the artificial intelligence company Benevolent AI for deep machine learning analyses.
ZAPI infectious diseases	EFPIA partners successfully performed large-scale manufacturing at high yields of vaccine candidates for Schmallenberg virus (SBV) and Rift Valley fever (RVFV) and of selected antibodies against Middle East Respiratory Syndrome (MERS) and RVFV. Although beyond its scope, ZAPI contributed to the fight against the SARS-CoV-2 pandemic through: i) the modular vaccine technology 'ZAPI-like' was used by several industry partners for research activities on SARS-CoV-2 vaccine candidates; ii) a SARS-CoV-2 cross-reacting antibody generated by ZAPI against MERS-CoV has been has been picked up by AbbVie for further development; iii) the H2020 MANCO project

Project title	Description of result(s)
	(Monoclonal Antibodies against the 2019 New COronavirus) will advance one lead (prophylactic and/or therapeutic) monoclonal antibody into a Phase I clinical trial; iv) the IMI2 CARE project (Corona Accelerated R&D in Europe) will build on ZAPI's methodology for the discovery, generation and characterisation of virus neutralising monoclonal antibodies targeting specifically the SARS-CoV-2 spike protein.

Accessibility of resources/outputs beyond consortium

Project title	Description of result(s)
COMBACTE-MAGNET antimicrobial resistance	The epidemiology network EPI-NET, in collaboration with the Joint Programming on Antimicrobial Resistance (JPIAMR) ARCH network, has published 4 white papers to facilitate the implementation of One Health antibiotic policy interventions driven by surveillance data on antimicrobial use (AMU) and antimicrobial resistance (AMR). The white paper series provides consensus-based practical guidance, as lists of actions tailored for different settings: hospital, out-patient, long-term care facility, or veterinary, and focusing on three main topics: 1) AMS (antimicrobial stewardship) leadership and accountability; 2) surveillance of AMU for AMS; 3) surveillance of AMR for AMS. The lists of actions for each setting have also been published as easy-to-follow checklists of targets as a baseline assessment that can be used by professionals and leaders working in the human healthcare and veterinary sectors to establish and/or monitor stewardship activities. EPI-NET has also released recommendations on how to implement semi-automated surveillance of healthcare-associated infections. These recommendations are expected to help infection control project leaders, epidemiologists and other professionals aiming to implement automated surveillance to start their project effectively.
COMBACTE-MAGNET antimicrobial resistance	COMBACTE-MAGNET launched the AMR travel tool as a free online tool to assess the risk of acquiring antimicrobial resistant bacteria in travellers and limit spread across borders. The tool is targets both travellers, with a dedicated section on risks and prevention measures that can be adopted to avoid transmission of multidrug-resistant pathogens while travelling, and healthcare professionals. It gathers data on AMR from several different sources and for pathogens classified as critical and high risk by the World Health Organization (WHO)
EPAD Alzheimer's disease	The Longitudinal Cohort Study (LCS) has screened a total of 2 096 participants, collecting a wide range of cognitive, clinical, neuroimaging and biomarker data to help further understanding of the early stages of Alzheimer's disease. The database including the final dataset Version.IMI (V.IMI) is open access and publicly available via an online request via EPAD LCS Research Access Process.
iABC antimicrobial resistance	The EU Bronchiectasis registry EMBARC continues to exceed original targets, with over 19 000 patients now enrolled. Partnerships have been formed with registries in India and Australia, providing access to the data of 23 000 patients for analysis including detailed longitudinal data, making EMBARC the largest such data resource in the world. All of the European collaborators of EMBARC have agreed to utilise the same electronic case report form and the registry is now primarily focusing on long term data collection. Access to the data is open to anyone with a valid research question. To date the registry has provided data to more than 50 unique users including 7 commercial organisations and multiple research groups as well as members of the iABC consortium.
ULTRA-DD drug discovery	Project outputs are made publicly available directly or through vendor partners. E.g. > 40 direct requests were made for chemical probes; and 25 antibodies are available from Immunoprecise. A total of 16 patient-derived cell assay datasets and protocols are published on the project website. The project has received external requests from AI companies to further mine these datasets.

Project title	Description of result(s)
ULTRA-DD drug development	An R package ‘Pi’, publicly deposited in the Bioconductor, enables the user to prioritise drug targets using their own GWAS summary data. The resource had 2 373 downloads in 2020, demonstrating its uptake and utility to the scientific community. An atlas of drug targets for 30 immune-related traits is available online.

IMI2 project outputs

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result(s)
ADAPTED Alzheimer's disease	The apolipoprotein E (APOE) gene is the best known risk factor for developing Alzheimer's disease (AD), but we still lack tools and methods enabling targeted drug discovery. The project validated for the first time a fully humanised assay that fits the quality control standards for the electrophysiological characterisation of neurons and astrocytes for functional study of the impact of astrocytic or neuronal APOE haplotypes in the electrophysiological properties of neurons. This assay is amenable for further pharmacologic studies, is easily scalable for use in pharma industry set ups, and represents one step closer to the reduction of animal use in pre-clinical research.
ADAPTED Alzheimer's disease	OrganoPlate neurovascular unit (NVU) models have been developed that are suitable for multi-omics measurements in vasculature models. These can be used in the future to advance research into the NVU in AD and other neurological conditions
ADAPTED Alzheimer's disease	There is increasing evidence of the importance of the immune system in the pathophysiology of Alzheimer's disease (AD), but it is still hard to determine which molecular targets should form a focus for drug discovery. rs72824905, p.P522R is a rare coding variant in the gene encoding the enzyme phospholipase-C-γ2 (PLCG2), which is expressed in microglia, the inflammatory cells in the brain. This variant confers protection against AD. The association of p.P522R with longitudinal cognitive decline was studied in 3 595 MCI patients, and 10 097 individuals from population-based studies. p.P522R in PLCG2 reduces AD disease progression by mitigating tau pathology in the presence of amyloid pathology and, as a consequence, maintains cognitive function. Thus targeting the enzyme PLCG2 might provide a new therapeutic approach for treating AD.
AIMS-2-TRIALS autism	Demonstrated with a new, highly specific, brain-penetrant inhibitor of MAP kinase-interacting kinases a novel molecular mechanism underpinning autistic-like behaviours in rodents. Targeting this mechanism could improve social behaviour - even in adults - providing proof of concept for a new 'druggable' target in autism R&D.
BIOMAP skin diseases	Data collected from datasets of atopic dermatitis and psoriasis patients was harmonised and analysed and shared in an open access manuscript. This analysis significantly increases the FAIRness of publicly available psoriasis and atopic dermatitis transcriptomics data and represents a valuable 'ready-to-use' resource available to the scientific community.
CARE coronaviruses	The first antiviral assets for the emergency response against SARS-CoV-2 have been developed, more specifically: 1) selection of 4 antibodies to be tested *in vivo*; 2) the first drug repositioning to be evaluated in animal models; and 3) identification of hits for at least 3 targets from screening activities on small molecules libraries (chemistry hit to lead optimisation is ongoing). In supporting the R&D activities other milestones have been reached: 1) animal models of SARS-CoV-2 infection have been established for safety and efficacy studies. 2) yeast-based synthetic genomics platforms to genetically reconstruct large RNA viruses have been developed, enabling the engineering and generation of chemically synthesised clones of SARS-CoV-2 in only a week after receipt of the synthetic DNA fragments. This technical advance enables the real-time generation and functional characterisation of evolving RNA virus variants during an outbreak, and makes this system an attractive alternative to providing infectious virus samples to health authorities and diagnostics teams.
ConcePTION safety	There is currently no good animal lactation model nor a physiologically based pharmacodynamic model to provide more reliable information on the safe use of medicines during lactation. The consortium has completed two literature researches as groundwork on establishing an advanced methodology.

Project title	Description of result(s)
	The first review showed that overall, the Göttingen Minipig seems to represent the most appropriate animal species to be further investigated. The second review provides a comprehensive state-of-the art overview of non-clinical (*in vitro, in vivo* and *in silico* - computational) methods that can be used to determine transfer of medication during lactation. This overview shows also how these methods can be combined to enable prediction of medicine transfer into breast milk when human lactation studies cannot be performed. The consortium is now working in further developing these models.
EBiSC2 stem cells	A cohort of 45 induced pluripotent stem cell (iPSC) lines derived from Huntington's disease (HD) gene-expansion carriers (HDGECs) and associated controls has been generated. These new lines will be used to further investigate the mechanisms of HD progression and for the development of novel therapeutics.
ERA4TB tuberculosis	The goal of the ERA4TB project is to accelerate the development of a new, more efficient treatment regimen that will help the world to meet the United Nations goal of ending the TB epidemic by 2030. A system to dynamically manage the drug development pipeline (dashboard) has been prototyped. Procedures to manage compounds into the pipeline (including via a Pipeline Development Committee and the Steering Committee) have been fully defined and implemented. Logistics for compound distribution to labs in charge of assays in the pipeline are defined and operational. Prototype of a drug development information management (DDIM) platform to leverage all data types generated in the project. New PET/CT molecular imager for the monitoring of TB progression in mice models.
ESCulab drug discovery	ESCulab has set up a publically accessible high throughput screening (HTS) centre based on a compound library (collection of high-quality chemical compounds) and screening facilities. Researchers in the early stages of drug development can screen this library to identify compounds that show an effect on a given disease target. To contribute to the discovery and development of potential SARS-CoV-2 antiviral drugs, the project fast-tracked coronavirus screening proposals. A proposal submitted by the Pivot Park Screening Centre has been selected focusing on the identification of small molecules that could stop the virus from getting into human cells. An additional initiative from Bayer AG to fight COVID-19 has been added to the project's portfolio.
ESCulab drug discovery	A collaboration between ESCulab and the SME Metabomed has empowered cancer metabolism research. Metabomed has used the ESCulab library and screening capabilities to discover novel potent and selective inhibitors of ACSS2 (AcetylCoA short chain synthase 2 enzyme) for the treatment of cancers dependent on acetate metabolism.
eTRANSAFE safety	The eTRANSAFE consortium has designed a protocol for the generation of virtual control groups (VCGs) to reduce the number of animals used in research. By sharing legacy data from in vivo toxicity studies across multiple pharmaceutical companies, historical animal control group data could be used to construct VCGs for future toxicity studies. The use of VCGs has the potential to reduce animal use by 25 % by replacing control group animals with existing randomised data sets.
GNA NOW antimicrobial resistance	GNA NOW will manage a portfolio of novel mode of action drugs against Gram-negative bacteria to progress one compound through completion of Phase I studies plus one compound reaching Investigational New Drug stage and/or up to two compounds reaching clinical development candidate stage. The GNA NOW portfolio includes three natural-product derived assets (NOSO-502, NOSO-2G and Corramycin) all exerting a novel mechanism of action on the bacteria. As such, they will be complementary to existing treatments and less susceptible for interfering resistance development. Overall, the main results so far are: ▪ NOSO-502: definition of an anticipated human dose (1g/day).

Project title	Description of result(s)
	▪ NOSO-2G: the NOSO-502 analogues are safer but the spectrum remains similar to that of NOSO-502; the NOSO-95753 subseries have a larger spectrum but for which tolerability needs to be improved. ▪ Corramycin: first estimations of efficacious doses in human with preliminary results supporting the strategy of targeting both complicated urinary tract infections and complicated intra-abdominal infections.
Hypo-RESOLVE diabetes	Hypo-RESOLVE investigates hypoglycaemia and its impact in diabetes. The project has established and validated a hypoglycaemia-associated autonomic failure (HAAF) model of impaired hypoglycaemia counter-regulation and impaired awareness in mice to enable the study of hypoglycaemia in animals.
Hypo-RESOLVE diabetes	Developed an *in vitro* glucose-sensing cell system to investigate the potential role of mitochondrial dysfunction in defective hypothalamic glucose sensing and subsequent blunting of the counter-regulatory responses to hypoglycaemia.
Hypo-RESOLVE diabetes	Developed animal models to study new pathways of hypoglycaemia sensing and the cardiovascular consequences of hypoglycaemia. In a rodent type 1 diabetes model, using involve non-invasive laser doppler imaging/iontophoresis, recurrent hypoglycaemia was found to further impair diabetes-induced endothelial dysfunction.
Hypo-RESOLVE diabetes	The error in estimating meal carbohydrates (CHO) amount is a critical mistake committed by type 1 diabetes (T1D) subjects. The consortium has developed models to identify carb counting error, and meal and snack timing. The most important predictors of CHO counting errors are CHO and meal type. The models are now being implemented in the T1D simulator - a state-of-the-art tool to perform realistic *in silico* clinical trials. The mathematical models proposed improve the description of patients' behaviour in the T1D patient decision simulator. The models are described in the journals Diabetes Technology & Therapeutics and the Journal of Diabetes Science and Technology.
iConsensus manufacturing technologies	New technologies in mammalian-cell based production of biopharmaceuticals lead to a better manufacturing control and are tools to reduce the time and costs of the process. In mammalian cell culture, the monitoring and controlling of factors such as dissolved oxygen (DO), CO_2 and pH is important to ensure stable cell growth and process reproducibility. iConsensus has developed novel optical O_2, CO_2 and pH sensors for long-term cell culture.
IMI-PainCare pain	The project discovered that the sigma-1 receptor (σ1-R) is a promising drug target in painful urinary bladder disorders. This paves the way for the development of novel medicines for a condition where no adequate treatment is available.
IMPRiND neuro-degenerative diseases	IMPRiND scientists characterised distinct human α-synuclein (αSYN) strains *in vivo* and provided new evidence that underline their relevance in synucleinopathies (aka progressive neurodegenerative disorders). They demonstrated that a specific signature can be attributed to Parkinson's disease (PD), multiple system atrophy (MSA) and Lewy bodies dementia (DLB)-derived strains that differs from previously described recombinant strains. Indeed, MSA strains provoke the most aggressive phenotype and have more similarities with PD compared to DLB strains. Therapeutic strategies specifically targeting disease-specific strains could open up new avenues aimed at slowing or stopping disease progression.
INNODIA diabetes	INNODIA aims to understand T1D and enable the delivery of disease modifying treatments. They have identified footprints of the immune assault on the beta cells and detected similarities between the beta cell signatures induced by cytokines present at different stages of the disease, pointing to a biological process and signalling pathways activated during early and late stages of the disease. Furthermore, by mining the beta cell signature in islets from T1D patients using the connectivity map (large database of chemical compounds/drugs). the project has identified interesting drug candidates to potentially revert the effects of insulitis on beta cells.

Project title	Description of result(s)
INNODIA diabetes	Performed an integrated multi-omics analysis and identified the landscape of interferon-α-mediated responses of human pancreatic beta cells. Based on the data mining of that multi-omics analysis the project identified two compound classes that antagonize IFNα effects on human beta cells. These serve as potential T1D drug targets.
INNODIA diabetes	Developed a nanobody-based nuclear imaging tracer for SPSCT/CT targeting a previously identified beta cell biomarker, dipeptidyl peptidase 6 (DPP6), to enable the quantification of human beta cell islet grafts. This represents a tool for clinical researchers in trials aiming to prevent beta cell loss in T1D and will lead to new criteria to evaluate therapy success.
INNODIA diabetes	Developed a new protocol of iPSC differentiation into islet like clusters, achieving for the first time glucose responsive human beta cells under purely *in vitro* conditions. This will be very useful for researchers studying beta cells T1D, and also for the future development of cell therapies.
INNODIA diabetes	Developed a novel and efficient purification method for murine alpha, beta, and delta cells for downstream analysis. The project has also identified for the first time CD71 as a postnatal beta cell-specific marker, and demonstrated a central role of iron metabolism in beta cell function.
INNODIA diabetes	Developed a new beta cell line, ECN90. The project is currently using this line to develop assays that aim at discovering compounds to protect human beta cells against their destruction by CD8+ T cells. Within this screen, they might have already identified protective compounds.
INNODIA diabetes	Discovered potential T1D drug candidates. Two TYK2 inhibitors were tested and shown dose dependant inhibition of the IFNα signalling in human beta cells, decreasing its pro-inflammatory and pro-apoptotic effects without sensitising the cells to viral infection. These preclinical findings could pave the way for future clinical trials with TYK2 inhibitors for the prevention and treatment of type 1 diabetes.
ITCC-P4 paediatrics, cancer	Out of more than 500 models registered in their R2 Genomics Analysis and Visualization Platform (r2.amc.nl), covering various paediatric tumour types including some rare cancer diagnoses, the consortium has now fully established over 237 patient-derived xenograft (PDX) models. Most of them are in the process of being molecularly characterised. Leukaemia and lymphoma models have been added to the platform as 5 new partners joined the consortium, including 2 new EFPIA companies. Each model is further pharmacologically characterised by *in vivo* testing. The first efficacy studies in PDX models, testing the various compounds selected by experts, have been initiated, starting with neuroblastoma models.
ITCC-P4 paediatrics, cancer	There is a need for novel treatments for children dying of rare cancers. To prioritise targeted drugs for paediatric clinical development, the consortium has developed a unique target actionability reviews (TARs) strategy that can be used to identify mechanism-of-action-based matches between targeted anti-cancer drugs and specific cancer subtypes. To test the TAR methodology, the consortium conducted a pilot review on the MDM2 and TP53 genes. The TAR strategy and the results of the pilot have been published and the consortium is completing four additional TARs. The TAR including study scores, key data summaries and source information, is also publicly available through the R2 platform, enabling researchers to access the data in its entirety in order to use it to support additional preclinical or clinical evaluation.
LITMUS liver disease	LITMUS aims at developing, validating and qualifying better biomarkers for testing non-alcoholic fatty liver disease (NAFLD). They have generated a novel non-rodent pre-clinical model of NASH using Göttingen Minipigs which presents with a valuable disease model that more closely recapitulates the condition in humans.
LITMUS liver disease	Optimised a 7-tier histological staging system (EPoS staging system) for NAFLD-associated fibrosis developed previously by the EU-funded EPoS (Elucidating Pathways of Steatohepatitis) project (and currently applied for histological scoring of

Project title	Description of result(s)
	fibrosis in NAFLD liver biopsies). This will allow for improved and harmonised fibrosis staging.
LITMUS liver disease	Established the proof-of-principle that NMR (nuclear magnetic resonance)-based metabolomics can be used to find non-invasive metabolic biomarkers to measure NASH onset and progression. This presents a possibility for a novel approach for metabolomics biomarkers for NASH diagnosis and progression assessment.
MAD-CoV 2 coronaviruses	MAD-CoV 2 demonstrated that a combination therapy using remdesivir (a drug that has received authorisation for COVID-19, improving outcomes but not decreasing mortality) with recombinant soluble angiotensin-converting enzyme 2 (ACE2), noticeably improved their therapeutic windows against SARS-CoV-2. This data lays the groundwork for the study of combinatorial regimens in future COVID-19 clinical trials and could lead to better therapy in future.
MELLODDY machine learning	MELLODDY aims to develop superior predictive models to speed up drug discovery by applying a machine learning algorithm to the private research data of 10 pharmaceutical partners, while keeping this data private. In 2020, the first version of the algorithm passed rigorous security audits ensuring the data is kept confidential. This allowed the pharma partners to allow the algorithm to be run on their massive datasets (>1 billion data points on >15 million chemical compounds). In 2021, the algorithm will be optimised to maximise its impact. Ultimately, using machine learning in this way should accelerate drug discovery.
PHAGO neuro-degenerative diseases	PHAGO has shown that antibodies against the stalk region of the triggering receptor expressed on myeloid cells 2 (TREM2) - essential for the transition of homeostatic microglia to a disease-associated microglial state - can enhance the protective clearance function of microglia and may have future potential for a clinical application in a variety of different clinical syndromes including Alzheimer's disease, frontotemporal lobar degeneration, amyotrophic lateral sclerosis, retinal degeneration, multiple sclerosis, and obesity-associated metabolic syndromes.
PHAGO neuro-degenerative diseases	PHAGO has identified a new, rare TREM2 variant, a glycine-to-tryptophan substitution at amino acid position 145 (Gly145Trp) that is associated with dementia. Gly145Trp is located in the intrinsically disordered region (IDR) of TREM2. Cellular studies showed that this variant led to IDR shortening and structural changes of the mutant protein resulting in an impairment of cellular responses upon receptor activation. These results suggest that a Gly145Trp-induced structural disturbance and functional impairment of TREM2 may contribute to the pathogenesis of an Alzheimer's-like form of dementia.
PREMIER environmental issues	PREMIER is developing a user-friendly digital system (database and assessment module) to help assess the environmental impact of pharmaceuticals more efficiently. A first version has been released to the consortium. The assessment tools are under development and a new version will be released every 6 months.
RESOLUTE drug development	Solute carriers (SLCs) are proteins that transfer nutrients into cells and are implicated in several neurological diseases, diabetes and cancer. Despite their importance, they are relatively understudied. RESOLUTE's objective is to intensify research on SLCs and, ultimately, make use of them as targets for drug development. The project has generated the following tools to advance research on SLCs: - expression plasmids for 447 human SLCs publically available through Addgene.org for fast and efficient sub-cloning into a wide range of expression vectors; - 536 cell lines expressing SLCs; - 20 different transport assays for 13 prioritised SLCs useful for functional characterisation of SLCs and new drugs testing.
RHAPSODY diabetes	Discovered a new transcription factor that protects β-cells against dedifferentiation, and which may be targeted to prevent diabetes development.

Project title	Description of result(s)
RTCure rheumatoid arthritis	Novel mechanisms that trigger arthritis-associated autoimmunity have been demonstrated whereby potentially pathogenic T and B cell immunity can be triggered at various sites of the body even before the onset of clinical arthritis. The findings resulted in 5 publications (PNAS, Scientific Report, Rheumatology, RMD Open and Ann Rheum Dis) and they are interesting for potential early interventions, for example at mucosal surfaces.
RTCure rheumatoid arthritis	Specific immune processes including a plethora of modified and unmodified antigens have been demonstrated to drive the expansion of autoreactive B cells conceivably present in the inflamed joint of RA-patients and which therefore may represent promising targets for tolerising immune therapies, the ultimate goal of the RTCure project.
RTCure rheumatoid arthritis	Regulatory mechanisms influencing disease-inducing immunity have been identified, for example it has been demonstrated that zonulin, a potent regulator for intestinal tight junctions associated to gut microbial disbiosis, is highly expressed in autoimmune mice and humans and can be used to predict transition from autoimmunity to inflammatory arthritis. Treatment with the zonulin antagonists effectively reduces arthritis onset. These data identify a preventive approach for the onset of autoimmune disease by specifically targeting impaired intestinal barrier function.
RTCure rheumatoid arthritis	Flow cytometric and CyTOF immunophenotyping assays have been standardised and validated to monitor immunological effects of various immunologic therapies (ongoing and planned) in consistent and comparable ways.
TransQST safety	BioModels Parameters - Enhancement of BioModels resource: One of the major bottlenecks in building systems biology models is identification and estimation of model parameters for model calibration. TransQST has developed a new service, BioModels Parameters, to facilitate search and retrieval of parameter values. Parameter values are extracted from over 1 370 kinetic models and made discoverable. The resource consists of over 84 000 biochemical reactions involving more than 56 000 entities and 95 000 parameters. Manuscript published. The data are accessible via web interface and API. BioModels Parameters is free to use and is publicly available. The retrieved rate equations and parameters can be used for scanning parameter ranges, model fitting and model extension. Thus, BioModels Parameters will be a valuable service for systems biology modellers.
VAC2VAC vaccines	Several animal-free methods/protocols (physicochemical, immunochemical, cell-based) have been developed with the aim of replacing the animal tests that are currently used by industries to ensure consistency among different vaccine batches. More specifically: ▪ tailor-made desorption protocols have been developed for human diphtheria, tetanus and acellular pertussis (DTaP) vaccines, facilitating the use of physicochemical, immunochemical, and cell-based assays; ▪ enzyme immunosorbent assay (ELISA) was confirmed to be efficacious for the determination of vaccine potency of tick-borne encephalitis virus (TBEV) and sensitive for testing *Clostridium chauvoei* vaccines; ▪ a monocyte-activation test using human peripheral mononuclear cells (PBMC) was validated and transferred to industry partners, for adaptation to GMP standards; ▪ a two-stage DNA-based method for the characterisation of tetani seed strains has been established and is ready for validation.

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

Project title	Description of result(s)
AIMS-2-TRIALS autism	Autism is a very heterogeneous condition, hence the need for a precision medicine approach. The consortium discovered 11 candidate stratification or prognostic biomarkers, including markers based on cognitive profile, eye-tracking, resting state functional connectivity and structural magnetic resonance imaging (MRI) with validation steps (pre-analytical validation, analytical validation and clinical validation to be achieved prior to application for qualification advice) in various stages of implementation. The markers will be critical enablers for the successful development of personalised treatment in autism.
AMYPAD Alzheimer's disease	Positron emission tomography (PET) imaging can identify amyloid-β (Aβ) plaques *in vivo* with high sensitivity and specificity in clinical populations, but better tools are needed to detect emerging amyloid pathology, and the extent of the pathologic burden. The project used data from 3 027 individuals (1 763 cognitively unimpaired, 658 impaired, 467 with Alzheimer disease [AD] dementia, 111 with non-AD dementia, and 28 with missing diagnosis) to develop a reliable model for staging cortical amyloid deposition using PET with high generalisability. The stage classification can help identify individuals with Alzheimer pathologic changes who have greater risk of amyloid-related long-term cognitive decline, a relevant population for secondary prevention trials.
AMYPAD Alzheimer's disease	Super-agers are individuals performing cognitively above the norm even at high age, thus with extraordinary resistance mechanisms against brain aging processes and/or neurodegeneration. By comparing the intracerebral amyloid and tau burden *in vivo* in 26 super-agers, 25 normal-agers and 25 patients with mild cognitive impairment (MCI), all above 80 years of age, super-aging associated with the resistance to tau and amyloid pathology, which likely permits maintenance of cognitive performance despite advanced age. These results points to potential novel treatment concepts based on the understanding of the responsible resistance factors.
DRIVE vaccines	DRIVE has developed a platform with the appropriate tools, protocols, infrastructure and sites network to estimate brand-specific influenza vaccine effectiveness (IVE) on a yearly basis, using real-world evidence and a collaborative public-private partnership governance model. Thus, DRIVE is able to provide vaccine effectiveness data as part of evaluation of influenza vaccines in post-marketing setting.
ERA4TB tuberculosis	A radiological score for the assessment of tuberculosis progression has been validated in mouse models. This radiological score integrated in the experimental workflow enables longitudinal monitoring for prospective efficacy studies in drug development programmes.
Hypo-RESOLVE diabetes	Identified potential novel regulators of hypoglycaemia detection involved in the control of glucose inhibited neurons. This sheds light on our understanding of the mechanisms and consequences of hypoglycaemia.
INNODIA diabetes	Discovered a potential link between SARS-CoV-2 and diabetes through putative infection of pancreatic microvasculature and/or ductal cells and/or through direct *β*-cell virus tropism. This suggests a link between inflammation and ACE2 expression levels in islet *β*-cells
INNODIA diabetes	Identified differential beta cell expression of 216 genes, identifying key pathways for T2D pathogenesis that comprised defective insulin secretion and oxidative stress. These novel approaches are enabling the project to compare type 1 diabetic vs non-diabetic single beta cell transcriptomes, to get insights into the pathophysiology of the beta cells in this form of diabetes and may lead to better understanding of the disease.

Project title	Description of result(s)
LITMUS liver disease	Identified and validated in a replication cohort 25 differentially expressed genes as fibrosing steatohepatitis progressed through stages F2 to F4. This finding provides insights into the pathophysiology of progressive fibrosing steatohepatitis, and proof of principle that transcriptomic changes represent potentially tractable and clinically relevant markers of disease progression. This may enable better diagnosis and staging of steatohepatitis.
LITMUS liver disease	Shortlisted 20 lipid biomarkers for further examination in the study cohort to validate their utility in diagnosing or staging the non-alcoholic liver diseases.
LITMUS liver disease	Potential bacterial and metabolic markers have been identified in the study cohort and are currently undergoing validation. These markers have been associated with non-alcoholic liver disease (NAFLD) progression, one of them also associated with the fibrosis and may be of diagnostic or prognostic utility.
MACUSTAR eye disease	There is an unmet need for treatment options in intermediate age-related macular degeneration (iAMD). To foster the development of new therapies, MACUSTAR is developing novel clinical endpoints with a regulatory and patient access intention. To do so, the consortium completed the recruitment of study patients in the low-interventional clinical multicentre study employing a novel two-part design. A total of 718 (96% of planned recruitment number) subjects were enrolled (screening and baseline visit performed and data documented): ▪ cross-sectional part (total duration, 1 month): 168 iAMD patients, 34 patients with early AMD, 43 patients with late AMD, and 56 age-matched, normal controls. ▪ longitudinal part (total duration, 36 months): 585 iAMD patients and 34 patients with early AMD. In addition, the consortium achieved 1 295 follow up visits (293 V3, 458 V4, 353 V5, 170 V6, 21 V7) as well as extensive data quality checks of functional testing and imaging data performed. The cross-sectional part of the study was completed successfully and data are being analysed. Preliminary analysis show that all tested outcome measures, i.e. functional, structural and patient reported outcomes (PROs), were successfully implemented and support being carried forward into the longitudinal study in order to assess their responsiveness to diseases progression over time or establish disease progression over time, respectively (structural outcomes). The protocol of the MACUSTAR low-interventional clinical multicentre study has been published, together with the manual of procedures to administer patient reported outcome (PRO) questionnaires, the manual of procedures to perform retinal imaging and the model consent form. These study procedures can be used by investigators for other clinical trials.
MOBILISE-D digital health	Because loss of mobility is an important feature of many health conditions, there is a need for regulatory accepted walking-related digital mobility outcomes (DMOs) as clinical trial endpoint measures in a variety of disease states. To achieve this, the consortium has elaborated a roadmap that is published (A Roadmap to Inform Development, Validation and Approval of Digital Mobility Outcomes: The Mobilise-D Approach). Part of the roadmap is the technical validation study. The consortium has started to recruit the 120 participants for this study (healthy older adults, Parkinson's disease, multiple sclerosis, chronic obstructive pulmonary disease, congestive heart failure, proximal femoral fracture) across sites in 3 countries: Germany, United Kingdom and Israel. The conduct of study is challenging due to the COVID-19 pandemic and recruitment is slower than anticipated. This study will identify the best algorithms to quantify real-world walking speed and other relevant characteristics to describe the way we walk using a variety of advanced technology that will then be taken for further clinical validation.

Project title	Description of result(s)
MOPEAD Alzheimer's disease	The usefulness of the diabetes specific dementia risk score (DSDRS) as a cognitive impairment screening tool is unknown. The project used DSDRS in 82 type 2 diabetes (T2D) patients for screening of cognitive impairment and found a high prevalence of unknown cognitive impairment in such patients. Thus DSDRS is a useful screening tool for detecting cognitive impairment in diabetic patients.
PERISCOPE vaccines	An assay to measure cellular responses to pertussis in infants was qualified in readiness for deployment in pertussis vaccination studies. A mucosal antibody assay against pertussis antigens not included in the aP vaccine was developed. An age-dependent increase in this non-aP response in aP vaccinated-children suggest this assay could yield a biomarker of asymptomatic infection in vaccinated children.
RADAR-AD Alzheimer's disease	Developed and deployed a technology-enabled system to measure identified functional domains via selected and bench tested devices (smartphone, wearable and fixed-home sensors) in people in the Alzheimer's disease (AD) spectrum, from preclinical AD to dementia stage. The achievement enables the start of the project studies that aim to demonstrate that such measures provide more sensitive indexes of functional decline than current approaches by integrating a combination of remote monitoring technologies (RMT)-based parameters.
RAPID-COVID coronaviruses	The project point of care (PoC) diagnostic prototype instrument, consisting of an all-in-one platform for extraction, amplification and detection, has being used for preliminary field testing in preparation for the large clinical validation study. This system combines quantitative polymerase chain reaction (qPCR) and patented chromatography technology for the detection of up to 6 pathogens in one test. The impact of this development is the provision of highly sensitive and specific detection for rapid front-line screening of multiple pathogens to ensure COVID-19 patients can be quickly isolated, limiting the spread of the disease.
RESCEU respiratory disease	By analysing and assessing 25 132 abstracts and studies, RESCEU published a review in the Journal of Infectious Diseases revealing the impact of respiratory syncytial virus (RSV), the most common cause of severe respiratory illness in infants and children worldwide. Although a wide range of biomarkers have been associated with RSV disease severity, the review illustrates the broad heterogeneity of study designs and high variability in the definition of severe RSV disease. This highlights the importance of performing additional research (including epigenetics, metabolomics, and microbiome) for the definition of robust biomarkers that need to be validated in prospective studies.
RHAPSODY diabetes	RHAPSODY works on assessing the risk and progression of prediabetes and type 2 diabetes to enable disease modification. They have progressed with 6 peptide/protein biomarker candidates by performing replication analysis using validated enzyme-linked immunosorbent assays (ELISAs), in samples from the ANDIS ACCELERATE and PLIC cohorts. The data generated is being used in the development of the T2D progression model, which will help to predict how type 2 diabetes will progress in patients..
RHAPSODY diabetes	Integrated multi-omics analysis of 121 partial pancreatectomies revealed the first islet gene co-expression modules and their correlation with plasma lipids, HbA1c and other diabetic parameters that leads to a predictive mechanistic model of beta-cell failure and may be helpful in predicting T2D progression linked to high plasma lipid levels.
RHAPSODY diabetes	New genes, including Scd1, have been discovered to provide resistance of beta-cells to gluco-lipotoxicity. This finding further expands our understanding of T2D.
RHAPSODY diabetes	A specific link between plasma triglycerides and liver carnitine transporters and beta-cell insulin secretion has been identified and is being validated by functional studies. This finding further expands our understanding of the T2D.
RHAPSODY diabetes	Identified candidate genes strongly associated with plasma triglycerides and potentially involved in the control of the pancreatic beta cell function that may be targeted to revert to the pre-diabetic state.

Project title	Description of result(s)
RHAPSODY diabetes	Developed assays for the candidate protein biomarker of pancreatic cell death, IL18Ra, for ultimate use in blood samples, based on aptamer technology.
RHAPSODY diabetes	Defined epigenetic markers for T2D in the exocrine pancreas in genes relevant to pancreatic cancer pathophysiology, providing insight into the link between T2D and pancreatic cancer.
TransBioLine safety	With the aim of developing novel safety biomarkers that will reliably indicate injury of the different target organs for drug development purposes, the project established specific research plans for each target organs with the input of health authority for future interactions/ submissions with both EMA and FDA. Notably, based on its Letter of Intent (LOI) submissions, the project's research approach to qualify biomarkers for drug-induced vascular injury drug-induced vascular injury (DIVI), drug-induced kidney injury (DIKI), and drug-induced CNS injury (DINI) were accepted into the FDA Biomarker Qualification Program.
TransQST safety	The development of all new medicines requires extensive nonclinical and clinical testing prior to drug approval by regulatory agencies and consequent marketing launch. Although clinical trials are generally conducted safely based on nonclinical results, a significant number of potential medicines (drug candidates) fail during clinical testing due to safety signals in human subjects, and high profile safety failures do occur. The TransQST project is gathering together existing data and generating new data to support the development of tools that should facilitate the assessment of drug candidates' safety before undergoing clinical testing. TransQST is working on understanding when results in non-clinical testing can be reliably extrapolated to humans. Since liver, kidney, cardiovascular and gastrointestinal-immune systems are among the more common target organs when safety signals are encountered during clinical testing, TransQST focuses on these four systems. Kidney QST model: A proof-of-concept quantitative systems toxicology (QST) model of drug-induced kidney injury was established by the project partners. It was fitted to data from rats dosed with cisplatin and applied for translational prediction of renal injury marker response in human with reasonable performance based on species-specific pharmacokinetics. It is under evaluation by a partner for potential internal use & further development.
TransQST safety	Multiscale QST model of oncotherapeutics induced gastrointestinal (GI) injury: The project developed a multiscale QST modelling approach to describe the dynamics of transcription, single cells, tissue, barrier integrity and risk of diarrhoea at relevant drug exposures. Model performance was demonstrated using an *in-vivo* multiscale dataset of 5-FU induced GI toxicity. Clinical predictions for 5-FU were generated at multiple scales and validated with reported clinical adverse effects. This would aid decision making on drug safety.
TransQST safety	Multiscale computer models of human cardiac electrophysiology and contractility: The project developed two human computer models: 1) ventricular electro-mechanics (Margara et al. 2020); 2) Cardiac purkinje electrophysiology (Trovato et al. 2020). These models can be used for early predictions of drug-induced changes in human cardiac electrophysiology and contractility.
TransQST safety	CAMDA DILI model: A machine learning model to predict drug induced liver injury (DILI) was evaluated in the CAMDA challenge for prediction of toxicity using CMap drug safety data. CAMDA focuses on the analysis of massive data in the life sciences. It introduces and evaluates new approaches and solutions to the big data challenge. An essential part of CAMDA is its open-ended data analysis challenge of complex data sets, often featuring novel technological platforms, exceptionally large cohorts, and heterogeneous data sources and types. Academic and industrial researchers worldwide alike are invited to take the CAMDA challenge. Accepted contributions are presented in short talks, and the results of analyses are discussed and compared at the CAMDA conference. Both contestants and other interested researchers are welcome at the meeting.

Project title	Description of result(s)
TRISTAN safety	The TRISTAN project has published a review providing a better overview and knowledge of the imaging techniques available and how they can be used in lung injury imaging. The review summarises the most useful molecular imaging tracers and outlines their potential for functional readout in a translational manner. This publication could be of great interest for future development of early biomarkers that could predict disease progression in interstitial lung disease (doi: 10.3390/jcm10010107).
TRISTAN safety	The project's preclinical team has demonstrated a successful multi-imaging approach (a novel positron emission tomography (PET) tracer for collagen-i recognition combined with multi-echo magnetic resonance imaging (MRI)) to monitor early and late stage fibrotic changes in bleomycin-induced lung injury in rats. This study supports the development of imaging biomarkers and their further introduction into clinical use where they can be used to improve diagnoses and choice of therapeutic.
TRISTAN safety	The TRISTAN project published a scientific paper describing a new radiotracer to image interleukin-2 receptor (IL-2R) positive immune cells. This tracer demonstrated improved positron emission tomography (PET) imaging characteristics compared to existing IL-2R imaging agents to image T-cells in mice. Based on these promising results, the project is currently preparing a clinical trial to evaluate the potential of this new IL-2 radiotracer to predict and monitor response to immune checkpoint inhibition in cancer patients. (DOI: 10.2967/jnumed.119.238782)
VITAL vaccines	The project developed a cytokine marker panel including 18 markers to study the inflammaging status of each individual and relate this to vaccination response. Inflammaging is the long-term result of the chronic physiological stimulation of the innate immune system, which can become damaging during ageing.

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
AB-Direct antimicrobial resistance	The aim of this project is to investigate the potential of gepotidacin as new novel antibiotic currently in Phase 3, for the treatment of a bacterial infection of the throat caused by the bacteria *Neisseria gonorrhoeae* or inflammation of the prostate caused by the bacteria *Escherichia coli*, by demonstrating sufficient penetration of gepotidacin into tonsils and prostate tissue. So far, the most important project achievement is the selection of the optimal microdialysis experimental conditions for animal and human tissues. In addition, the consortium has made considerable progress in developing a mathematical model that relates the gepotidacin tissue exposure with the killing activity of the antibiotic on the relevant bacteria (*E. coli* and *N. gonorrhoeae*) *in vitro*.
AIMS2-TRIALS autism	Started to pilot the use of passive and active remote digital monitoring (RDM) in a subset of participants in the arbaclofen clinical trial. The results will ascertain the feasibility and validity of using digital tools to assess outcomes in autism that may be poorly captured by more traditional laboratory- and clinic-based approaches – including treatment-related change in everyday social skills and communication for autistic people.
CARDIATEAM diabetes	Amendment of the clinical study protocol for the homogeneous detection of COVID infection using the same rapid kits in all clinical centres. (The result of the COVID test determined whether or not the patients could be included in the clinical trials.) Version 3.9 : Standard of procedures on imaging modalities.
COMBINE antimicrobial resistance	One of the objectives of this project is to propose innovative methods to optimise preclinical and clinical research for the development of products against antimicrobial resistant infections. COMBINE aims to increase the success rate of vaccine and antibiotic trials by proposing innovative study designs and novel strategies to analyse clinical trial data.

Project title	Description of result(s)
	COMBINE has issued an open data call within the antimicrobial resistance community for parties interested in sharing their data. Moreover, to identify current gaps in vaccine development and to guide the data analysis work, the consortium published a literature review on vaccines for nosocomial antimicrobial resistant pathogens (Frontiers in Immunology).
DRIVE vaccines	The DRIVE test-negative design protocol for brand-specific vaccine effectiveness has been improved in 2020 and significantly updated taking into account the fact that the SARS-CoV-2 virus was spreading in the different countries at the same time as flu viruses, contrary to previous years for influenza vaccine effectiveness interpretation.
ERA4TB tuberculosis	Two compounds, TBAJ-1 and GSK-1, are already in FTIH (first time in human) trials. The clinical protocol trial design has been improved by establishing in both of them two parts: 1) single ascending dose (SAD) design l with a food-effect cohort; 2) multiple ascending dose (MAD) design. The design allows to evaluate safety, tolerability and pharmacokinetics.
INNODIA INNODIA HARVEST diabetes	The master protocol developed in INNODIA has been incorporated in the MELD-ATG trial (collaboration with Sanofi) and in the IMPACT trial (sponsored by IMCYSE) in INNODIA and INNODIA HARVEST respectively. The home measured C-peptide, the miRNA testing and the whole INNODIA-developed 'omics' tool is implemented in these industry-sponsored or industry supported clinical trials. The INNODIA master protocol was also the inspiration for the Novartis-sponsored Iscalimab trial (INNODIA HARVEST).
PERISCOPE vaccines	An outpatient controlled human infection study was initiated to confirm results obtained previously in in-patient studies and evaluate risk of asymptomatic transmission to household contacts. Approved and launched a randomised clinical trial to investigate and compare immunogenicity of aP vs wP vaccines in infants born to aP-vaccinated mothers.
PREFER patient involvement in R&D	There is a value in integrating patient preferences for decision-making throughout the medical product lifecycle (MPLC). However, to do it effectively, it is important first to understand existing processes and decision-points. The consortium has identified 15 critical decision points in the industry, regulatory and HTA decision-making where patient preference information can support the process: 6 for industry, 3 for regulatory bodies, and 6 for HTA.
RADAR-AD Alzheimer's disease	It is critical to define appropriately the targets functional domains for remote monitoring technologies (RMT) used in clinical studies of Alzheimer's disease (AD) patients. The project published a prioritised list of functional domains that are likely to be specific and sensitive to early stages of AD progression and predictive of deleterious long-term outcomes such as loss of independence and nursing home entry. These findings can be applied to any clinical study that wishes to measure function in early AD or employ RMTs to measure health parameters and disease progression remotely.
Trials@Home digital health	In 2020, the Trials@Home project published draft recommendations on ongoing experiences with remote and decentralised clinical trial (RDCT) technologies. The recommendations are based on in-depth interviews with key stakeholders including patient representatives and an extensive systematic literature review. They apply to all aspects of RDCTs from design, planning and set-up to close-out and reporting. The key recommendations are: ▪ answer an important research question; ▪ keep the focus on participants; ▪ simplify the participant experience whilst maintaining quality and scientific rigour.
Trials@Home digital health	To link terminologies used in remote and decentralised clinical trials (RDCT) with those used in traditional clinical trials, the Trials@Home project published a glossary which provides updated definitions of already used terms in clinical trials as well as new terms, specific for RDCTs. Multiple external glossary sources were analysed for this work, gaps and conflicts were resolved and resulted in re-defining some terms and

Project title	Description of result(s)
	introducing new ones where necessary. This glossary is already being used by other stakeholders in the industry.
Trials@Home digital health	In 2020, the Trials@Home project launched a call to recruit innovative technologies that could be used to implement remote decentralised clinical trials. The technologies should cover the full clinical trial process, including data acquisition & processing, patient engagement, setup & design, closeout & reporting, operation & coordination, intervention & follow-up and recruitment & enrolment. The successful technologies will be used in the clinical study to be launched in 2022.
Trials@Home digital health	In 2020, the Trials@Home consortium collaborated with ECSEL JU to help define an ECSEL call for technology developers who could develop/fine-tune their devices to meet the exact needs of the Trials@Home remote clinical trials. The collaboration included a public information campaign and brokerage event.
TRIC-TB tuberculosis	TRIC-TB has started a first in human (FIH) clinical trial in December 2020. It is a single centre trial with single ascending dose followed by multiple ascending dose protocol. The FIH study evaluates safety and tolerability and pharmacokinetics of the drug in healthy volunteers and thus the trial design is standard.
VALUE-Dx diagnostics	The goal of VALUE-Dx is to generate evidence on the medical, economic, and public health value of diagnostics in treating AMR. The VALUE-Dx trial has been divided into two separate protocols for community care settings and hospital settings. This was considered most feasible and appropriate, since point of care diagnostics should be evaluated in the setting where they are intended to be used. The PRUDENCE trial will include participants recruited by primary care clinicians and in long term care facilities (LTCF). The LTCF network will be managed by University of Verona, LOTTA-Net and RAMBAM. The following networks have agreed to participate: UK, Greece, Georgia, Ireland, Poland, Germany, Belgium, Hungary, Spain, France, Italy, Switzerland, and Israel. The UOXF has reviewed the PRUDENCE trial protocol and have agreed to act as trial Sponsor for the whole PRUDENCE trial. The sponsor letter, confirmation of insurance, protocol and associated documents have been sent to the networks for translation and submission to their national regulatory agencies. By the end of 2020 the UK, Georgia and Hungary had received all regulatory approvals and executed the contractual agreements to enable them to start in January 2021. However, the PRUDENCE Trial Management Group met on the 22nd December 2020, and due to the pressures on primary care with the COVID-19 pandemic, the vaccine roll-out and lack of flu circulating, they proposed postponing the start of PRUDENCE to September 2021. The VALUE-Dx Executive Board and other work packages have agreed to this postponement. The ADEQUATE study consists of an adult and a paediatric protocol. The adult part will be executed by the UMCU and the paediatric part will be executed by the PENTA Network. UMCU remains study sponsor. The adult protocol has been registered in clinicaltrials.gov NCT04547556. During 2020, 8 adult sites and 6 paediatric sites have been selected. EC submissions have been completed for the first sites (4), and first approvals.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s)
PERISCOPE vaccines	Maternal vaccination study: differences in mucosal antibody binding to *B. pertussis* between infants born to mothers vaccinated with acellular pertussis (aP) or with a control tetanus vaccine during pregnancy; the study of differences between infants after vaccination with aP vs whole-cell (wP) vaccines is ongoing. The development of non-invasive mucosal sampling and antibody assay enables large-scale and repeated immune monitoring of vaccines in populations normally difficult to sample, including infants.

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

Project title	Description of result(s)
HARMONY big data, cancer	HARMONY, in close collaboration with the European Myeloma Network (EMN), collected data from more than 7 000 patients with multiple myeloma from 15 European clinical trials enrolling newly diagnosed multiple myeloma (NDMM) patients from 2005 to 2014. The aim of this analysis has been to revise the Revised International Staging System risk stratification model, by analysing the prognostic value of each single baseline risk feature, to improve prognostication in NDMM patients. The new scoring system improves risk stratification in NDMM, representing a first step towards a risk-adapted approach. Results have been presented and published at the EMN 2020 Congress, the EHA and ASH annual conferences.
INNODIA diabetes	Discovered that type 1 diabetes may be a case of one name but two diseases (i.e. younger-onset with primary T cell-driven mechanisms and older-onset with primary beta cell-driven mechanisms), leading to similar clinical presentations but requiring different treatments. This might enable more targeted treatment approached for T1D in the future.
INNODIA diabetes	Discovered that T1D may be a disease of both the immune system and beta cells, resulting from a conflicting dialogue between them. This is seen in an overlap between the hyper-immune (CD20high) immunohistological endotype of insulitis and altered proinsulin processing in beta cells, and exemplifies the intertwining of the two participants in the dialogue.
RHAPSODY diabetes	Discovered that prediabetes is causally related with coronary artery disease, and its prevention is likely to be most effective if initiated prior to the onset of diabetes.
TransQST safety	Histopathology terms standardisation: a FAIR-compliant (findable, accessible, interoperable & reusable) nomenclature for histopathology standardisation was developed. DrugMatrix and TG-GATES pathology terms were standardised for integrative analysis. The current collection has 326 standardised terms comprising 84 distinct pathology terms, 39 distinct anatomical regions, and 32 distinct cell types. The modified underlying ontologies can be accessed at the EBI Ontology lookup service and annotation of TransQST datasets using the standardised terminology is ongoing. This standardised approach should support harmonisation of histopathological data across public and private resources.

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

Project title	Description of result(s)
AIMS-2-TRIALS autism	The AIMS-2-TRIALS clinical trials network (CTN) has grown to include 120 sites across 38 countries, with access to >28 000 newly diagnosed autistic individuals each year and trained to Good Clinical Practice standards. The network is an important resource to enable clinical trials of new medicines for autism in Europe.
AIMS-2-TRIALS autism	The Synaptic Gene Study (SynaG) consists of two sub-studies in patients with rare diseases causing autism. The first has consented 15 neurexin-1 deletion individuals and 3 controls. The second has recruited 14 controls, one Phelan McDermid Syndrome (PMS) participant, three participants with idiopathic autism, and two carriers of other copy number variation. Participants completed the protocols as far as the COVID-19 restrictions allowed. The study will identify biomarkers linked to these monogenic forms of autism to enable clinical trials for these rare disease populations.

Project title	Description of result(s)
AIMS-2-TRIALS autism	The recruitment for the foetal / neonatal prognostic study has started and some brain scans acquired before the study was halted due to the COVID-19 lockdown. Furthermore, ethics approval has been received to conduct the first ever prospective study of the impact of prenatal exposure to maternal immune activation (to COVID-19) on early brain development in relation to autism. The studies will provide important data on bio-behavioural markers to predict which of those children at increased risk of neurodevelopmental disorders will receive a diagnosis of autism.
AIMS-2-TRIALS autism	The consortium is running two single dose 'shiftability' studies with repurposed compounds in adults with autism and non-autistic controls. For the study with the GABA-A a2/a3 subtype positive modulator (AZD7325) baseline data are available from 43 autistic individuals (ASD) and 50 non-autistic controls, and 11 ASD and 13 controls completed the study before it was paused due to the COVID 19 pandemic. For the tianeptine (selective serotonin reuptake enhancer) study, data were obtained from 24 autistic individuals and 23 non-autistic controls at both baseline (i.e. placebo) and tianeptine time points. Both compounds were well tolerated. The studies will show the ability of any of the two compounds after acute dosing to 'shift' abnormal brain signalling in individuals with autism towards functional signatures seen in controls, validating two potential novel treatment mechanisms.
AIMS-2-TRIALS autism	The Phase 2 trial to explore the efficacy, safety and tolerability of arbaclofen in children and adolescents (ages 5-18) for the treatment of social adaptive behaviours disorders in autism has started. Ethics and regulatory approval are secured in 7 clinical trial sites in 3 European countries and 12 patients have been randomised. This study will provide critical data for the validation of the N170 biomarker and the Vineland Socialisation composite score in the context of use of stratification of the autistic population in a trial.
AMYPAD Alzheimer's disease	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 (DPMS), despite the significant challenges of the COVID-19 pandemic, concluded recruitment with a total of 844 randomised patients, out of the expected 900, of which 679 have already undergone an amyloid scan. The initial analysis of the primary endpoint strongly suggests that the main objective of DPMS will be reached in spite of the COVID-19 crisis.
AMYPAD Alzheimer's disease	Amyloid imaging is an important tool for identifying patients with Alzheimer's disease for clinical trials and detecting the efficacy of a treatment. During 2020, the prognostic and natural history study (PNHS) saw great progress in the inclusion of additional parent cohorts (PCs) to boost recruitment, reaching a total of 17 recruitment sites activated. Despite significant challenges due to the COVID-19 pandemic, this strategy allowed the project, by end of 2020, to reach 731 research participants consented, of which 546 have undergone an amyloid scan. The study results will provide precious information on the value and optimised use of amyloid imaging to detect the effects of treatments in a clinical trial.
BIOMAP skin diseases	BIOMAP (operating in the area of skin diseases: atopic dermatitis and psoriasis) finalised a mapping exercise on 60 cohorts, and developed a glossary for clinical and -OMICS data, essential to ensure the efficient harmonisation of the existing heterogeneous datasets. These glossaries will now be used to harmonise the data which are in the process of being uploaded to centralised database at University of Luxembourg. This will have the potential to become a gold standard for new, prospective cohorts.
c4c paediatric clinical trials	To ensure good paediatric development programmes, the consortium is setting up standing expert groups to provide strategic feasibility advice (scientific advice) to study sponsors as part of the network. So far, 12 advice requests have been received from 6 of the c4c industry partners requiring contributions from clinical experts, methodology experts and in some cases requesting patient and public involvement. Out of the 12, 5 of these advice requests have been addressed. The experience with the process and the quality of the advice provided are being gathered with the view to having an optimised input of the c4c network into study design.

Project title	Description of result(s)
c4c paediatric clinical trials	To test the viability of the c4c paediatric clinical trial network, in particular the processes and infrastructure provided by the network, the three proof-of-viability non-industry studies that were selected through a defined selection process are now starting. KD-CAAP started with the first clinical site open as of 28 September 2020 at Great Ormond Street Hospital NHS Foundation Trust, UK. While piloting the network, this KD-CAAP (Kawasaki Disease Coronary Artery Aneurysm Prevention trial) study will answer the important question on the best way to treat children and adolescents aged between 30 days and 15 years who have Kawasaki disease. (EudraCT number 2019-004433-17) For the cASPerCF clinical trial, the preparation phase is finalised with competent authorities and ethic committees' approval obtained to start the recruitment of children. This prospective trial aims at validation and clinical evaluation of a new posaconazole dosing regimen for children and adolescents with cystic fibrosis and Aspergillus infection (EudraCT number 2019-004511-31) The TREOPACA trial, which will assess the effectiveness of paracetamol on the closure of the ductus arteriosus and the increase in surviving without severe morbidity in extremely premature infants, is in preparation phase with finalisation of the protocol and clinical trial applications to ethics committees and competent authorities. (EudraCT number 2019-004297- 26)
c4c paediatric clinical trials	The c4c clinical paediatric network of national hubs and qualified sites in order to deliver high quality clinical trials across Europe, is being strengthened notably with the implementation of governance, processes, and a single fully operational point of contact for all sponsors, sites and investigators. In setting up the network, c4c has stimulated the setting up of 12 national paediatric networks (NO, DE, PT, IE, GR, SE, PL, EE, IT, CZ, HU, ES) complementing the existing national networks. In total, there are 19 national hubs across 20 countries (with the Finnish National Hub covering both Finland and Iceland).
COMBACTE-CDI antimicrobial resistance	*Clostridioides difficile* infection (CDI) remains a severe, or even fatal, infection with a large burden on the healthcare system worldwide. The preliminary results from the sample testing study, case/control study and the survey highlight key differences between community and hospital CDI across Europe in terms of diagnosis, risks and outcomes; important factors to understand to improve patient care. An overview of these first results are presented in an infographic developed by the consortium.
COMBACTE-CDI antimicrobial resistance	A dynamic transmission model of CDI has been developed to estimate the true incidence of colonised and infected cases in the hospital setting within different European countries by accounting for differences in national sampling and testing rates. Based on the data from the case control study, predictions from the model suggest that many European countries are significantly underestimating the incidence of CDI. Overall these preliminary results improve the understanding of the epidemiology and clinical impact of *Clostridioides difficile* infection (CDI) across Europe.
COMBINE antimicrobial resistance	One of the objectives of the project is the coordination of the Antimicrobial Resistance Accelerator that was created to respond to the challenge of developing new treatment and prevention approaches to antimicrobial resistant infections. COMBINE aims to develop a clinical and interpersonal network between AMR Accelerator participants and antimicrobial resistance stakeholders across the EU and globally to improve the design of the clinical trials and develop more predictive and reliable infection models for preclinical studies, to accelerate antibacterial drug and vaccine development. So far, the consortium has developed a software to support a wide range of data formats, from simple office documents and chemical structures to preclinical and clinical data sets, while retaining compatibility with all common operating systems. They also developed the documentation covering data governance, quality, access, and analysis procedures for the projects within the Accelerator.

Project title	Description of result(s)
DRIVE vaccines	For 2019/2020, the Finland Terveyden ja hyvinvoinnin laitos (THL) register-based cohort included children aged 6m-6y (100 942 person years) and older adults 65-100y (410 911 person years). The population-based cohort covered a total of 511 854 person-years and two vaccine brands. In children aged 2-6y, the influenza vaccine effectiveness (IVE) against any influenza was 68 % (95 % CI 58-75) for Fluenz Tetra and 71 % (56-80) for Vaxigrip Tetra. In adults ≥65y, IVE against any influenza was 29 % (20-36) for Vaxigrip Tetra. One of the implication if that the vaccine effectiveness of Vaxigrip Tetra is less effective for adults over 65 years old than for children aged 2 to 6 years old.
EHDEN big data	To demonstrate the utility of their health data and evidence network, the EHDEN consortium carried out two 'study-a-thons' in 2020. These events compress what would normally take months of research into just five days: Rheumatoid arthritis: In January 2020 approximately 40 people of all disciplines, from clinical to academic to data partners assembled to evaluate the utilisation of disease modifying anti rheumatic drugs (DMARDs), their safety profiles and outcomes, as well as prediction modelling. 15 databases from 6 countries were used in the study. The results have already been presented at the European League Against Rheumatism congress in June 2020 and may lead to recommendations on how to monitor these drugs. COVID-19: In March 2020, EHDEN and the OHDSI community organised a 3-day remote COVID-19 study-a-thon involving more than 330 researchers, with 37 healthcare databases from 30 different countries. The aim was to rapidly design and execute studies to inform healthcare decision-making during the COVID-19 pandemic. Initial results include the largest ever assessment of the safety of hydroxyl-chloroquine, and a comparison of the characteristics of hospitalised influenza patients with COVID-19 patients. Other pre-print publications are available online.
ERA4TB tuberculosis	Two trials are ongoing. TBAJ-1: Is a two-part, partially blinded, placebo-controlled, combined single ascending dose (SAD) trial with a food-effect cohort (Part 1) and multiple ascending dose (MAD) trial (Part 2). GSK-1: The study is a randomised, double blind, placebo-controlled study. There are two parts to the study: a) SAD design (8 cohorts) with a food effect cohort; and b) MAD design including up to 4 cohorts.
IDEA-FAST digital health	In 2020, the IDEA-FAST project started recruiting patients to a feasibility study in 4 clinical sites across 3 countries. The aim of the study is to explore which of a variety of wearable digital devices are most suitable to measure sleep disturbances or fatigue. The study will also establish which devices participants find easy or enjoyable to use and are as unobtrusive as possible. A larger clinical validation study using the best devices will start in 2022.
IMI-PainCare pain	Pain is a very subjective phenomenon and reliable and standardised patient reported outcome measures (PROMs) for pain are missing. By end of 2020 the observational study PROMPT NIT-1 recruited and collected PROMS in 518 patients from 17 hospitals across Europe. The results of the study will show the PROMs that measure acute post-surgical pain outcomes accurately and respond sensitively to any changes in daily routine care of patients after different surgical procedures. These tools will help clinicians to give the best treatment to their patients.
INNODIA diabetes	INNODIA has built a competitive pan-European clinical trial network for T1D. It consists of more than 50 fully qualified and accredited clinical centres and satellites across Europe. Beyond the execution of the first trial in INNODIA, MELD-ATG, the project is actively collaborating with INNODIA HARVEST where 3 novel trials have recently been initiated.

Project title	Description of result(s)
LITMUS liver disease	Established the largest global cohort of patients containing 11 813 records across 7 910 individual patients recruited to November 2020, with histologically characterised NAFLD/NASH under longitudinal follow-up by expanding the European NAFLD Registry. It represents a valuable resource for research and biomarker development at scale and pace.
PERISCOPE vaccines	Developed a clinical network in Finland to perform a maternal-infant vaccination study. The objective is to study whether pertussis immunity from mothers can be transmitted to their infant (and if yes from which month onward).
RADAR-AD Alzheimer's disease	In October 2020 the first participant (of 200) of the main RADAR- Alzheimer's disease (AD) study completed the two-month assessment period. During this period the participant interacted with apps and wearable devices which measured physical activity, sleep and heart rate, as well as thinking abilities and spatial navigation. The data will provide important learnings to optimise studies for the development and validation of technology-enabled, quantitative and sensitive measures of functional decline in people with early stage AD.
RADAR-CNS neurological disorders	Three of the RADAR-CNS clinical studies have completed recruitment and are actively gathering data (multiple sclerosis (MS) disability study, the depression study and the epilepsy hospital study). Overall recruitment for second MS study (MS and depression) is strong, despite the difficulties due to the COVID-19 pandemic. These studies have already indicated that remote monitoring technologies are acceptable to participants, and once complete, they will contain the largest dataset on the use of these technologies in the three conditions which will be used to build insights into disease management and outcomes.
RTCure rheumatoid arthritis	The RTCure registry containing information on individual at risk of developing rheumatoid arthritis (RA) has been expanded and currently combines cohort of approximately 3 000 at-risk patients and a further 11 000 patients with early disease, for inclusion in proof of concept validation studies and prospective studies. The register and the harmonisation of clinical data, biobanking and 'omics' data for risk estimation, patient subsetting and disease monitoring, will provide an internationally unique resource for understanding of the longitudinal development of RA, and also provide pharma and academia with a unique potential to perform clinical trials intended to prevent the development of RA.
VALUE-Dx diagnostics	In the point prevalence audit survey 1 in Jan-Feb 2020, patient characteristics, treatment and diagnostic testing were registered for 4 500 patients in 18 countries. Profound between-country differences were seen in clinical investigation, antibiotic prescribing (33 % overall, ranging from 18 % in Belgium to 54 % in Ireland) and the use of POC and lab diagnostics. CRP and total white blood count were most frequently tested. It demonstrates that in terms of infection controls in point of care (POC) or lab, there are different practices which may explain different results in the point prevalence survey.
VITAL vaccines	VITAL performed 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 points after influenza vaccination (2 days, 1 week and one month) and after pneumococcal vaccination (up to 1 month). In total VITAL has performed over 2 600 blood draws, stored isolated cells in 16 000 vials and performed over 1 600 real time analyses of cell constitution.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
ConcePTION safety	A first prototype of the FAIR ConcePTION data catalogue has been developed. This catalogue aims to identify relevant data access providers and data sources (e.g. pharmacovigilance data, data on reported pregnancies, data on congenital anomaly surveillance, registries, plus routine electronic health care data) for the conduct of studies to generate evidence on the safety of medicines in pregnancy. Further testing by researchers and data access providers are ongoing to allow further development of the data catalogue and release next prototype versions.
EHDEN big data	Evidence on how patients experience their conditions is crucial to understand the safety and effectiveness of treatments in everyday use. Huge volumes of this 'real world data' exist in hospital medical records, but they are difficult to access and analyse. In 2020, the EHDEN project ran two open calls to recruit data partners to contribute to their health data and evidence network. This included a rapid call to address the COVID-19 pandemic. To date, the project has recruited 62 data partners across 16 countries with over 200 million patient records. These partners will be funded to make their data available for research in a GDPR compliant manner.
eTRANSAFE safety	Capturing 'treatment-related' findings from animal studies is essential to fully understand potential side-effects of medicines. However, there are currently no standardised tools to report and process this information. To address this issue, the eTRANSAFE consortium released a study report (SR) domain template and editor. This is based on the internationally recognised SEND standard and defines all the key entities that describe a treatment-related finding. In addition, the consortium developed a desktop application to allow SR-domain templates to be visualised, amended and updated. The SR-domain concept has raised wide interest with several external stakeholders comprising an industry-wide audience of CROs (contract research organisations), sponsors and regulators.
eTRANSAFE safety	To help understand the risk-benefit balance of medicinal products, the eTRANSAFE consortium launched a Periodic Safety Update Reports (PSUR) database in December 2020. The database, which includes web-based query functionality, incorporates summarised quantitative information on the adverse health events observed during clinical trials and the pharmacovigilance of medicines, constituting key documents in regulatory procedures.
FAIRplus knowledge management	The FAIRplus project has further expanded their FAIR Cookbook, with 17 'recipes' to make data findable, accessible, interoperable, and reusable. The cookbook recipes allow other researchers to make their data FAIR and have already been applied to four IMI projects, whose data is outlined in the Elixir Luxembourg data catalogue. The consortium is now FAIRifying an additional 9 datasets and working to enhance and extend the cookbook.
PERISCOPE vaccines	Developed a vertical analysis plan to enable direct comparison of results across all clinical studies in PERISCOPE. Time points and an integrative bioassay panel were selected. A statistical analysis framework was developed to analyse the impact of various parameters on clinical/immunological endpoints
PharmaLedger machine learning	In 2020, the PharmaLedger project selected the use cases they will use to advance adoption of blockchain in healthcare. These are: Supply chain. By simply scanning a data matrix (QR) code on a packet of medicine, a patient would be able to check product authenticity and obtain reliable information, which should help to boost trust in medicines. Health data. This would strengthen patients' ownership of their data, giving them greater control over who can access their health data and when, with a view to enabling a health data marketplace.

Project title	Description of result(s)
	Clinical trial data. This would facilitate the matching of patients to clinical trials while preserving patient privacy and also support remote data capture during clinical trials, cutting down on the number of times patients would need to visit the clinic for tests.
PIONEER prostate cancer, big data	96 prostate cancer data sources from 16 countries have been identified. 35 are catalogued and prioritised for OMOP mapping (Observational Medical Outcomes Partnership). 9 are mapped to OMOP and available in the platform. 5 are due to start early 2021 with 9 in the pipeline to begin mapping soon after.
RADAR-AD Alzheimer's disease	Integration of data from digital apps that measure different functions is a big challenge. The project modified the open source RADARbase platform so that it can seamlessly integrate data streams of passively and actively collected digital biomarkers of function across motor, cognitive, neurophysiological and emotional domains. This is a critical enabler for the project clinical study and may be exploited for any other future remote monitoring of function study in early Alzheimer's disease.
RADAR-CNS neurological disorders	A key result that has already had significant impact is the RADAR-Base platform that gathers and manages data from wearables and smart-phones. This platform has continued to be deployed including to facilitate a study on the physical and mental health effects of COVID-19. A key feature of this study is the use of wearable data which will be used to investigate changes in measurements such as heart rate during infection with coronavirus.
RADAR-CNS neurological disorders	The RADAR-CNS consortium leveraged their participant data to assess whether there was an increased risk of COVID-19 symptoms among multiple sclerosis (MS) patients. 399 patients already participating in the RADAR-MS study were assessed. The results were published in Neurological Sciences and indicate that remote monitoring technologies may provide support to health authorities in monitoring and containing the pandemic.
RADAR-CNS neurological disorders	As part of their effort to address the COVID-19 pandemic, the RADAR-CNS consortium analysed data from smartphone and wearable devices to rapidly test the effect of non-pharmaceutical interventions (NPIs) such as social distancing and full lockdown. 1 062 participants in five countries were included and the results indicate that remote monitoring technologies may be a viable approach to passively assess the local compliance to interventions in epidemics and pandemics, and could help countries ease out of lockdown.
RHAPSODY diabetes	Established a unique bioinformatics network, a federated database with data from 12 large human cohorts (over 68 000 individuals displaying different diabetes disease stages) and from 3 different mouse models of type 2 diabetes. Notably, the project collected, generated and harmonised multi-omics data and genetic data in addition to biochemical and clinical data. Within the database they have developed new statistical tools to maximise the power of federated analysis and foster efficient discovery of blood biomarkers.
RHAPSODY diabetes	Developed and validated computer simulation models (the 'Modelling Integrated Care for Diabetes based on Observational data' - MICADO model and the United Kingdom Prospective Diabetes Study (UKPDS) -Outcomes Model) able to predict type 2 diabetes progression, health benefits and costs in order to calculate long-term outcomes and develop scenarios for new treatment approaches. Those tools have the potential to support decision making by European agencies for the adoption and reimbursement of medicines in diabetes.
TransQST safety	Contributed TransQST data to the DisGeNET knowledge platform, integrating and standardising data on disease genomics and drug adverse phenotypes, which is used by more than 55 000 users/year worldwide and cited in more than 2 000 publications. DisGeNET is a knowledge management platform integrating and standardising data about disease associated genes and variants from multiple sources, including the scientific literature. It is an interoperable resource supporting a variety of applications in genomic medicine and drug R&D.

Project title	Description of result(s)
TransQST safety	Platinum quantification: ICP-MS method was established for platinum (Pt) quantification, which is needed for pharmacokinetics/toxicokinetics of platinum for *in vivo* studies, but also to measure Pt content in cell lysates and medium of *in vitro* studies.
TransQST safety	Preservation between human and rat: Publicly available transcriptomic data from human liver (1 100 samples) and human kidney (2 100 samples) were retrieved, curated and processed. The data allow the preservation assessment of rat liver and kidney WGCNA networks with the human liver and kidney. This will provide a step towards building a human liver and kidney TXG-MAPr, used for drug safety assessment and interspecies translation.
VALUE-Dx diagnostics	An AMR data ready model was created in Observational Medical Outcomes Partnership (OMOP) / Common Data Model (CDM) using Logical Observation Identifiers Names and Codes (LOINC) and Standard Nomenclature of Medicine (SNOMED) clinical trial standard vocabularies. In a proof of concept, AMR data coming from Dx systems were converted to the OMOP/CDM tables and uploaded in various 'satellite' databases which were queried by the central observatory using an OHDSI federated architecture. This allows federated AMR repositories to be accessed without compromising data sovereignty.
VITAL vaccines	The burden of specific diseases is changing over time, and hence burden of disease estimates should preferably be regularly updated over time. Secondary database use has, as compared to primary data collection, the main advantage of being relatively resource efficient, and hence burden of disease estimates based on secondary data use can be more easily updated. Generic master protocols to obtain burden of disease estimates from databases are being written to facilitate the future estimation of burden of disease from database.
WEB-RADR 2 pharmaco-vigilance	A key output of the WEB-RADR 2 project is bi-directional mappings between two health data terminologies, MedDRA and SNOMED CT. These mappings will allow for electronic health record data to be easily used by regulators & vice versa. Ultimately, these mappings should better facilitate epidemiological studies between databases encoded in different terminologies and provide the potential for the use of real-world evidence in clinical trials. A successful proof of concept pilot for EHR connectivity within the Danish healthcare system has already been carried out.
WEB-RADR 2 pharmaco-vigilance	A COVID-19 reporting form has been specifically designed for the reporting of medicines used to treat coronavirus symptoms. Since being made available in the Med Safety App, a number of countries have implemented the form. This includes Armenia, Botswana, Burkina Faso, Ethiopia, Uganda, Zambia, Pakistan and Nigeria.

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

Project title	Description of result(s)
AIMS-2-TRIALS autism	To support and accelerate the involvement of people with autism (A-Reps) in the project research activities, the consortium arranged a webinar series to learn more about the project and to engage in an interactive Q&A, with A-Reps able to provide their input and feedback on research. Furthermore, all webinars were recorded and made available via the A-Reps Slack platform to broaden the reach of these materials.
c4c paediatric clinical trials	The consortium has continued to develop an integrated educational programme to address best practice in paediatric clinical trials and paediatric medicine development, notably with the creation of two short thematic courses focusing on trial start up and monitoring aspects of clinical trials. The c4c e-learning platform is now offers a large range of training courses and more than more than 500 clinical trial staff have been trained so far.
c4c paediatric clinical trials	To empower children and families through the COVID-19 pandemic, the consortium has gathered a range of reliable information and resources about COVID-19, in a variety of European languages.
ConcePTION safety	Preliminary results of a survey targeting both women and healthcare professionals in Europe were presented during the workshop on the benefits/risks of medicines used during pregnancy and breastfeeding held by EMA in September 2020. These preliminary results showed that out of a total of 1 910 women from 74 countries who completed the questionnaire, approximately 85 % reported a need for information about medications during pregnancy/lactation and medical doctors (33.1 %) and the internet (33.0 %) were the most used information sources. Out of 665 healthcare providers (HCPs) who completed the survey, more than 60 % reported being asked information use on a daily/weekly basis. A study analysing the frequency and nature of discrepancies between different online information sources for patients in four European languages showed that information discrepancies are frequent for medicine use during pregnancy/lactation, especially for lactation (abstract 2650 here). Overall the preliminary results contribute to building a targeted education programme and knowledge bank to empower women and healthcare professionals to make informed decisions on the use of medicines during pregnancy and lactation.
EBODAC Ebola and related diseases	Training has been delivered by the EBODAC consortium in 2020 on the use of biometric tools, community engagement, rumour management and use of remote training platforms for community health workers in the Democratic Republic of the Congo (DRC) and Rwanda. In total 2 935 people received training from the EBODAC consortium in 2020.
EBOVAC projects Ebola and related diseases	In 2020, the EBOVAC projects organised 35 training events in Sierra Leone and 5 training events in the DRC in topics related to clinical studies conduct.
EFOEUPATI education and training	EFOEUPATI, which was set up to ensure the sustainability of the IMI EUPATI project achievements, contributed to the establishment of the EUPATI self-sustaining independent foundation, as EFOEUPATI has developed a viable sustainability/business model for the mid- to long-term future of the EUPATI objectives and activities in the form of the European Patients' Academy.
EFOEUPATI education and training	EFOEUPATI redesigned the www.eupati.eu website, including EUPATI National Platforms and a collaborative interface. They will enhance the access of users to information about EUPATI at a global and national levels and contribute to networking across the different stakeholders.

Project title	Description of result(s)
EFOEUPATI education and training	Contribution to the EUPATI Toolbox design with currently over 4 million users worldwide, envisaged to grow through the extension of content topics (e.g. medical technology, digital health, personalised medicine). The addition of 4 further languages beyond the existing 9 will extend its reach further.
EHDEN big data	In April 2020, EHDEN launched EHDEN academy, a web-based educational platform offering free courses on harmonisation and analysis of heath data using the OMOP common data model. Ten courses are now available, and have already been used to remotely train SMEs for EHDEN data harmonisation activities. By the end of 2020, 550 students were enrolled in the platform, which is free to access.
EHDEN big data	One of the challenges in making real world data available for research & timely decision making is that the different databases across Europe use many different data standards. This makes carrying out research across different countries slow and expensive. Harmonising these databases to a single standard can facilitate rapid research, but there is limited expertise to carry this out this harmonisation at scale. The EHDEN project trains and certifies SMEs and other organisations to ensure these skills are available in Europe. In 2020 EHDEN trained an additional 15 SMEs which allows them to work with the EHDEN data partners. There are now 28 certified organisations in the EHDEN business directory, several of which are already working on data sets.
GetReal Initiative relative effectiveness	Three online course sessions on real world evidence in medicines development were held in 2020. The course, which consists of 5 learning units running over a period of approximately 8 weeks, is addressed to anyone from pharmaceutical companies, regulatory authorities, health technology assessment bodies, patients' organisations, consultancy companies and academia who wishes to broaden their expertise.
HARMONY blood cancers, big data	Regular monthly training sessions and videoconferences related to data analysis have been organised for data scientist and biostatistician teams of different partners participating in the analysis of the data in the platform.
PERISCOPE vaccines	A whole blood stimulation assay for measuring pertussis-specific cellular responses in small blood volumes was established. Knowledge transfer to consortium partners was initiated and the assay was implemented in all infant vaccination studies (Africa, UK, Finland).
PIONEER prostate cancer, big data	A training programme was established to increase capacity for OMOP mapping of datasets within PIONEER. A training group of 18 young academic urologist, R&D scientists and guideline developers was established and engaged in the guided theory training via the EHDEN academy and hands on training in mapping.
TransQST safety	Mathematics of Life 2020: Virtual course on modelling. 28th September to 2nd October 2020. BioModels and BioModels parameters training provided. 28 participants including PhD students, Postdocs, scientists, full professors and industrial researchers.

Impact on regulatory framework

Project title	Description of result(s)
AIMS-2-TRIALS autism	The consortium is progressing to regulatory validation of an autism stratification biomarker based on electroencephalographic (EEG) measurement of brain response to faces ('N170 latency'). 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. The EMA provided qualification advice on the biomarker and its intended use in June 2020 and in November 2020 issued a letter of support encouraging to continue working to produce data for applying to qualification opinion.

Project title	Description of result(s)
ConcePTION medicines safety	The tools (distributed analytics) and common data model to harmonise data collected in healthcare being developed by the consortium will be used for secondary use of real world data by the project CONSIGN. The CONSIGN project was tendered by EMA to guide evidence based decision-making about COVID-19 vaccine indications, vaccination policies, and treatment options for pregnant women by regulators.
DRIVE vaccines	Providing brand-specific influenza vaccine effectiveness (IVE) estimates is a regulatory requirement by EMA to influenza vaccine manufacturers. This is being addressed in the DRIVE project. Regular EMA exchanges and national scientific advice (PEI) were conducted in 2020: regulators welcomed the DRIVE initiative and acknowledged its value and the good progress made so far.
EBOVAC projects Ebola and related diseases	Janssen (EBOVAC projects partner) has been in constant dialogue with the EMA and other regulators and stakeholders (FDA, WHO, SAGE [Strategic Advisory Group of Experts on Immunization]…) to obtain more clarity on the pathway towards licensure (in absence of efficacy data) and to explore the possibilities to roll out the vaccine in case of an outbreak. Janssen received Marketing Authorisation from the European Commission for its vaccine regimen for the prevention of Ebola virus disease under 'exceptional circumstances' on the basis of an immunobridging approach rather than clinical efficacy data: the Marketing Authorisation is supported by data from Phase 1, 2 and 3 clinical studies evaluating the safety and immunogenicity (ability to induce an immune response) of the vaccine regimen in more than 6 500 adults and children aged one year and above across the US, Europe and Africa, preclinical studies, and immunobridging analyses comparing the results of clinical and preclinical efficacy studies.
EHDEN big data	In 2020, EHDEN started working with the EMA to establish a European framework and research network for the conduct of multicentre cohort studies on the use of medicines in COVID-19 patients. The outcomes of the projects will feed into the work of EMA's COVID-19 EMA pandemic Task Force (COVID-ETF) and EMA's scientific committees, to ensure that the evidence is translated into scientific opinions on the optimal use of the medicines concerned.
HYPO-RESOLVE diabetes	The project has undergone a formal scientific advice with the EMA to obtain qualification advice regarding the patient reported outcome tool (PRO) under development that will be ultimately used to evaluate the impact and burden of continuous glucose monitoring (CGM) on detected, as well as self-reported, hypoglycaemia.
INNODIA diabetes	Obtained support from the European Medicines Agency (EMA) on the INNODIA's master protocol. Furthermore, to ensure improvement in prevention or delay of T1D disease manifestation in the near future, the consortium is already in exchange with EMA to plan for advice on master protocol II (MP-II) for upcoming INNODIA prevention studies.
LITMUS liver disease	Participated in two scientific advice meetings with EMA and submitted two briefing packages and two questionnaires. Also participated in two scientific meetings with EMA. Submitted documents to FDA on the diagnostic screening and prognostics enrichment contexts of use. The Letter of Intent (LOI) for diagnostic screening has been accepted by the FDA. The prognostic enrichment LOI is pending approval. Initiated the regulatory qualification process for the patient reported outcome tool NASH-CHECK PRO with both EMA and FDA.
MOBILISE-D digital health	The EMA has issued a letter of support that publicly endorses the approach undertaken by the consortium to pursue the qualification of digital mobility outcomes (DMOs) as monitoring biomarkers of mobility performance in regulatory drug trials. This is a major achievement for the consortium to pursue with its approach.

Project title	Description of result(s)
PIONEER prostate cancer, big data	The project has written a policy paper that outlined 4 key evidence themes, related specifically to prostate cancer, that need to be addressed in order to close the gap between regulatory and HTA decisions on innovative medicines.
PREFER patient involvement in R&D	The consortium has completed a framework and points for consideration on method selection that describes a structured approach to assess and use patient preferences as input in medical product decision-making (taken by industry, regulators, HTA bodies and payers). The framework offers a set of principles, guidelines and tools to guide those who conduct preference studies in study design, conduct and analysis. The framework also guides decision-makers through assessing and using preference study results in their decisions. The points to consider provide specific applications of the framework across different preference study examples and methods. This framework has now been submitted to the EMA and EUnetHTA (European Network for Health Technology Assessment) through the qualification of methodology. This is the first joint EMA-EUnetHTA joint qualification procedure and the opinion is expected soon.
RADAR-CNS neurological disorders	In 2020, the RADAR-CNS consortium successfully engaged with the EMA and FDA to provide evidence on the potential of remote monitoring technologies (RMTs): ▪ A meeting with the EMA ITF (Innovation Task Force) discussed scientific and regulatory topics relevant to the development of new medicinal products and technologies using RMTs to complement and reinforce existing procedures. ▪ A meeting of the FNIH Biomarkers Consortium discussed 'Remote Digital Monitoring for Medical Product Development'.
RESCEU respiratory disease	Guidelines providing a basis for feasible and affordable surveillance of RSV, and allowing comparison of surveillance results at European and global level have been produced. Three different levels of surveillance are presented (active sentinel community surveillance, active sentinel hospital surveillance and passive laboratory registry surveillance) and recommendations for optimal diagnostics and virus characterisation provided. The guidelines influence health policies upon establishment or upgrading of an existing RSV surveillance system.
VAC2VAC vaccines	Pyrogen content is a key quality feature that must be checked in all injectable products, including vaccines. Extensive work was carried out to implement and validate the European Pharmacopoeia (Ph. Eur.) method 'monocyte activation test' (MAT) for pyrogenicity testing of a vaccine against tick-borne encephalitis virus produced by GSK. The method was finally validated in GSK and implemented in July 2020 after approval by the competent authorities. This is the first method within VAC2VAC to reach regulatory acceptance and implementation and thus represents an important milestone in our effort to implement the consistency approach.
WEB-RADR 2 pharmaco-vigilance	A key output of the WEB-RADR 2 project is the Vigilance Hub, which allows for the reporting of adverse drug reactions (ADRs) to national competent authorities (NCAs). This has been made available as an app: MedSafety, which allows for the easy reporting of ADRs by patients and physicians and can also deliver trusted regulatory news to the users. The app is available in multiple languages, and, with the support of the World Health Organization (WHO) and Uppsala Monitoring Centre, has been rolled out in an additional five countries in 2020.

Implementation of project results inside industry

Project title	Description of result(s)
ADAPTED Alzheimer's disease	The inducible pluripotent stem cells (iPSC) models and ADAPTED database have been used by all the industry participants during the course of ADAPTED and will continue to be used after the project ends.
AIMS-2-TRIALS autism	Many of the centres of the project clinical trial network have been selected by industry for three multicentre clinical trials for development of innovative medicines in autism, a phase 3 trial of balovaptan for adults, a phase 1 trial of balovaptan in children, and a phase 3 trial of bumetanide for autistic young people.
AMYPAD Alzheimer's disease	The industry partner GE Healthcare has adapted the quantitative tool Cortex ID developed in the project for the analysis of brain positron emission tomography (PET) images. Cortex ID suite provides easy, robust review/analysis of PET and PET-computed tomography (CT) neuro scans.
DRIVE vaccines	DRIVE is part of risk management plan of vaccine company partners to answer to their regulatory obligations (regular updates in periodic benefit-risk evaluation reports (PBRE)/ Periodic Safety Update Report (PSUR) and submission of yearly seasonal joint report to EMA).
EBiSC2 stem cells	12 novel cell lines and iPSC derived cell types such as hiPSC-derived cardiomyocytes, neurons and astrocytes have been used by industry partners as *in vitro* models for testing activities.
EBOVAC projects Ebola and related diseases	The clinical trial results generated in EBOVAC projects contributed to the vaccine licensure packages. In July 2020, the European Commission has granted Marketing Authorisation for its Janssen Pharmaceutical Companies' Ebola vaccine regimen for the prevention of Ebola virus disease. Experience has been gained via the EBOVAC projects in conducting clinical studies in sub-Saharan Africa and more specifically in resource-limited settings. The lessons learned in EBOVAC projects have contributed to assist other vaccine programmes within Janssen. ▪ HIV vaccine studies (developed by J&J) are being conducted or have been conducted in the following countries. ▪ HIV-V-A004: S. Africa, Uganda, Rwanda, Thailand ▪ HPX2004: Rwanda ▪ HPX2003: Rwanda, Kenya ▪ HPX2008: S. Africa, Zambia, Zimbabwe, Malawi, Mozambique ▪ HPX3002: Brazil, Argentina, Peru, Mexico This HIV vaccine consists of multiple doses of vaccine and thus the ability to ensure how many doses and when the doses have been given is critically important once the vaccine is administered outside the carefully controlled clinical trial setting. The WHO has shown great interest in both the one-step biometric scanning (using the tablet's camera rather than a peripheral camera) as well as the mobile messaging in the native language and is investigating the possibilities to use the platform for deployment of the COVID vaccine. The experience gained from the IMI-sponsored development of the iris scanning biometric platform and the mobile messaging will be utilised for successful deployment of vaccines in the future.
ERA4TB tuberculosis	Preliminary CT-based image biomarkers are being incorporated to the *in-vivo* analysis on mouse models carried out in GSK to study drug candidate efficacy.
IMPRIND neurodegenerative disease	An improved seeded aggregation assay for tau (a microtubule-associated protein), generated by the IMPRiND project, is used by the industry to perform a genome wide screen and identify several hundred hits in pathways that modify tau aggregation. These hits are undergoing further prioritisation within industry based on bioinformatic analysis and additional secondary screens in primary neurons, for the development of future therapeutics in neurodegeneration.

Project title	Description of result(s)
LITMUS liver disease	Developed a new disease-specific PROM (NASH-CHECK) that will be the first measure developed for NASH F1-F3 and F4 patients. This instrument, once qualified as a novel methodology (biomarker), could become a well-accepted measure to assess symptoms and health-related quality of life in clinical drug development programmes and clinical practice. A NASH-CHECK user license has already been provided to Pfizer, Boehringer-Ingelheim and Novo Nordisk to be included in their interventional studies. In addition, TARGET-NASH, a US prospective registry, also implemented NASH-CHECK.
NeuroDeRisk safety	The NeuroDeRisk *in silico* Toolbox for screening chemical structures, such as drug candidates against a panel of models developed for neurotoxic adverse effects predictions, has been deployed to EFPIA consortium partners. This allows scientists interested in assessing compounds for potential neurotoxic effects to use the tool in-house, thus excluding any risk of unveiling confidential data.
PERISCOPE vaccines	The following models developed in the project have been used in the industry for vaccine development: ▪ stream-lined cellular immunity assay against pertussis antigens using small volumes of whole blood rather than isolated lymphocytes; ▪ serology assays to measure pertussis responses in preclinical infection models. Scientific validation and positioning of preclinical infection model in the screening and selection of vaccine for clinical development.
TransQST safety	Kidney QST model: A proof-of-concept quantitative systems toxicology (QST) model of drug-induced kidney injury established by AbbVie, SIMCYP & Leiden University. Fitted to data from rats dosed with cisplatin and applied for translational prediction of renal injury marker response in human with reasonable performance based on species-specific pharmacokinetics. Under evaluation by AbbVie for potential internal use & further development.
TransQST safety	Multiscale QST model of oncotherapeutics induced GI injury: AstraZeneca is assessing the application of the multiscale QST oncotherapeutics-induced gastrointestinal (GI) injury for clinical translation of preclinical GI safety (*in vivo* and organoids) prior to clinical trials for study design.
TransQST safety	The TXG-MAPr tools have been tested by the EFPIA partners. Mechanisms for final implementation within EFPIA partners are being explored. This will enable the tools to be evaluated using proprietary data from live/terminated drug candidates.
VHFMODRAD Ebola and related diseases	The Ebola-Ag K-SeT developed by Coris BioConcept is being prepared for registration. CORIS has demonstrated capacities to develop and bring new product (rapid antigen and antibody test for COVID-19) to the market rapidly, which will benefit the introduction of new assays for VHFMODRAD. FlexCart-04 open cartridges, developed by CEPHEID (for bedside diagnostics using in-house reagents) will be available from the CEPHEID catalogue after internal validation. Privileged candidates are CCHFV and YFV at this time of the project. FDA or CE IVD (in vitro diagnostic) registration are not in the scope of VHFMODRAD and not being considered by CEPHEID.
WEB-RADR 2 pharmaco-vigilance	The utility of the WEB-RADR2 adverse drug reaction reporting platform to the pharmaceutical industry was demonstrated by a pilot run by AbbVie. The platform was used by 5 patient support programme (PSP) nurses to report adverse events (AEs) to the pharmacovigilance team. A total of 100 AE reports were submitted. The overall user experience was very positive with most nurses feeling that the app added value to their role and was much faster and easier than traditional reporting methods. The team intends to publish the results in 2021.

Accessibility of resources/outputs beyond consortium

Project title	Description of result(s)
ADAPTED Alzheimer's disease	ADAPTED has produced four fully characterised sets of isogenic inducible pluripotent stem cells (iPSC) lines carrying one of the following APOE genotypes: APOE-Ɛ2/Ɛ2, APOE-Ɛ3/Ɛ3, APOE-Ɛ4/Ɛ4, APOE-Ɛ3/Ɛ4, or APOE-KO. These cells are available to the scientific community, distributed by the European Collection of Authenticated Cell Cultures (ECACC).
DRIVE vaccines	Results of influenza vaccine effectiveness IVE for the 2019/2020 season are publicly available on DRIVE website. Moreover, results of all site-specific, pooled, and population-based analyses are available in a web annex, which increased the transparency and accessibility of the project outcomes – also publicly available.
EBiSC2 stem cells	Building on the EBiSC project (2014-2017), the overall goal of the EBiSC2 is the establishment of a self-sustainable European-based and globally operating biobanking facility and mirror bank for quality-assured human induced pluripotent stem cells (hiPSCs). EBiSC2 enlarged the total storage capacity of the biobank, which now exceeds 110 000 vials. All hiPSC lines available through EBiSC have been deposited by organisations who support fair and open research and are willing to share these critical tools with other researchers. An EBiSC2 infographic summarises at one glance the implications and benefits of deposition, the ethical and legal governance sourcing EBiSC lines and how iPSC lines can be deposited into and purchased from EBiSC. EBiSC2 has developed protocols for the derivation and cryopreservation of hiPSC-derived cells to meet long-term economic and scientific sustainability goals and engaged new channels for marketing and dissemination such as publication of an EBiSC specific Wikipedia page and completed international trademark to protect both the EBiSC and EBiSC2 logos, and the name 'EBiSC, the European Bank for induced Pluripotent Stem Cells'.
EQIPD data quality, neuro-degenerative diseases	The project operating in the area of the preclinical data quality in neurosciences developed the database/data catalogue: Shiny-App which can be used for pre-clinical Alzheimer's disease (AD) decision modelling. The tool provides a summary of all transgenic drug testing studies in AD; it is therefore of value in informing scoping exercises where scientists or companies wish to contextualise their proposed research against what has gone before; and as a starting point (with the opportunity to download a bibliographic record of the search) for those wishing to conduct a systematic review.
EU-PEARL clinical trial design	Platform trials testing novel techniques and treatments developed by multiple companies offer opportunities for more efficient drug development. This became again apparent during the COVID-19 response, as hundreds of individual trials were set up but many struggled to achieve meaningful outcomes quickly. To build and share knowledge around platform trials within the stakeholder community, EU-PEARL developed: 1) a comprehensive glossary with key terminology and scenarios for platform trials; 2) a clinical operations best practices guide, presenting lessons learned from ongoing platform trials and areas of priority for future trials design and execution. These tools form the groundwork for common understanding around integrated research platform concept and operational guidances for platforms trials set up.
GetReal Initiative relative effectiveness	The PragMagic tool developed by the IMI1 GetReal project has been updated to the GetReal Trial Tool with more effective functionalities. The tool is open access and can be used without entering any real trial information, and offers researchers step by step guidance to evaluate the options and implications of introducing RWE elements in a trial design, to assess the impact of design choices on generalisability of the clinical trial to routine clinical practice, while taking into account other aspects of the trial, such as risk of bias, precision, acceptability and operational feasibility.

Project title	Description of result(s)
INNODIA diabetes	CDAs (confidential disclosure agreements) signed with companies for scientific advice and guidance in design of protocol for clinical intervention trials in T1D. Services are ongoing.
LITMUS liver disease	Developed, qualitatively validated and published the NASH-CHECK patient reported outcome measure for non-alcoholic liver disease. The tool is now being used in a number of clinical trials and available for licencing (at no cost) through RWS (NovartisPROrequest@rws.com). The tool was linguistically adapted for use in 39 languages across 29 countries.
LITMUS liver disease	Developed and released the NAFLD Pathology Atlas as an educational/training tool. The Atlas is available for download on the European Society of Pathology website and includes multiple choice test questions.
NeuroDeRisk safety	Deployed the NeuroDeRisk *in silico* Toolbox for screening chemical structures against a panel of models developed for neurotoxic adverse effects predictions. It is provided as an extension of the KNIME Analytics Platform, an open-source software for data science workflows. This approach allows rapid prototyping, ensures re-usability, and facilitates combination of tools from multiple consortium partners. The tools are available on request at no costs for scientists interested in assessing compounds for potential neurotoxic effects. Comprehensive information is available on the *in silico* Toolbox page of the project website, and detailed instructions for installing the tools are provided on both the Inte:Ligand and Biovista documentation websites.
NGN-PET pain	NGN-PET has generated several transcriptomic and proteomic data sets. Many of these are publicly available at the 'Neuro-Immune interactions in the Periphery (NIPPY)' resource.
NGN-PET pain	The NGN-PET project has developed 13 assays to study neuropathic pain: ▪ Assay 1 - *in vitro* testing of rat DRG cells in 384 MTP starting from frozen cells ▪ Assay 2 - *in vitro* testing of primary rat DRG cells in 384 MTP ▪ Assay 3 - functional characterisation of neurotoxic effect of vincristine on rat-DRG ▪ Assay 4 - functional test performed at FLIPRTETRA on rDRG cells in 384 MTP with fluorescent dyes ▪ Assay 5 - fluorescent labelling of neurites, mitochondria and nuclei on rDRG in 384 format (HC) ▪ Assay 6 - microscope parameter for image acquisition and algorithm for image analysis on rDRG (HC) ▪ Assay 7 - functional test performed at FLIPRTETRA on idSN in 384 MTP fluorescent dyes ▪ Assay 8 - fluorescent labelling of neurites, mitochondria and nuclei on idSN in 384 format (HC) ▪ Assay 9 - microscope parameter for image acquisition and algorithm for image analysis on idSN (HC) ▪ Assay 10 - functional test performed at FLIPRTETRA on direct and indirect co-cultures of idSN and idMacrophages in 384 MTP fluorescent dyes ▪ Assay 11 - fluorescent labelling of neurites, mitochondria and nuclei on direct and indirect cocultures of idSN and idMacrophages in 384 format (HC). ▪ Assay 12 - functional assays on MEA platforms with rodent non-purified and purified sensory neurons ▪ Assay 13 - functional assays on MEA platforms with hiPSC-derived sensory neurons in monocultures. These assays and related cell lines are accessible for use by scientific and industrial community through the collaboration with NGN-PET partners
PIONEER prostate cancer, big data	The project's first policy paper, which attempts to identify the key issues and make recommendations for next steps that will support action and alignment for the project's prostate cancer evidence framework, is available on the project website.

Project title	Description of result(s)
TransQST safety	Omnipath database: Omnipathdb.org; Universitätsklinikum Heidelberg; collection of 103 protein interaction databases in one place. Covering more than 100k protein-protein interaction, 29k transcriptional regulations, 22k complexes, more than 4 million annotations, intra- and intercellular interactions. Paper under review at Molecular Systems Biology.
TransQST safety	COSMOS (Causal Oriented Search of Multi-Omic Space): Computational tool developed by Universitätsklinikum Heidelberg that facilitates the integration of multiple omics data (proteomics, phosphoproteomics, transcriptomics and metabolomics) using networks. It reveals the pathways and key molecular players of drug response. Paper accepted at Molecular Systems Biology.
TransQST safety	CellNOpt (Cell Network Optimiser): Available at Cellnopt.org (Universitätsklinikum Heidelberg). Modelling toolbox to reveal the mechanistic effects of drug perturbations on the signalling pathways. Recent development includes probabilistic models, improved optimisation that allows to handle large scale networks. Published at Bioinformatics
TransQST safety	The TGX-MAPr web tools are available for free to consortium partners (TransQST, eTRANSAFE, EUTOXRISK) at. Access details need to be requested (transqst.org/contact-us/). The TXG-MAPr app is displaying gene co-expression network analysis (WGCNA) applied to publicly available transcriptomic datasets from the TG-GATEs database.

Annex 3 – Publications from projects

Hot publications in 2020

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

- Okba, Nisreen M. A. et al. (2020) Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibody Responses in Coronavirus Disease Patients, Emerging Infectious Diseases 26: 1478
- Wang, Chunyan et al. (2020) A human monoclonal antibody blocking SARS-CoV-2 infection, Nature Communications 11:
- Zhang, Wenjuan et al. (2020) Novel tau filament fold in corticobasal degeneration, Nature 580: 283
- Aguet, Francois et al. (2020) The GTEx Consortium atlas of genetic regulatory effects across human tissues, Science 369: 1318
- Nemeth, Tamas et al. (2020) Neutrophils as emerging therapeutic targets, Nature Reviews Drug Discovery 19: 253
- Moreno, Carmen et al. (2020) How mental health care should change as a consequence of the COVID-19 pandemic, Lancet Psychiatry 7: 813

2020 publications featured in in the top 10 journals

- Nemeth, Tamas et al. (2020) Neutrophils as emerging therapeutic targets, Nature Reviews Drug Discovery 19: 253
- Weaver, Richard J. et al. (2020) Managing the challenge of drug-induced liver injury: a roadmap for the development and deployment of preclinical predictive models, Nature Reviews Drug Discovery 19: 131
- Langan, Sinead M. et al. (2020) Atopic dermatitis, Lancet 396: 345
- Zhang, Wenjuan et al. (2020) Novel tau filament fold in corticobasal degeneration, Nature 580: 283
- Maisonnasse, Pauline et al. (2020) Hydroxychloroquine use against SARS-CoV-2 infection in non-human primates, Nature 585: 584
- Deniston, C. K. et al. (2020) Structure of LRRK2 in Parkinson's disease and model for microtubule interaction, Nature 588: n/a
- Rodstrom, Karin E. J. et al. (2020) A lower X-gate in TASK channels traps inhibitors within the vestibule, Nature n/a: n/a
- Hornberg, Hanna et al. (2020) Rescue of oxytocin response and social behaviour in a mouse model of autism, Nature 584: 252
- Bar, Noam et al. (2020) A reference map of potential determinants for the human serum metabolome, Nature 588: n/a
- Meyer, Hannah V. et al. (2020) Genetic and functional insights into the fractal structure of the heart, Nature 584: 589

Highly cited publications in 2020

- Okba, Nisreen M. A. et al. (2020) Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibody Responses in Coronavirus Disease Patients, Emerging Infectious Diseases 26: 1478
- Wang, Chunyan et al. (2020) A human monoclonal antibody blocking SARS-CoV-2 infection, Nature Communications 11: n/a
- Zwanenburg, Alex et al. (2020) The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping, Radiology 295: 328
- Pinero, Janet et al. (2020) The DisGeNET knowledge platform for disease genomics: 2019 update, Nucleic Acids Research 48: D845
- Zhang, Wenjuan et al. (2020) Novel tau filament fold in corticobasal degeneration, Nature 580: 283
- Aguet, Francois et al. (2020) The GTEx Consortium atlas of genetic regulatory effects across human tissues, SCIENCE 369: 1318
- Lord, Catherine et al. (2020) Autism spectrum disorder, Nature Reviews Disease Primers 6: n/a
- Nemeth, Tamas et al. (2020) Neutrophils as emerging therapeutic targets, Nature Reviews Drug Discovery 19: 253
- Moreno, Carmen et al. (2020) How mental health care should change as a consequence of the COVID-19 pandemic, Lancet Psychiatry 7: 813

- Bean, Daniel M. et al. (2020) Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are not associated with severeCOVID-19infection in a multi-site UK acute hospital trust, European Journal of Heart Failure 22: 967
- Wang, Xin et al. (2020) Global burden of respiratory infections associated with seasonal influenza in children under 5 years in 2018: a systematic review and modelling study, Lancet Global Health 8: E497
- Lazarus, Jeffrey, V et al. (2020) A cross-sectional study of the public health response to non-alcoholic fatty liver disease in Europe, Journal of Hepatology 72: 14
- Kjolbaek, Louise et al. (2020) Arabinoxylan oligosaccharides and polyunsaturated fatty acid effects on gut microbiota and metabolic markers in overweight individuals with signs of metabolic syndrome: A randomized cross-over trial, Clinical Nutrition 39: 67
- Couto, Narciso et al. (2020) Quantitative Proteomics of Clinically Relevant Drug-Metabolizing Enzymes and Drug Transporters and Their Intercorrelations in the Human Small Intestine, Drug Metabolism and Disposition 48: 245
- Jian, Ching et al. (2020) Quantitative PCR provides a simple and accessible method for quantitative microbiota profiling, PLoS ONE 15: n/a
- Schlepckow, Kai et al. (2020) Enhancing protective microglial activities with a dual function TREM2 antibody to the stalk region, EMBO Molecular Medicine 12: n/a
- Picca, Anna et al. (2020) Mitochondrial Signatures in Circulating Extracellular Vesicles of Older Adults with Parkinson's Disease: Results from the EXosomes in PArkiNson's Disease (EXPAND) Study, Journal of Clinical Medicine 9: n/a
- Picca, Anna et al. (2020) Gut Microbial, Inflammatory and Metabolic Signatures in Older People with Physical Frailty and Sarcopenia: Results from the BIOSPHERE Study, Nutrients 12: n/a
- van de Kreeke, Jacoba Alida et al. (2020) Optical coherence tomography angiography in preclinical Alzheimer's disease, British Journal of Ophthalmology 104: 157
- Warmerdam, Elke et al. (2020) Long-term unsupervised mobility assessment in movement disorders, Lancet Neurology 19: 462
- Magri, Alessandro et al. (2020) High-dose vitamin C enhances cancer immunotherapy, Science Translational Medicine 12: n/a
- Nanou, Afroditi et al. (2020) Tumour-derived extracellular vesicles in blood of metastatic cancer patients associate with overall survival, British Journal of Cancer n/a: n/a
- Rodriguez-Espigares, Ismael et al. (2020) GPCRmd uncovers the dynamics of the 3D-GPCRome, Nature Methods 17: 777
- Grandjean, Joanes et al. (2020) Common functional networks in the mouse brain revealed by multi-centre resting-state fMRI analysis, Neuroimage 205: n/a
- Coleman, Jonathan R., I et al. (2020) The Genetics of the Mood Disorder Spectrum: Genome-wide Association Analyses of More Than 185,000 Cases and 439,000 Controls, Biological Psychiatry 88: 169
- Simblett, Sara Katherine et al. (2020) Patients' experience of wearing multimodal sensor devices intended to detect epileptic seizures: A qualitative analysis, Epilepsy & Behavior 102: n/a

Annex 4 – Patents from projects

Since the start of IMI2 programme, IMI projects have been patenting developed technologies. The statistics below encompass 9 patent/trademark/registered design applications and 2 patents awarded from the beginning of IMI2 until 31 December 2020.

FILODAG – 1 patent application on ‘superparamagnetic particles modified with samarium, gadolinium and yttrium for use in the detection of Ebola virus’.

MOFINA – 1 registered design and 1 trademark application on ‘Alere Q filovirus detector’.

EBOVAC 1 – 1 patent awarded on ‘methods and compositions for inducing protective immunity against filovirus infection’; 2 patent applications on ‘methods and compositions for enhancing immune responses’ and ‘methods and compositions for inducing protective immunity against filovirus infection’.

PHAGO – 1 patent awarded on ‘TREM2 cleavage modulators and uses thereof’.

PEVIA – 2 patent applications on ‘mélanges d’epitopes t cd8 immunogènes du virus Ebola’ and ‘peptides immunogènes issus de la nucléoprotéine du virus Ebola’.

EBiSC2 – 2 trademark applications for the EBiSC trademark.

Annex 5 – 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:[63]

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

- 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[64]:

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

Where:

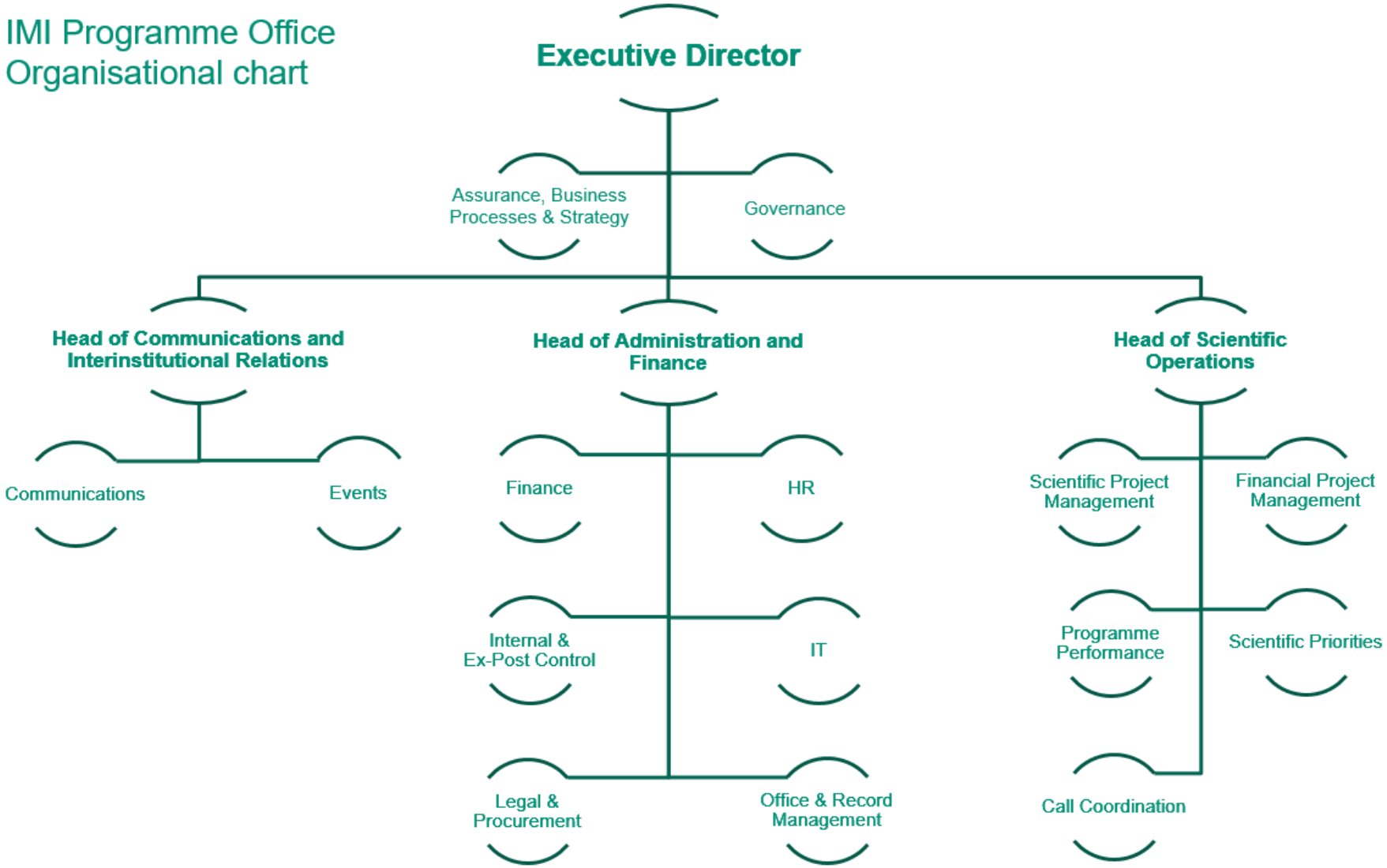
- **ResER%** = residual error rate, expressed as a percentage;
- **RepER%** = representative error rate, or error rate detected in the representative JU sample, calculated as described above;
- **RepERsys%** = systematic portion of the RepER% (the RepER% is composed of complementary portions reflecting 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.

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

64 Idem.

Annex 6 – Organisational chart



Annex 7 – Staff establishment plan

Grade	Year 2019			Year 2020												
	Establishment plan 2019			Evolution in posts						Organisational evolution			Establishment plan 2020			Posts filled on 31/12/20
				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		0	0		+ 1									1	1	1
AD9		6	6		+ 1									7	7	5
AD8		7	7		- 1									6	6	5
AD7		3	3		- 1									2	2	4
AD6		4	4		+ 4									8	8	5
AD5		8	8		- 4									4	4	8
Total AD		**33**	**33**											**33**	**33**	**32**
AST11																
AST10																
AST9																
AST8		1	1											1	1	1
AST7																

AST6																
AST5																
AST4		4	4											**4**	**4**	3
AST3		0	0											**0**	**0**	1
AST2		0	0		**+1**									**1**	**1**	0
AST1		1	1		**-1**											
Total AST		**6**	**6**											**6**	**6**	**5**
SC6																
SC5																
SC4																
SC3																
SC2																
SC1																
Total SC																
Overall total		**39**	**39**											**39**	**39**	**37**

Notes

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

Contract agents

Grade	2019	2020	Posts filled on 31/12/20
CA FG IV	2	3	3
CA FG III	12	11	11
CA FG II	1	1	1
CA FG I			
Total CA	**15**	**15**	**15**

Notes:

- CA = contract agent
- FG = function group

Seconded national experts (SNEs)

SNEs	2019	2020	Posts filled on 31/12/20
Total	**2**	**2**	**1**

Annex 8 – Final annual accounts

BALANCE SHEET

EUR '000

	Note	31.12.2020	31.12.2019
NON-CURRENT ASSETS			
Intangible assets	*2.1*	*37*	*46*
Property, plant and equipment	*2.2*	*219*	*126*
Pre-financing	*2.3*	*232 241*	*244 200*
		232 497	**244 372**
CURRENT ASSETS			
Pre-financing	*2.3*	*133 967*	*113 577*
Exchange receivables and non-exchange recoverables	*2.4*	*24 696*	*25 584*
		158 664	**139 161**
TOTAL ASSETS		**391 160**	**383 533**
CURRENT LIABILITIES			
Payables and other liabilities	*2.5*	*(326 391)*	*(241 139)*
Accrued charges	*2.6*	*(146 112)*	*(156 186)*
		(472 503)	**(397 324)**
TOTAL LIABILITIES		**(472 503)**	**(397 324)**
NET ASSETS		**(81 343)**	**(13 791)**
Contribution from Members	*2.7*	*2 713 664*	*2 290 993*
Accumulated deficit		*(2 304 783)*	*(1 930 477)*
Economic result of the year		*(490 223)*	*(374 306)*
NET ASSETS		**(81 343)**	**(13 791)**

STATEMENT OF FINANCIAL PERFORMANCE

EUR '000

	Note	2020	2019
REVENUE			
Revenue from non-exchange transactions			
Recovery of expenses	*3.1*	*1 218*	*2 721*
Other	*3.2*	*32*	*1*
		1 250	**2 722**
Revenue from exchange transactions			
Other	*3.3*	*69*	*51*
		69	**51**
Total revenue		**1 319**	**2 773**
EXPENSES			
Operational costs	*3.4*	*(483 182)*	*(368 441)*
Staff costs	*3.5*	*(4 993)*	*(4 644)*
Finance costs	*3.6*	*(19)*	*–*
Other expenses	*3.7*	*(3 348)*	*(3 994)*
Total expenses		**(491 542)**	**(377 080)**
ECONOMIC RESULT OF THE YEAR		**(490 223)**	**(374 306)**

CASHFLOW STATEMENT[65]

EUR '000

	2020	2019
Economic result of the year	*(490 223)*	*(374 306)*
Operating activities		
Depreciation and amortization	*73*	*65*
(Increase)/decrease in pre-financing	*(8 431)*	*(61 536)*
(Increase)/decrease in exchange receivables and non-exchange recoverables	*888*	*24 155*
Increase/(decrease) in payables	*85 253*	*55 143*
Increase/(decrease) in accrued charges & deferred income	*(10 074)*	*22 782*
Increase/(decrease) in cash contributions	*232 301*	*198 265*
Increase/(decrease) in in-kind contributions	*190 370*	*135 481*
Investing activities		
(Increase)/decrease in intangible assets and property, plant and equipment	*(156)*	*(47)*
NET CASHFLOW		
Net increase/(decrease) in cash and cash equivalents	*–*	*–*
Cash and cash equivalents at the beginning of the year	*–*	*–*
Cash and cash equivalents at year-end	*–*	*–*

STATEMENT OF CHANGES IN NET ASSETS

EUR '000

	Contribution from Members	Accumulated Surplus/ (Deficit)	Economic result of the year	Net Assets
BALANCE AS AT 31.12.2018	**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)**
Allocation 2019 economic result	*–*	*(374 306)*	*374 306*	*–*
Cash contribution	*232 301*	*–*	*–*	*232 301*
Contribution in-kind	*190 370*	*–*	*–*	*190 370*
Economic result of the year	*–*	*–*	*(490 223)*	*(490 223)*
BALANCE AS AT 31.12.2020	**2 713 664**	**(2 304 783)**	**(490 223)**	**(81 343)**

[65] Following the appointment of the Accounting Officer of the Commission as the Accounting Officer of IMI2 JU, the treasury of IMI2 JU was integrated into the Commission's treasury system. Because of this, IMI2 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 9 – List of IMI projects

(Grant agreements signed as of 31 December 2020)

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	vac4eu.org	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		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		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		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		knowledge management
ELF	European Lead Factory	www.europeanleadfactory.eu	drug discovery
EMIF	European medical information framework	www.emif.eu	knowledge management, Alzheimer's disease, metabolic syndromes
EMTRAIN	European medicines research training network	www.emtrain.eu	education and training
ENABLE	European Gram negative antibacterial engine	www.nd4bb-enable.eu	antimicrobial resistance
EPAD	European prevention of Alzheimer's dementia consortium	ep-ad.org	Alzheimer's disease
eTOX	Integrating bioinformatics and chemoinformatics approaches for the development of expert systems allowing the *in silico* prediction of toxicities	www.e-tox.net	knowledge management, drug safety
eTRIKS	Delivering European translational information & knowledge management services	www.etriks.org	knowledge management
Eu2P	European programme in pharmacovigilance and pharmacoepidemiology	www.eu2p.org	education and training
EU-AIMS	European autism interventions - a multicentre study for developing new medications	www.eu-aims.eu	autism
EUPATI	European patients' academy on therapeutic innovation	www.eupati.eu	education and training
EUROPAIN	Understanding chronic pain and improving its treatment	www.imieuropain.org	chronic pain
FLUCOP	Standardization and development of assays for assessment of influenza vaccines correlates of protection	www.flucop.eu	vaccines
GetReal	Incorporating real-life clinical data into drug development	www.getreal-institute.org	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		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		schizophrenia, depression
OncoTrack	Methods for systematic next generation oncology biomarker development	www.oncotrack.eu	cancer
Open PHACTS	The open pharmacological concepts triple store	www.openphactsfoundation.org	knowledge management
OrBiTo	Oral biopharmaceutics tools		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		rheumatoid arthritis and lupus
PREDECT	New models for preclinical evaluation of drug efficacy in common solid tumours		cancer
PreDiCT-TB	Model-based preclinical development of anti-tuberculosis drug combinations		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		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		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		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	amr-accelerator.eu/project/ab-direct	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
ARDAT	Accelerating research & development for advanced therapies	ardat.org	advanced therapies
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
BIGPICTURE	Central repository for digital pathology	www.bigpicture.eu	artificial intelligence
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
CARE	Corona accelerated R&D in Europe	www.imi-care.eu	coronaviruses
COMBACTE-CDI	Combatting bacterial resistance in Europe - clostridium difficile infections	www.combacte.com/about/combacte-cdi-understanding-of-the-epidemiology-and-clinical-	antimicrobial resistance

Project acronym	Full project title	Website	Subject area
		impact-of-clostridium-difficile-infection/	
COMBINE	Collaboration for prevention and treatment of MDR bacterial infections	amr-accelerator.eu/project/combine	antimicrobial resistance
ConcePTION	Building an ecosystem for better monitoring and communicating of medication safety in pregnancy and breastfeeding: validated and regulatory endorsed workflows for fast, optimised evidence generation	www.imi-conception.eu	medicines safety
COVID-RED	COVID-19 infections - remote early detection	www.covid-red.eu	coronaviruses
DECISION	A minituarized disposable molecular diagnostics platform for combatting coronavirus infections		coronaviruses
DO>IT	Big data for better outcomes, policy innovation and healthcare system transformation		big data
DRAGON	Rapid and secure AI imaging based diagnosis, stratification, follow-up, and preparedness for coronavirus pandemics	europeanlung.org/dragon	coronaviruses
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	stem cells
EBODAC	Communication strategy and tools for optimizing the impact of Ebola vaccination deployment (Compliance with vaccine regimens)	www.ebovac.org/ebodac	Ebola and related diseases
EbolaMoDRAD	Ebola virus: modern approaches for developing bedside rapid diagnostics	www.ebolamodrad.eu	Ebola and related diseases
EBOMAN	Manufacturing and development for rapid access Ebola vaccine	www.ebovac.org/eboman	Ebola and related diseases
EBOVAC1	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	www.ebovac.org	Ebola and related diseases

Project acronym	Full project title	Website	Subject area
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: Phase II	www.ebovac2.com	Ebola and related diseases
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	eupati.eu	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
EUbOPEN	EUbOPEN: Enabling and unlocking biology in the OPEN	www.eubopen.org	drug discovery
eTRANSAFE	Enhancing translational safety assessment through integrative knowledge management	etransafe.eu	safety
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.getreal-institute.org	relative effectiveness
GNA NOW	Novel Gram-negative antibiotic now	amr-accelerator.eu/project/gna-now/	antimicrobial resistance
GRAVITATE-HEALTH	Gravitate–Health: Empowering and equipping Europeans with health information for active personal health management and adherence to treatment	www.gravitatehealth.eu	digital health
H2O	H2O Health outcomes observatory	health-outcomes-observatory.eu	digital health
HARMONY	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology	www.harmony-alliance.eu	big data, cancer

Project acronym	Full project title	Website	Subject area
HARMONY PLUS	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology – PLUS	www.harmony-alliance.eu/harmony-plus/story	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	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 tissue signatures and their correlates in liquid biopsies	www.immuniverse.eu	autoimmune diseases
Impentri	Development of Impentri, an intravenous imatinib formulation for COVID-19 acute respiratory distress syndrome (ARDS)	impentri.exvastat.com	coronaviruses
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	imsavar.eu	autoimmune diseases, cancer
INNODIA	Translational approaches to disease modifying therapy of type I diabetes: an innovative	innodia.eu	diabetes

Project acronym	Full project title	Website	Subject area
	approach towards understanding and arresting type I diabetes		
INNODIA HARVEST	Translational approaches to disease modifying therapy of type 1 diabetes - HARVESTing the fruits of INNODIA	www.innodia.eu/harvest	diabetes
ITCC-P4	ITCC pediatric preclinical POC platform	www.itccp4.eu	paediatrics, cancer
KRONO	Evaluation of a production ready portable, point-of-need platform (instrument and reagents), direct from nasal swab test for the molecular diagnostic detection of COVID-19 infection		coronaviruses
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
MAD-COV 2	Modern approaches for developing antivirals against SARS-CoV 2	mad-cov2.eu	coronaviruses
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	ngn-pet.com	pain

Project acronym	Full project title	Website	Subject area
	platform for pain efficacious treatments		
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
PREMIER	Prioritisation and risk evaluation of medicines in the environment	imi-premier.eu	environmental issues
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

Project acronym	Full project title	Website	Subject area
RADAR-CNS	Remote assessment of disease and relapse in central nervous system disorders	www.radar-cns.org	neurological disorders
RAPID-COVID	Robust automation and point of care identification of COVID		coronaviruses
RESCEU	Respiratory syncytial virus consortium in Europe	resc-eu.org	respiratory disease
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
SISAQOL-IMI	Establishing international standards in the analysis of patient reported outcomes and health-related quality of life data in cancer clinical trials		cancer
SOPHIA	Stratification of obese phenotypes to optimize future obesity therapy	imisophia.eu	obesity
STOPFOP	Saracatinib trial to prevent FOP	www.stopfop.com	rare / orphan diseases
T2EVOLVE	Accelerating development and improving access to CAR and TCR-engineered T cell therapy	t2evolve.eu	advanced therapies, cancer
TransBioLine	Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease	transbioline.com	safety

Project acronym	Full project title	Website	Subject area
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
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 10 – 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
ACSS2	AcetylCoA Short chain Synthase 2 enzyme
AD	Alzheimer's disease
ADNI	Alzheimer's Disease Neuroimaging Initiative
ADR	Adverse drug reaction
AFS	Anti-fraud strategy
AI	Artificial intelligence
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
AP	Associated Partner
API	Application programing interface
ApoE	Apolipoprotein E
ARES	Advanced Records System
ASD	Autism spectrum disorder
ATM-AVI	Aztreonam-avibactam
ATMP	Advanced therapy medicinal product
AURI	Audit Result Implementation Workflow
AWP	Annual Work Plan
BARDA	Biomedical Advanced Research and Development Authority
BBI JU	Bio-based Industries Joint Undertaking
BD4BO	Big Data for Better Outcomes
BMGF	Bill and Melinda Gates Foundation
CA	Commitment appropriations
CA	Contract agent
CAFS	Commission Anti-Fraud Strategy
CAS	Common Audit Service
CDA	Confidential disclosure agreement
CDI	*Clostridioides difficile* infection
CDM	Common data model
CEOS	Conditions of Employment of Other Servants
CERT-EU	Computer Emergency Response Team

Acronym	Meaning
CFS	Certificate on Financial Statements
CGM	Continuous glucose monitoring
CHO	Carbohydrate
CIRS	Centre for Innovation in Regulatory Science
CMM	Capability maturity model
CNS	Central nervous system
COMPASS	H2020 workflow tool providing harmonisation between business processes & validation workflows
CONT	European Parliament Budgetary Control Committee
COPD	Chronic obstructive pulmonary disease
CORDA	Common Research Data Warehouse
COVID-19	Coronavirus disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
COVID-ETF	COVID-19 EMA pandemic Task Force
C-Path	Critical Path Institute
CRAB	Carbapenem-resistant *Acinetobacter baumannii*
CRE	Carbapenem-resistant Enterobacteriaceae
CRO	Contract research organisation
CRS	Common representative sample
CSF	Cerebrospinal fluid
CT	Computed tomography
CTN	Clinical trials network
DDIM	Drug Development Information Management
DG	Directorate-General
DG BUDGET	European Commission Directorate-General for Budget
DG CNECT	European Commission Directorate-General for Communications Networks, Content and Technology
DG DIGIT	European Commission Directorate-General for Informatics
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
DIKI	Drug-induced kidney injury
DILI	Drug-induced liver injury
DIVI	Drug-induced CNS (central nervous system) injury
DKD	Diabetic kidney disease
DKFZ	German Cancer Research Centre
DLB	Dementia with Lewy bodies
DMARD	Disease modifying anti rheumatic drugs

Acronym	Meaning
DMO	Digital mobility outcome
DO	Dissolved oxygen
DoA	Description of Action
DOI	Digital object identifiers
DPA	Data protection authority
DPIA	Data protection impact analysis
DPMS	Diagnostic and patient management study
DPP6	Dipeptidyl peptidase 6
DRC	Democratic Republic of the Congo
DSDRS	Diabetes specific dementia risk score
DTAP	Diphtheria, tetanus and acellular pertussis
DW	Data warehouse
DZIF	German Centre for Infection Research
EC	European Commission
ECA	European Court of Auditors
ECACC	European Collection of Authenticated Cell Cultures
ECSEL JU	Electronic Components and Systems for European Leadership Joint Undertaking
EDES	Early Detection and Exclusion System
EDPS	European Data Protection Supervisor
EEG	Electroencephalogram
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHA	European Hematology Association
EHR	Electronic health record
EJP RD	European Joint Programme on Rare Diseases
ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EMBARC	EU bronchiectasis registry
EMN	European Myeloma Network
ENISA	European Union Agency for Network and Information Security
ENSO	Exploring New Scientific Opportunities
EPoS	Elucidating Pathways of Steatohepatitis
ERCEA	European Research Council Executive Agency
ERM	Enterprise risk management
ESOF	EuroScience Open Forum
EU	European Union
EU-IN	EU-Innovation Network
EUnetHTA	European Network for Health Technology Assessment

Acronym	Meaning
EUSA	European School of Administration
ExPEC	Extra-intestinal pathogenic *Escherichia coli*
F4E	Fusion for Energy
FAIR	Fraud and irregularity in research
FAIR	Findable, accessible, interoperable, reusable
FC	Financial contribution
FCH JU	Fuel Cells and Hydrogen Joint Undertaking
FDA	US Food and Drug Administration
FG	Function group
FIA	Financial initiating agent
FIH	First in human
FNIH	Foundation for the National Institutes of Health
FOP	Fibrodysplasia ossificans progressiva
FP	Full proposal
FP7	Seventh Framework Programme
FTE	Full time equivalent
FWC	Framework contract
GA	Grant Agreement
GAP	Grant Agreement preparation
GB	Governing Board
GCGH	Grand Challenges in Global Health
GDPR	General Data Protection Regulation
GHDDI	Global Health Drug Discovery Institute
GI	Gastrointestinal
GMP	Good manufacturing practice
GP	General practitioner
GPPAD	Global Platform for the Prevention of Autoimmune Diabetes
GWAS	Genome-wide association study
H2020	Horizon 2020
HAAF	Hypoglycaemia-associated autonomic failure
HALE	Healthy aging lifestyle education
HAP	Hospital-acquired pneumonia
HCP	Healthcare provider
HDGEC	Huntington’s disease gene-expansion carrier
hiPSC	Human induced pluripotent stem cell
HIV	Human immunodeficiency virus
HR	Human resources

Acronym	Meaning
HRQOL	Health-related quality of life
HTA	Health technology assessment
HTS	High throughput screening
IA	Innovation Action
IaaS	Infrastructure as a Service
iACT	Institute for Advanced Clinical Trials for Children
iAMD	Intermediate age-related macular degeneration
IAS	Internal Audit Service of the European Commission
IBA	Ion Beam Applications SA
IBD	Inflammatory bowel disease
IC	Internal control
ICF	Internal control framework
ICU	Intensive care unit
IDR	intrinsically disordered region
IED	Invasive ExPEC disease
IKC	In-kind contribution
IL-2R	Interleukin-2 receptor
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
iPSC	Induced pluripotent stem cell
IRDiRC	International Rare Diseases Research Consortium
IT	Information technology
ITF	Innovation Task Force
IVD	*In vitro* diagnostic device
IVE	Influenza vaccine effectiveness
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
JTI	Joint Technology Initiative
JUs	Joint Undertakings
KD-CAAP	Kawasaki Disease Coronary Artery Aneurysm Prevention
KMP	Knowledge management platform
KPI	Key performance indicator
LCS	Longitudinal cohort study
LOI	Letter of intent
LOINC	Logical observation identifiers names and codes

Acronym	Meaning
LT	Long-term contract
MAD	Multiple ascending dose
MANCO	Monoclonal antibodies against COVID-19
MAT	Monocyte activation test
MCI	Mild cognitive impairment
MCI	Multicomponent intervention
MEP	Member of the European Parliament
MERS	Middle East respiratory syndrome
MICADO	Modelling Integrated Care for Diabetes based on Observational data
MiPS	Mission Processing System
MPLC	Medical product lifecycle
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MSA	Multiple system atrophy
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCP	National Contact Point
NDMM	Newly diagnosed multiple myeloma
NIH	National Institutes of Health
NIH HEAL	National Institutes of Health Helping to End Addiction Long-term Initiative
NMR	Nuclear magnetic resonance
NPI	Non-pharmaceutical interventions
NVU	Neurovascular unit
OHDSI	Observational Health Data Sciences and Informatics
OLAF	European Anti-Fraud Office
OMOP	Observational Medical Outcomes Partnership
PA	Payment appropriations
PBRE	Periodic benefit-risk evaluation reports
PC	Parent cohort
PD	Parkinson’s disease
PDX	Patient derived xenografts
PET	Positron emission tomography
PF&S	Physical frailty and sarcopaenia
PFMD	Patient Focused Medicines Development
PfMF	Platform master file
PiR	Partner in Research

Acronym	Meaning
PLoS	Public Library of Science
PMO	Paymaster Office
PNHS	Prognostic and natural history study
PoC	Point of care
PP	Patient preference
PPP	Public-private partnership
PRO	Patient reported outcome
PROM	Patient reported outcome measure
PSUR	Periodic Safety Update Reports
QIDP	Qualified Infectious Disease Product
qPCR	quantitative polymerase chain reaction
QST	Quantitative systems toxicology
R&D	Research and development
RA	Rheumatoid arthritis
RAE	Risk assessment exercise
RAFS	Common Research Family Anti-fraud Strategy
RDCT	Remote and decentralised clinical trial
RDM	Remote digital monitoring
REA	Research Executive Agency
REMAP-CAP	Randomised, embedded, multi-factorial, adaptive platform trial for community-acquired pneumonia
RepER	Representative error rate
ResER	Residual error rate
RIA	Research and Innovation Action
RMIC	Risk Management and Internal Control manager
RMT	Remote monitoring technology
RPT	Rabbit pyrogen test
RSV	Respiratory syncytial virus
RTO	Research and Technology Organisation
RVFV	Rift Valley fever virus
S2R JU	Shift2Rail Joint Undertaking
SAD	Single ascending dose
SAGE	Strategic Advisory Group of Experts on Immunization
SAIP	*Staphylococcus aureus* intensive care-acquired pneumonia
SA-PJI	*Staphylococcus aureus* prosthesis joint infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SBV	Schmallenberg virus

Acronym	Meaning
SC	Scientific Committee
SEP	Staff establishment plan
SEP	H2020 IT tool for submission and evaluation of proposals
SEP DS	SEP Data Store
SGG	Strategic Governing Group
SIP	Security Implementation Plan
SLC	Solute carrier
SME	Small and medium-sized enterprise
SNE	Seconded national expert
SNOMED	Standard Nomenclature of Medicine
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SPOC	Single Point of Contact
SR	Study report
SRA	Strategic Research Agenda
SRG	States Representatives Group
SSI	Surgical site infection
ST	Short-term contract
SyGMa	H2020 IT tool for grant management
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TA	Temporary agent
TAR	Target actionability review
TB	Tuberculosis
TBEV	Tick-borne encephalitis virus
THL	Terveyden ja hyvinvoinnin laitos
TOMI	Trial Outcome Markers Initiative in T1D
TREM2	Triggering receptor expressed on myeloid cells 2
TRL	Technology readiness level
TTG	Time to grant
TTI	Time to inform
TTP	Time to pay
TTS	Time to sign
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Stud
US	United States

Acronym	Meaning
VAC4EU	Vaccine Monitoring Collaboration for Europe
VAP	Ventilator-associated pneumonia
VCG	Virtual control group
WA	White Atrium
WHO	World Health Organisation
WP	Work package

Annex 11 – Analysis and assessment of the IMI2 JU Annual Activity Report 2020 (AAR 2020) 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 2020 (Authorising Officer's report) was presented to the IMI2 JU Governing Board at the end of February 2021 and it is planned to have it approved by the Governing Board in June 2021.

The Governing Board is of the opinion that the IMI2 JU AAR 2020 covers well the main activities and achievements of the IMI2 JU in 2020 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 2020 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 2020 together with the draft Budget 2020 was approved by the Governing Board on 13 December 2019 (Decision IMI2-GB-DEC-2019-24), first amended by the Governing Board on 28 February 2020 (Decision IMI2-GB-DEC-2020-8), second amended on 8 May 2020 (Decision IMI2-GB-DEC-2020-13), third amended on 19 June 2020 (Decision IMI2-GB-DEC-2020-20), and last amendment on 6 October 2020 (Decision IMI2-GB-DEC-2020-31). The financial details of these amendments are duly explained in the Annual Activity Report.
- In 2020, the JU implemented the final stage (grant agreement signature) of the IMI2 Calls for proposals 17, 18, 19, 21, and two Calls were at various stages of the evaluation and granting process (IMI2 - Calls 20 and 22) initiated under the Horizon 2020 Framework Programme. Of note is the fast-track Call 21 (Development of therapeutics and diagnostics combatting coronavirus infections) launched in response to COVID-19 pandemic. Despite the emergency of the situation, the Call was successfully prepared and launched extremely rapidly. The JU launched four new Calls under Horizon 2020, IMI2 Calls 20, 21, 22 and 23. Those Calls represent the commitment of a total value of €501 million: €264 million of EU contribution; €199 million of contribution from EFPIA companies; and €38 million of contribution from Associated Partners.
- In 2020, the JU signed 19 new grant agreements from IMI2 Calls 17, 18, 19, 21 initiated under Horizon 2020. As on 31 December 2020, the portfolio of projects consisted of 11 projects from the first phase of IMI (initiated under Framework Programme 7) of which 8 still running, plus Grant Agreements signed from IMI2 Calls 1 to 17, 19 and 21 (initiated under Horizon 2020) of which 92 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 2020, 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 10 projects in 2020. 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) Results that were implemented in industrial processes; (j) Accessibility of resources/outputs beyond consortium.

- By 31 December 2020, IMI2 projects had led to 9 patent applications and 2 patent awards (up from 7 patents applications and 1 patent award in 2019), and IMI1 and IMI2 projects had produced 6 963 publications in peer reviewed journals, around 15 % of which (1 052) were published in year 2020. The latest biblio-metric analysis demonstrated that the citation impact of papers associated with IMI projects is at 1.99 (unchanged from 2019), twice the world average (baseline of 1), and almost twice the EU‘s average (1.10). Also 35.7 % (increased from 22.3 % in 2019) of IMI2 publications are published in top 10 % of publications. This confirms, like for previous year 2019, the scientific excellence of IMI projects.

- Impacts of projects on the regulatory framework start emerging. Several project results are also implemented within 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 2020, the IMI2 JU States Representatives Group met 3 times. The IMI2 JU Scientific Committee held 3 meetings. Notably, this Committee prepared five position papers with recommendations, on 1) data infrastructure and integration, 2) involvement of regulators and regulatory science, and 3) equitable access, as well as topics related to the research programme i.e. recommendations on 4) rare diseases within and 5) drugs repurposing. 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), were in existence, with variable number of meetings as some of the related activities were not prominent in the calls launched in 2020.

- In 2020, 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 online Stakeholder Forum in 10 November 2020 with the theme of ‘‘Broader horizons: growing Europe’s health partnership”, which attracted almost 600 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 2020, IMI2 JU conducted 14 interim reviews of projects from the IMI2 Calls 1, 3, 6, 7, 9, 10, 12, 13 and 16. Overall, the reviewers were generally satisfied with the progress made by these projects, but noted some delays mainly due to the outbreak of COVID-19 pandemic. In addition, the experts provided a number of constructive recommendations to the consortia.

- The “Time To Pay” is similar to 2019 and below the maxima foreseen for the Horizon 2020 Programme, with 6 days for pre-financings, 63 days for interim payments, and 72 days for final payments. The “Time To Grant” (190 days) again improved from 2019 and 2020, and is below the maximum foreseen for the Horizon 2020 Programme.

- For IMI projects (operating under Framework Programme 7), 80% of the €965.7 million EU contribution committed in total have been claimed, validated and paid, while 75.5% of the €975.5 million EFPIA contributions committed in total have been reported and validated, as on 31 December 2020. For IMI2 projects (operating under Horizon 2020), 20% of the €1,455 million JU contribution already committed have been claimed, validated and paid, while 28.4% of the €1,279.6 million EFPIA and Associated Partners contributions already committed have been reported and validated, as of 31 December 2020. Out of the EUR 1,474.5 million committed by EFPIA and Associated Partners over the full IMI2 programme duration, EUR 1,022.3 million is coming from the EU and H2020 associated countries which represents 70.4% of the EU's commitment.

- In total, 281 ex-post audits of beneficiaries under Framework Programme 7 have been launched since 2011, out of which a total of 272 have been finalised, of which 14 during the year 2020. 89 ex-post audits of beneficiaries under Horizon 2020 have been launched since 2016, out of which 57 have been finalised, including 28 during the year 2020. In 2020, the cumulative residual error rate from the finalised audits was 1.14% for operational expenditure under Framework Programme 7, and was 0.74% 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 2020, IMI has completed ex-post audits of 21 EFPIA companies, covering a total of EUR 709.7 millions of accepted contributions or 96 % of all EFPIA contributions to IMI projects under Framework Programme 7.

- 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).

- The European Court of Auditors in its report on the financial year 2019, 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 report notes that the JU has in particular improved their implementation of the 2019 budget, and significantly stabilised the staff turnover. Furthermore, the auditors have substantiated that audits of randomly selected IMI payments to H2020 beneficiaries showed no significant errors or control weaknesses.

- In 2020 IAS performed an audit on Horizon 2020 grant implementation in IMI2 JU as originally foreseen in 2019-2021 Strategic Internal Audit Plan[66]. The objective of this audit was to assess the adequacy of the design and the efficiency and effectiveness of the internal control system in place in for the implementation of grant agreements under Horizon 2020 programme. Preliminary survey and fieldwork phases of the audit were completed during 2020 while the final report was issued in 2021.

- In relation to the use of human resources, activities carried out by the IMI2 JU staff in 2020 were in line with the IMI objectives. On 31 December 2020, 53 of the 56 positions as in the Staff Establishment Plan of the IMI2 JU were occupied. Five positions were filled during 2020, three for temporary agents and two for contract agents.

- During 2020 the monitoring tools were fully operational and the IMI2 JU AAR 2020 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 2020 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 2020 in a realistic way.

The Governing Board is recommending that efforts be continued in 2021 to execute all the remaining commitment appropriations.

[66] Ares(2019)4058461 - 26/06/2019.

Assessment

The declaration of the Executive Director and the IMI2 JU AAR 2020 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 2020.

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 2020 of the authorizing officer. This analysis and assessment will be included into the IMI2 JU AAR 2020.

Done at Brussels, on 25 June 2021

For the Innovative Medicines Initiative 2 Joint Undertaking,

signed

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Olivier Laureau
Chairperson of the Governing Board

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