innovative health initiative

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Consolidated annual activity report 2023

In accordance with Article 26 of Council Regulation (EU) 2021/2085 of 19 November 2021 and with Article 23 of the Financial Rules of IHI JU. The consolidated annual activity report will be made publicly available after its approval by the Governing Board.

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Factsheet

Name of the JU	**Innovative Health Initiative (IHI)**
Objectives	IHI's general objectives are to: • turn health research and innovation into real benefits for patients and society; • deliver safe, effective health innovations that cover the entire spectrum of care – from prevention to diagnosis and treatment – particularly in areas where there is an unmet public health need; • make Europe's health industries globally competitive.
Legal Basis	Article 187 of the Treaty on the Functioning of the European Union Regulation (EU) 2021/695 of the European Parliament and of the Council of 28 April 2021 establishing Horizon Europe Council Regulation (EU) 2021/2085 of 19 November 2021 establishing the Joint Undertakings under Horizon Europe and repealing Regulations (EC) No 219/2007, (EU) No 557/2014, (EU) No 558/2014, (EU) No 559/2014, (EU) No 560/2014, (EU) No 561/2014 and (EU) No 642/2014
Executive Director	Hugh Laverty was interim/acting Executive Director throughout 2023. Niklas Blomberg was appointed Executive Director in 2023 and joined IHI in January 2024.
Governing Board	Chair: Irene Norstedt, European Commission Vice-Chair: Nathalie Virag, Medtronic / MedTech Europe 8 members in total: 4 from the European Commission, and 4 from the industry partners. More information on the Governing Board can be found here.
Other bodies	Science and Innovation Panel (SIP) • 18 members from the scientific community, wider healthcare community, European Commission, IHI industry partners, and the States' Representatives Group • provides the Governing Board with science-based advice on a range of matters. States' Representatives Group • up to two representatives from each EU Member State and country associated to Horizon Europe • is consulted on a range of issues, including draft call topics • acts as a link between IHI and relevant national and regional research and innovation programmes.
Staff number	44 positions were occupied at the end of 2023.
Total budget 2023[1]	Commitment appropriations: EUR 223 231 575 Payment appropriations: EUR 225 848 975
Budget implementation / execution	Commitment appropriations: total consumption: EUR 206 830 838 (92.65%) Title 1 – EUR 5 674 330 (2.54%) Title 2 – EUR 2 173 337 (0.97%) Title 3 – EUR 198 983 171 (89.14%) Payment appropriations: 203 917 585 (90.29%) Title 1 – EUR 5 602 300 (2.48%) Title 2 – EUR 2 129 790 (0.94%) Title 3 –EUR 196 185 496 (86.87%)

[1] Total budget includes operational budget (used for funding selected projects) & administrative (used for funding Programme Office activities)

Grants	16 grants signed for a total value of EUR 184 million EU contribution plus EUR 190 million in contributions from IHI industry members and contributing partners.
Strategic Research & Innovation Agenda	The Strategic Research and Innovation Agenda (SRIA) was adopted by the Governing Board on 20 January 2022.
Call implementation	Number of calls launched in 2023: 2 (one single-stage, one two-stage) Single-stage calls[2] • Number of full proposals submitted: 19 • Number of eligible proposals: 14 • Number of proposals granted: 14 Two stage calls[3] • Number of short proposals submitted: 17 • Number of eligible proposals: 15 • Number of proposals invited to stage 2: 6 • Number of proposals granted: 2 Number of IHI projects as of end of 2023: 16 IMI1 projects: 59 | IMI2 projects: 123
Participation including SMEs	Total participations: 404 / Total (unique) participants: 315 Breakdown of participants by organisation type: • Academia, secondary / higher education establishment: 25% • IHI industry partners: 27% • Contributing partners: 7% • Non-profit research organisations: 16% • Small and medium-sized enterprises (SMEs): 10% • Patient organisations: 4% • Regulatory / community bodies: 1% • Other: 10% Number of newcomer beneficiaries: 160

[2] Figures on proposals submitted and eligible come from IHI call 3. The figure on proposals granted comes from IHI calls 1 and 3.

[3] Figures on proposals submitted, eligible, and invited to stage 2 come from IHI call 4. The figure on proposals granted comes from IHI call 2.

Foreword

As I sit down to write this, I have been in post as the IHI Executive Director for two months and it has been a true privilege to join this organisation at an exciting moment: 2023 was the pivotal year when the programme went from an ambition to reality, with the first 16 IHI projects signing their grant agreements and launching the IHI portfolio.

IHI is a true partnership of public and industry actors –our projects draw half of their support from our industry members. A large fraction of this support comes in the form of people, as Europe's leading pharmaceutical, health technology and medical device companies contribute the time and expertise of their engineers and scientists to our projects.

This makes the IHI programme unique globally; there is no other programme that drives interdisciplinary research at this level – each of IHI's project teams is composed of diverse experts, including medical researchers, healthcare practitioners, patients, and health industry representatives.

IHI is an ambitious programme that will help to develop a novel, interdisciplinary ecosystem for health research. The ambition to foster truly cross-sectorial research can be seen in the projects started during the year. For instance, we have projects that bring together expertise in medical and pharmaceutical research with health technologies and artificial intelligence to address novel modes for cancer treatments, or projects that work with healthcare practitioners to assess the capability of novel technologies to reduce stress and cognitive load in healthcare staff working in intensive care units.

IHI's ambition to foster research for the long-term sustainability of the European health industry can also be seen in the calls launched during the year: in addition to topics on novel methods for combining diagnostics and treatment and patient-centric care, we also launched two exciting topics on sustainable-by-design solutions for healthcare products and new manufacturing methods in the circular economy.

With IHI launched and the project portfolio steadily building, we must now turn our attention to creating partnerships that ensure the long-term uptake of project outcomes. The most important aspect of this partnership is with patients. In 2023 the IHI Patient Pool was established and as we move forward, they will be an important part of IHI – both in discussions on individual projects and for the shaping of the overall programme.

We are also looking to deepen our connections with other important actors: regulators, health technology assessment bodies, and national and regional healthcare systems to help embed project outcomes in European healthcare.

I would like to close by thanking the many people whose hard work and dedication make possible the results presented in this report.

Setting up and implementing a new partnership is not an easy task, and the successful launch of the IHI portfolio in 2023 is in large part thanks to the many people in all the IHI member organisations, public and private, who work tirelessly behind the scenes to make the programme a success. Thanks also to the participants in our projects – in IHI and in the predecessor IMI programmes. It is their ingenuity and willingness to collaborate across sectors and boundaries that makes a difference.

I would also like to thank the members of the Governing Board, States' Representatives Group and Science and Innovation Panel, whose commitment to the programme, independent advice and willingness to contribute time and expertise are instrumental to IHI's success.

Finally, I would like to thank my new colleagues in the IHI Programme Office. It has been a joy and privilege to join this talented, knowledgeable and extraordinarily hardworking team. Thank you for the warm welcome and thank you for the committed work to launch the projects, nurture the budding consortia, and manage new calls, all while managing the portfolio and outcomes of the ongoing IMI projects. I would also like to thank Hugh Laverty, Head of Scientific Operations and interim Executive Director in 2023: the accomplishments set out in this 2023 report are all on his watch.

Niklas Blomberg
IHI Executive Director

Executive summary

IHI highlights in 2023

- Launch of the first IHI projects – 16 grant agreements signed for projects covering all objectives outlined in the Strategic Research and Innovation Agenda and addressing diverse unmet public health needs.
- Launch of two new calls for proposals (IHI calls 4 and 5) with a total of 10 topics.
- Establishment of the IHI Patient Pool comprising around 120 patients and caregivers who are well placed to contribute their knowledge, expertise and experience to IHI's work.
- Creation of synergies with related initiatives, including a Memorandum of Understanding with EIT Health.
- Results from IMI projects continue to highlight the ability of public-private partnerships to deliver results in challenging areas and create long-lasting networks that continue to collaborate long after the end of the funding period.
- Strong administrative performance, with good results on budget execution and achievement of all key targets relating to the management of calls and payments.

Launch of the first IHI projects

The signature of the first IHI grant agreements in spring 2023 was a major milestone for the partnership. The five projects, funded under IHI call 1, address key challenges in health research that will benefit from the public-private, cross-sector approach exemplified by IHI. These include the use of big data, imaging and diagnostics to advance cancer diagnosis and treatment, and the creation of digital platforms to improve the care of people with neurodegenerative diseases (namely Alzheimer's disease and multiple sclerosis) plus other health problems.

Later in the year, IHI signed a further 11 grant agreements for projects funded under IHI calls 2 and 3. Among other things, these new projects address conditions such as heart disease, diabetes and rare diseases as well as Alzheimer's disease and liver disease. There is a strong emphasis on prevention, with a number of projects working on screening platforms to identify people at risk of or in the very early stages of a disease, when there is still time to slow or even reverse the progress of the disease.

Between them, the 16 projects cover all five specific objectives set out in the IHI Strategic Research and Innovation Agenda (SRIA) and the legislation creating IHI.

Launch of new IHI calls for proposals

On 27 July, IHI launched two new calls for proposals: IHI call 4 (a two-stage call with 6 topics) and IHI call 5 (a single-stage call with 4 topics). The topics show how IHI makes contributions to key European policies. For example, two topics on the environmental impacts of healthcare are in line with the goals of the European Green Deal. Two further topics advance the EU's aims of replacing, reducing and refining the use of animals in research (the '3Rs'). The other topics featured in the calls aim to improve the experience of blood tests; boost the diversity of clinical studies by increasing the involvement of underserved patient populations; speed up development of treatments for rare diseases; improve the care of stroke patients; advance the potential of synthetic data in health research; and explore theranostics (in which a diagnostic test and therapy are twinned).

The Programme Office also organised online info sessions on all call topics as well as IHI's rules and procedures (for both single- and two-stage calls) and the financial aspects of single-stage calls. To facilitate networking and the formation of strong consortia, IHI also organised pitching sessions on the single-stage topics, during which people could showcase their potential as project partners. In addition, the online brokerage platform was updated for the new calls – the platform allows users to find, contact and even meet with potential project partners.

In October, IHI published the draft topics slated for inclusion in IHI calls 6 and 7, which were launched at the beginning of 2024. Publishing draft topics ahead of the call launch gives applicants additional time to start preparing their proposals. The brokerage platform was updated at the same time to make it easier for applicants to highlight their own interest in the topics and start identifying and networking with potential partners.

Promotion of the IHI brand

While much of IHI's communication efforts focused on new and forthcoming calls for proposals, the team also put efforts into promoting IHI more broadly, including through an online communication campaign. With powerful visuals, the campaign effectively told IHI's story by linking the way we work to the stories of fictional patients and their families.

Creation of the IHI patient pool

Today, it's widely recognised that patients (and informal caregivers) can and should be involved in all aspects of health research and innovation. This includes the activities of organisations like IHI that fund projects in this area.

That's why the IHI Programme Office set up the IHI Patient Pool – to create a group of patients and informal caregivers who can support IHI activities by bringing their unique perspective, experience, and expertise to the table. People interested in being part of the pool were invited to submit an expression of interest. Currently there are some 120 people in the pool, a quarter of whom were also in the IMI patient pool.

Members of the pool may be invited to participate in project meetings, scientific events, webinars, or trainings organised by IHI. Crucially, IHI will turn to the pool if patient / caregiver expertise is needed in core activities such as the evaluation of proposals, reviews of ongoing projects, and discussions on future funding opportunities.

Announcing IHI's new Executive Director

In summer 2023, IHI was able to announce that Dr Niklas Blomberg had been appointed as IHI's next Executive Director, with a start date in January 2024. Dr Blomberg has worked in both research and leadership roles in Europe's life sciences sector, and at the time of his appointment was Director of ELIXIR, the life sciences data infrastructure.

Supporting synergies

The research and innovation funding landscape counts many organisations working on similar topics to IHI. Throughout 2023, the IHI team sought to explore ways of exploiting synergies with these organisations. A highlight here was the signature of a Memorandum of Understanding (MoU) with EIT Health that will facilitate collaboration and allow the two organisations to leverage their strengths, networks and expertise.

The MoU between EIT Health and IHI is a significant step towards contributing meaningfully to EU priorities by creating a collaborative innovation ecosystem that promotes entrepreneurship and innovation in healthcare. By leveraging their unique strengths and resources, the two organisations aim to create a platform that supports healthcare entrepreneurs, researchers, and healthcare professionals across Europe.

Project results continue to highlight added value of PPP approach

While the first IHI projects are just getting up and running, IMI projects are continuing to deliver results that demonstrate the added value of the public-private partnership approach in diverse ways.

Ensuring the long-lasting legacy of high-performing projects

Many projects set up organisations to build on the projects' results after the IMI funding period has finished. For example, ITCC-P4 has developed a platform of over 400 patient-derived models, based on cells and tissues obtained from patients covering more than 20 common childhood cancers. These models are designed to facilitate research into these diseases and develop much-needed new treatments.
In 2023, the project set up a spin-off company, ITCC-P4 gGmbH, to make the models developed by the project available to the wider research community.

Similarly, the conect4children launched a non-profit foundation to sustain the pan-European paediatric clinical trial network, and associated support services, set up by the project since its launch back in 2018.

Meanwhile results from projects that finished several years ago are testament to the long-lasting bonds forged between partners in our projects. IMI severe asthma project U-BIOPRED ended in 2015, but the partners are still working together, thanks in large part to the strong involvement of patients in the project – this provided the researchers with inspiration and motivation for further collaborations. In 2023 the team published a paper exploring how the community of microbes living in the sputum (mucus and phlegm) contributes to childhood asthma or wheezing.

And although IMI project DIRECT ended in 2019, the team is still collaborating and delivering fresh insights into the drivers of diabetes; a recent paper sheds new light on why the efficacy of diabetes drugs called GLP-1 agonists varies so much from patient to another. These findings could help to personalise the treatment of people with diabetes.

Projects also secure their legacy when their results are taken up and used. IMI project EU-PEARL delivered a range of resources to guide the planning and development of platform trials, in which multiple organisations can test candidate drugs simultaneously against a shared placebo group. Project partner the Children's Tumor Foundation (CTF) has announced its plans to use the methodology and structure established by EU-PEARL to set up a platform trial for neurofibromatosis 1 (NF-1) and schwannomatosis. As of the end of 2023, CTF and the Global Coalition for Adaptive Research were working together to select sites and speaking to pharmaceutical companies who could want to test drugs via the trial.

Cross-sector collaborations deliver results

Cross-sector collaboration is embedded in IHI at all levels. However, many IMI projects already include a strong cross-sector component, and their results speak to the added value of this approach.

For example, the AMYPAD project demonstrated the usefulness of PET (positron emission tomography) brain scans in securing an earlier diagnosis of Alzheimer's disease. RADAR-CNS investigated how an app designed to detect difficulties in thinking skills such as concentration and memory could help to monitor and manage depression.

IDEA-FAST is testing the ability of a small wearable sensor to pick up on signs of fatigue in people with conditions such as Parkinson's disease, inflammatory bowel disease, and rheumatoid arthritis. This is important because many patients rate fatigue among their most disabling symptoms, yet measuring fatigue, and its impact on people's lives, is very difficult.

IMI projects are also addressing the many and diverse challenges associated with the gathering and use of health data for research. There have been decades of research to find biomarkers relating to neurodegenerative diseases, but the samples and data from this research are spread across laboratories in multiple countries. The IMI European Platform for Neurodegenerative Diseases (EPND) project aims to bring these disparate sources together in a central hub. In 2023, the project launched the first component of its platform: the cohort catalogue, which covers neurodegeneration research from 12 disease areas. This version already contains over 60 cohort studies, and users can filter them by disease area and the kinds of biological samples, imaging and other data available.

Today, data on the safety of using medicines during pregnancy is gathered in different ways by different organisations. This makes it much harder for researchers to combine data from different studies for large-scale analyses which could yield useful new results on this important subject. To address this issue, CONCEPTION developed a reference framework of core data elements (CDEs) designed to standardise the collection of data on the benefits and risks of medications used in pregnancy.

Striving for excellence in administration

The IHI Programme Office is currently managing three programmes in parallel (IMI1, IMI2 and IHI), each of which has different rules, management tools and procedures. Thanks to strong collaboration between the teams at IHI and robust procedures, IHI continues to manage these programmes efficiently, meeting all targets in terms of making payments and managing calls for proposals, and achieving a good budget execution rate.

- Time to inform (TTI) applicants of evaluation results (target 153 days): 68 days
- Time to grant (TTG) (target 245 days): 234 days

- Time to pay (TTP) project pre-financing (target 30 days): 7 days
- Time to pay (TTP) interim payments to projects (target 90 days): 65 days
- Budget execution: 92.65% (commitment appropriations) and 90.29% (payment appropriations)

The cumulative residual error rate for the IMI1 and IMI2 programmes is under the 2% materiality threshold.

In its 'Annual report on the EU Joint Undertakings for the financial year 2022', the European Court of Auditors (ECA) gave a clean bill of health for IHI JU, issuing an unqualified ('clean') opinion on the reliability of the accounts as well as on the legality and regularity of the revenue and payments underlying the annual accounts.

Gender balance at IHI

The statistics show that IHI has a good gender balance in a wide range of areas. As of the end of 2023, the statistics showed that:

- IHI Programme Office: 70% of staff are female.
- IHI Governing Board: 6 of the 7 named members are female[4]
- IHI Science and Innovation Panel: 9 of the 16 members are female.
- IHI States Representatives Group: 17 out of 35 main delegates are female.
- Expert evaluators for IHI calls for proposals: 46% are female.

Women are also well represented in leadership roles; at the end of the year, the chairs of the Governing Board, SRG and SIP were all female, as was the vice-chair of the Governing Board, and two of the three line managers at the Programme Office.

[4] One post out of the eight was unfilled at the end of the year.

1 Implementation of the annual work programme for 2023

1.1 Key objectives for 2023, associated risks and corrective measures

1. Execute the Strategic Research and Innovation Agenda priorities, enabling the active engagement of industry sectors covering the pharmaceutical, the biopharmaceutical, biotechnology and medical technology sectors, including companies active in the digital area, and a range of other key stakeholders involved in health care (including SMEs, academia, health care authorities, health care professionals and providers, and patient organisations), in particular through the launch of open and competitive calls for proposals.

- Signed 16 grant agreements launching the first IHI projects. The new projects cover all specific objectives set out in the SRIA and bring together diverse sectors and stakeholder types.
- Launched two new calls for proposals (one single-stage, one two-stage) with a total of 10 topics.
- Established the IHI Patient Pool to facilitate the direct involvement of patients and caregivers in IHI activities.
- Gathered 16 ideas for IHI call topics via the Ideas Incubator, 6 of which passed the basic checks and were reviewed by the SIP.

2. Ensure continuity with, and manage the legacy from, the Innovative Medicines Initiative 2 Joint Undertaking.

- Assessed technical interim / final reports and cost claims as well as reported in-kind contributions for IMI1 and IMI2 projects. 99 operational transactions were made during the year (15 pre-financing payments, 80 interim and final payments and 4 recoveries related to final payments).
- Held 15 interim reviews of ongoing IMI2 projects to assess progress and obtain recommendations for the future.
- Held 4 close-out meetings to gain insights into the results, impact and legacy of projects that have finished.
- Continued to communicate about and promote IMI projects via all communication channels.

3. Ensure sound budget implementation through the effective and efficient management of calls for proposals, grant award processes, close monitoring of projects and error rate.

- For operational payment appropriations, maintained a good execution rate of 90%.
- Met our targets for time to inform (TTI) applicants of the outcome of evaluations and time to grant TTG).
- Comfortably met our targets for time to pay (TTP) pre-financing, interim and final payments to projects.
- Maintained a residual error rate below the 2 % materiality threshold for ex-post audits (demonstrating the effectiveness of IHI's ex ante control procedures).
- Continued the development of processes and IT tools needed to allow the reporting of IKOP (in-kind contributions to operational activities) and IKAA (in-kind contributions to additional activities) for IHI projects.
- Hit all targets for TTP pay administrative payments.

4. Promote the cross sectorial partnership in health through proactive outreach strategies to attract high quality applications to IHI JU calls for proposals and engage with new players and newcomers.

- Ensured the early publication and continuous promotion of call topics through all communication channels, from draft topic stage until the call deadline.
- Organised IHI Call Days for calls 4 and 5, featuring info sessions, pitching sessions, and an online brokerage platform.
- Contributed to external events by sending speakers and materials to promote IHI calls.

5. Demonstrate the EU added value of IHI JU through assertive communication to target audiences with an emphasis on the openness, transparency, relevance, and coherence of IHI JU activities with its defined objectives and those of Horizon Europe.

- Ran the #IHITransformingHealth campaign which used simple language and powerful visuals to raise awareness about who we are, what we do, and why. The campaign was shared with IHI's partners and the SRG and triggered a marked increase in IHI website page views.
- Ran the multi-lingual #IdeasIncubator campaign to promote the Ideas Incubator.

6. Explore synergies with relevant programmes at Union, national, and regional level, in particular with those supporting the deployment and uptake of innovative solutions, training, education and regional development.

- Signed a Memorandum of Understanding with EIT Health and ran a joint workshop with them to support the sharing of opportunities between our communities.
- Interacted with IHI's sister joint undertakings GH EDCTP3 (Global Health - European and Developing Countries Clinical Trials Partnership) and Chips JU.
- Interacted with other health-oriented initiatives including the Cancer Mission, the Rare Diseases partnership, the partnership on Transforming Health and Care Systems, the Member States driven initiative Important Project of Common European Interest (IPCEI) on Health, the World Health Organisation (WHO).
- Met with EC teams leading key European political priorities such as EU4Health and the Digital Europe programme.

7. Improve and broaden access to project outcomes by embedding dissemination and exploitation activities in all stages of the project lifecycle.

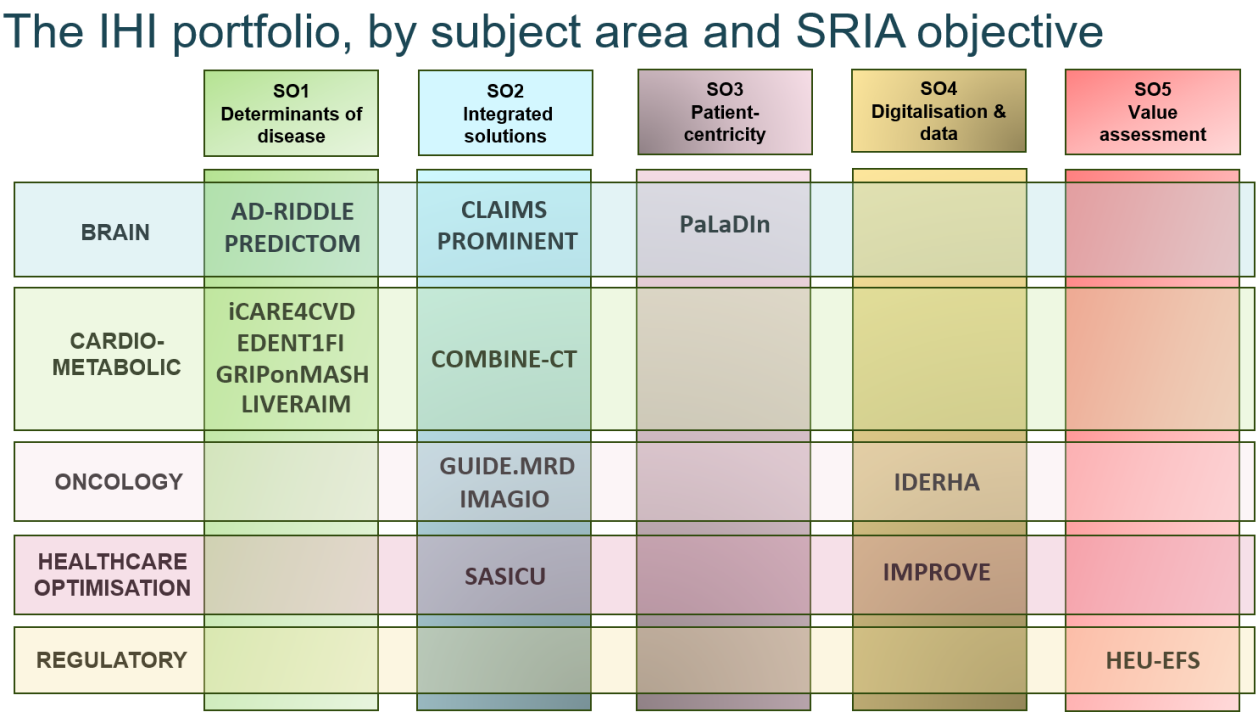
- Participated in the "inter-JU working group on KPIs monitoring & reporting" to establish a common approach to the monitoring of the various Horizon Europe performance indicators.
- Contributed to the second Biannual Monitoring Report (BMR) which monitors the performance of partnerships.
- Participated in a panel at the European Partnerships Stakeholder Forum in December 2023.

1.2 Research & innovation activities and achievements

IHI's first projects get started

A highlight of 2023 was the launch of the first IHI projects. In total, IHI signed 16 grant agreements for new projects. Addressing a range of disease areas and bringing on board sectors as diverse as pharmaceuticals, medical technology, big data and imaging, the projects exemplify IHI's cross-sector approach.

The diagram below shows the different disease and research areas addressed in the first IHI projects. It also shows that even at this early stage in the programme, the portfolio already includes at least one project under each specific objective (SO) of the Strategic Research and Innovation Agenda (SRIA).



SO1 – determinants of disease

- AD-RIDDLE aims to revolutionise the way Alzheimer's disease is detected, diagnosed, prevented and treated. It will do this by delivering a modular, customisable 'toolbox platform' of resources designed for patients, caregivers and healthcare providers.
- PREDICTOM's goal is to develop an AI-based screening platform capable of identifying people at risk of dementia, before the first symptoms appear. Crucially, patients would be able to start the screening process from the comfort of their own homes.
- iCARE4CVD aims to improve the care of cardiovascular disease (CVD), starting from those at risk of developing CVD to those with advanced disease. Among other things, the project will develop AI-based models to identify different subgroups of patients and the best treatments for them.
- EDENT1FI plans to set up a pan-European open platform to screen 200 000 children and adolescents for type 1 diabetes (T1D). Ultimately, EDENT1FI hopes to pioneer a new approach to T1D diagnosis and care, with a much stronger focus on early detection and prevention of the disease.

- GRIPonMASH plans to develop a diagnostic platform to identify people with the common liver disease MASLD (metabolic dysfunction-associated steatotic liver disease), so that they can take steps to protect their liver and avoid developing MASH (metabolic associated steatohepatitis) which is more severe and is on track to become the leading cause of liver transplants worldwide.

- LIVERAIM focuses on cirrhosis and liver cancer, both of which tend to be diagnosed quite late, when significant damage to the liver has already occurred. The project aims to develop a screening platform to detect liver disease early, when severe damage can still be reversed and prevented.

SO2 – integrated solutions

- CLAIMS addresses the challenge of finding the best treatment for people with multiple sclerosis (MS). The project aims to develop a diagnostic platform that would offer clinicians a holistic overview of the MS patient and would be able to predict how the patient's MS would likely progress with different treatments.

- PROMINENT aims to set up a digital platform to improve the diagnosis and personalised treatment of people with Alzheimer's disease coupled with other diseases. It will draw on existing artificial intelligence tools to create an open, interoperable platform capable of interacting with multiple systems.

- COMBINE-CT's goal is to deliver a workflow that will optimise the use of a non-invasive imaging technique called coronary computed tomography angiography (CCTA) in the diagnosis and care of people with coronary artery disease (CAD).

- GUIDE.MRD is exploring how blood tests could be used to detect minute traces of cancer in the blood following surgery to remove a tumour. This would help clinicians to identify which cancer patients would benefit from further treatment such as chemotherapy or radiotherapy.

- IMAGIO is working to advance interventional oncology (IO), a technique in which miniaturised instruments are inserted into a cancer patient's body and guided to the tumour with the help of imaging technologies. Once at the tumour, they can apply the treatment (e.g. chemotherapy, radiotherapy, etc.) directly and precisely, thereby limiting damage to health cells and tissues.

- SASICU aims to make intensive care units (ICUs) more peaceful environments for patients and staff alike. It is doing this by using smart technologies to reduce the frequency of alarms and making it easier for staff to identify patients at risk of certain problems.

SO3 – Patient-centricity

- PaLaDIn aims to develop and implement an innovative, global, patient-centric data platform to accelerate the development of effective treatments and care for neuromuscular and other rare diseases.

SO4 – Digitalisation & data

- IDERHA is setting up an open platform that will facilitate the integration and analysis of diverse types of health data. The platform will link up multiple public and private data sources and put in place interoperable tools and services that will make it possible for key groups to use the data. To focus their efforts, the IDERHA team is using lung cancer as a use case to design the platform.

- IMPROVE will use patient-generated health data, gathered via m-health and e-health technologies, to gain improved insights into the real-life behaviour of, and challenges faced by, patients with complex, chronic diseases and comorbidities.

SO5 – Value assessment

- HEU-EFS is developing a harmonised framework and accompanying recommendations for conducting early feasibility studies (EFS) in the EU. An EFS is a clinical study conducted on a medical device in the early developmental stages, and it is a key step in the journey towards device approval.

IMI projects – delivering results with impact

The IHI Programme Office continues to manage the large number of projects launched under the IMI1 and IMI2 programmes. Both programmes had ambitious goals; for example, the aims of IMI2 include improving and accelerating the drug development process; developing diagnostic and treatment biomarkers for disease; and developing new therapies for diseases where there is a high unmet need.

In order to track progress against these ambitious goals, the Programme Office follows the projects' outputs closely, and an extensive list of project achievements can be found in Annex 3. Meanwhile, a selection of these outputs is presented below. Between them, they demonstrate how our projects are delivering results that address major unmet health needs, including infectious diseases such as tuberculosis (TB), metabolic disorders such as diabetes, and more.

They also highlight how the projects are delivering knowledge and resources that can be used by the wider research community. In addition, the many results in fields such as health data and medical devices demonstrate how IMI paved the way for IHI by launching projects with a strong cross-sectoral element.

Finally, we feature a number of results from projects that actually ended several years ago. The fact that the consortia are still collaborating and publishing new papers is testament to the way IMI projects are creating long-lasting, productive networks.

IMI projects deliver tools and resources for the wider research community

Many projects make their outputs accessible to the wider research community, thereby increasing their potential impact dramatically.

EBiSC teams up with EIT Health project to facilitate access to cells for research

IMI project EBiSC has developed a not-for-profit bank of almost 1 000 high quality induced pluripotent stem cells (iPSCs) for use by researchers in academia and industry. Human iPSCs are mature adult cells that have been reprogrammed to make them 'pluripotent', i.e. they can be differentiated into any type of cell found in the human body. As such they are widely used health research. Meanwhile R2U-Tox Assay, a project funded by EIT Health, has developed a test for drug toxicity testing using heart and nerve cells derived from iPSCs. Now, the two projects have teamed up so that EBiSC can distribute the R2U-Tox Assay tests via their channels.

For R2U-Tox Assay, the collaboration contributes to the uptake of their product, while for EBiSC, the R2U-Tox Assay represents a useful additional product that they can offer to their customers. The collaboration also underscores the synergies between IMI/IHI and EIT Health, and the Memorandum of Understanding signed by IHI and EIT Health in 2023 makes future collaborations like this one more likely.

- Read more in the EBiSC project's news story

3TR project creates common standards to boost severe asthma research

People with mild-to-moderate asthma can often rely on common inhalers to treat their symptoms. But those with a severe form of the disease find it more difficult to control, even with higher doses of medication.

Although researchers across the world are developing better treatments for severe asthma, they often use different tools to assess how well they work (the outcomes). This makes it difficult to compare or combine results of any research on the condition.

Until now, asthma researchers have not used a consistent, standard set of results (called core outcome measures) to understand whether or not certain asthma therapies work. To remedy this, a European multi-stakeholder working group has developed the 'core outcome measures sets for paediatric and adult severe asthma' (COMSA). By having a minimum set of outcome measures for all future clinical trials, the hope is that COMSA will speed up finding which treatment works best for individuals with severe asthma.

The development of COMSA was led by IMI project 3TR, and the working group behind it included doctors, people both young and old living with severe asthma, patient representatives, pharmaceutical companies, and health policymakers. They looked at what individual outcome measures were being used in severe asthma research, for example ways of measuring changes in lung function during a clinical trial, and surveyed patients living with severe asthma and their carers across Europe.

The full COMSA set of core outcome measures includes measures of lung function, frequency and severity of severe asthma attacks, and regular steroid tablet use. It also includes standards for patient-reported outcomes, such as asthma control questionnaires and asthma quality of life questionnaires for adults and children.

The COMSA is described in a paper in the European Respiratory Journal and in a video prepared by the 3TR team.

- Read our success story

EUbOPEN opens its gates to a library of chemical compounds

When developing new medicines, scientists need to understand the underlying causes of disease.
To do that, they need to be able to study in detail the role of the different proteins involved in the disease, which requires chemical compounds capable of altering or blocking the action of individual proteins.

By end of 2023, the EUbOPEN Gateway sustainably provided scientists with access to a library of 2 300 very precisely annotated chemical compounds covering roughly 850 different proteins. The EUbOPEN team aims to create the largest and most deeply characterised open collection of chemical modulators of protein function. In addition, 88 probe compounds of very high quality co-developed between academics and pharmaceutical industries have been made available to the global scientific community.

Both initiatives will help researchers in academia and industry alike to use the tools to design drugs capable of blocking specific proteins involved in diseases, as well as identifying proteins that play a key role in disease development and deepening our understanding of disease mechanisms.

- Visit the EUbOPEN Gateway

IMI projects are adding to our understanding of diseases of unmet need

IMI projects are adding to our understanding of a range of diseases, including heart disease, liver disease, and chronic pain, to name just a few. These results also highlight an important area of alignment between IMI and IHI; one of the specific objectives of IHI is to 'improve our understanding of the factors that affect our health and the development and treatment of certain diseases'.

Examining data in new ways highlights genetic differences in psoriatic skin

Psoriasis is a skin disease that manifest in scaly skin patches. There is no cure and the treatments do not work well for all patients. IMI project BIOMAP carried out an extensive analysis of a wide range of molecular data from people with psoriasis, and uncovered some previously unknown genetic factors that are associated with the onset of the disease. They published their findings in the journal Human Genomics.

People with psoriasis experience flare-ups – for example, if you have psoriasis on your elbow, it may appear scaly, red and sore for a few weeks – but then the skin will recover, and you'll experience another flare-up a few weeks later. One thing that the data showed was that skin from a psoriatic lesion showed genetic differences to healthy skin from the same person. Even more intriguingly, the genetic pattern looked different again when you compared it to the healthy skin of someone who didn't have psoriasis at all.

Another aspect of the study was the discovery of "bridge genes" – a group of genes that form connections between genes that are known to be associated with psoriasis. These bridge genes were never described in scientific literature before. Looking to the future, some of the genes identified could be investigated as a potential drug target or biological marker for psoriasis.

- Read more in our success story

Research shows the hidden biases in cardiovascular disease data

Heart disease is a major cause of death for both women and men, but it remains under-diagnosed and undertreated in women because they often have different symptoms, and this has not been taken into account in past research. IMI project BigData@Heart published two papers on this issue. The first paper, published in the European Journal of Heart Failure, draws on data from clinical trials on heart failure and a reduced ejection fraction (where a weakened heartbeat pumps out less blood) and observational registries on heart failure.

The project identified three groups of people: people who actually took part in a randomised clinical trial (RCT); people who were eligible to take part in an RCT but did not; and people who did not qualify to be included in an RCT.

Their results showed that generalising the results of RCTs towards all patients with heart failure and reduced ejection fraction is likely unwise, since females were under-represented in clinical trials. The women who did enrol in trials also had a lower-than-expected mortality rate (5.6%) compared to women in the registries who were eligible to take part in trials (14%) and those who were not eligible (28.6%).

There could be many reasons behind this. One is that cardiovascular symptoms show up later in women, which gives time for other health issues to also play a role in their health, which in turn might cause them to be excluded from some trials. Social factors may also play a role.

- Read more in our success story

Biomarkers, not biopsies, indicate who will fall foul of liver disease

Although most people will never have heard of it, MASLD (metabolic dysfunction-associated steatotic liver disease) is common, affecting around a quarter of adults. MASLD (which was known until recently as NAFLD, or non-alcoholic fatty liver disease) is characterised by a build-up of fat in the liver, and most of those affected will have little to no symptoms at all. However, a small proportion of people with MASLD will go on to develop a more serious condition called metabolic dysfunction-associated steatohepatitis (MASH), which places them at a greater risk of developing liver cirrhosis and liver cancer.

Today, a biopsy is needed to confirm which MASLD patients have progressed to MASH and to determine the severity of the condition. IMI project LITMUS wants to revolutionise the testing process so that patients can opt for a simple blood test or scan. The project team has already identified a range of biological markers that offer important clues as to the state of a person's liver. Crucially, they have also generated data that shows that these biomarkers may be as good as biopsies, or better at predicting long-term outcomes.

The project worked closely with regulators to ensure that their approach to biomarker identification and validation was sound, and in October 2023 they submitted a qualification package for certain key biomarkers to the US Food and Drug Administration (FDA). They also shared their lessons learned on working with regulators in an article in the Journal of Hepatology.

- Read more in our success story

Better understanding the genetic link between obesity and type 2 diabetes

Clinicians have long known that there's a link between obesity and type 2 diabetes (T2D), but the nature of the link is unclear, as evidenced by the fact that not everyone with obesity will develop T2D, while many people who do develop T2D are not obese.

Writing in Nature Metabolism, IMI project SOPHIA explained how they identified 48 genetic changes called single nucleotide polymorphisms (SNPs) associated with having both obesity and T2D, and 19 SNPs associated with having obesity but being protected from T2D. They also worked out some of the mechanisms behind T2D caused by obesity. For example, a person's higher capacity to expand fat tissue around the thigh area plays an important role in genetically-determined obesity without T2D. Other such 'biomarkers' include blood pressure, the cholesterol content of high-density lipoproteins, and levels of the protein HS6ST2.

Finding and understanding these biomarkers marks an important step to precisely identify whether a person with obesity is susceptible or resistant to developing T2D, while knowing the genetic background to these biomarkers can help when designing future medications.

- Read more in our success story

Getting to grips with pain management with IMI-PainCare

Pain is the leading cause of disability worldwide among adults but despite this, treatment options are limited. Furthermore, roughly one in five people that suffer from chronic pain have been diagnosed with depression because of it, and two-thirds were less able or unable to work outside the home. The IMI-PainCare project is delivering knowledge and tools to help in the development of novel painkillers.

Chronic pelvic pain affects more than one in four women, yet it remains difficult to treat and affects patients in a range of different ways. IMI-PainCare conducted a study involving 769 women which illustrated the negative effect that chronic pelvic pain has on a patient's quality of life, impacting their mental health and sexual relationships, and demonstrating the need for novel approaches to be taken to classify patients with pelvic pain.

It is not always easy to determine how best to measure how effective existing pain management strategies are. IMI-PainCare conducted a trial to evaluate how effective patient-reported outcome measures were at assessing changes in pain in patients who had just undergone surgery. They found that using self-reported pain measures alone was not a good indicator of changes in pain, suggesting that a patient should report on a range of domains instead in order to reliably estimate the efficacy of pain management strategies.

To develop new painkillers, a specialised series of tools is needed, and the IMI-PainCare project is putting together a toolbox, including biomarkers and core outcomes sets, to help drug manufacturers develop more targeted treatments. 'Core Outcome Sets' (COS) are a minimum set of outcomes that should be measured and standardised in clinical trials for a specific health condition, and can then be used to develop better targeted drugs, and in 2023, the IMI-PainCare project was the first to identify four COS relating to pain.

Contributing to efforts to tackle infectious diseases

IMI boasts an extensive infectious disease portfolio, with projects addressing antimicrobial resistance, tuberculosis, and vaccines. Despite advances in research, infectious diseases remain a major threat to public health worldwide, meaning the results presented here are more relevant than ever.

New treatment shows promise for combating dangerous drug-resistant bacteria

Antibiotic-resistant carbapenem-resistant Enterobacteriaceae (CRE) are widely considered to be among the most dangerous drug-resistant bacteria in the world. They can cause infections in almost any body part and can be fatal. IMI project COMBACTE-CARE has been supporting the development of a combination treatment called aztreonam and avibactam (ATM-AVI). Aztreonam is an antibiotic, but it falls prey to beta-lactamases, which are released by the carbapenem-resistant Enterobacteriaceae. Avibactam targets the beta-lactamases, effectively protecting the aztreonam so that it can do its job.

In 2023, a phase 3 study of ATM-AVI called REVISIT suggested that ATM-AVI was effective in treating serious bacterial infections due to Gram-negative bacteria, including metallo-β-lactamase (MBL)-producing multidrug-resistant pathogens for which there are limited or no treatment options. It was also tolerated well by patients, with no new safety concerns arising.

Data from the REVISIT study will enable the ATM-AVI combination to be formally submitted for marketing authorisation to health regulators across the globe, and in fact the EMA started an accelerated procedure to review the marketing authorisation application of ATM-AVI in September 2023. If approved, ATM-AVI would be an important treatment option for patients with life-threatening bacterial infections that are resistant to almost all currently available antibiotics.

- Read more in our success story

Categorising people according to 'immunotype' could predict vaccine effectiveness

Not everyone responds in the same way to influenza vaccines. In fact, the variability in effectiveness of the vaccine among older adults ranges from 17-53%, leaving a significant proportion of the population unprotected even when vaccinated.

Researchers from IMI project VITAL analysed the immune profiles of more than 300 people aged 25-98, both before and after they received a flu vaccine. They identified two pre-vaccination immunotypes, one of which was associated with a weak response and one with a strong response. These results, published in the journal Aging Cell, highlight that age is not a good predictor of flu vaccine responsiveness, whereas baseline immune profiles are.

This work could help to identify individuals who would most benefit from a flu vaccine, with a view to developing new vaccination strategies for those who are not protected via current vaccines.

- Read more in our success story

Research reveals characteristics of 'neglected' lung disease

Bronchiectasis occurs when the airways in the lungs permanently widen because of damage caused by inflammation and infection. This widening in turn makes it difficult for the lungs to remove mucus.
The mucus lining the lung helps to clear particles and bacteria from the airways, and as the mucus builds up, it becomes easier for bacteria to multiply and infect the lung system. Bronchiectasis is growing in prevalence, but clinicians still do not fully understand the disease's causes, levels of severity, and treatment options.

One important output of IMI project iABC is the European Bronchiectasis Registry (EMBARC), which includes data on bronchiectasis patients from across Europe and Israel. The iABC team drew on EMBARC to analyse the characteristics of the disease in almost 17 000 people, providing the most comprehensive description of disease burden to date. Their findings are published in The Lancet Respiratory Medicine.

The results showed that the most common identified cause of the disease was a 'post-infective disease'; when patients contracted an earlier infection or disease that later caused bronchiectasis.

Bacterial infections causing the disease were most common in Southern Europe; *Pseudomonas aeruginosa* was prevalent in over 50% of cases, perhaps owing to the bacteria flourishing in warm, damp environments.

Perhaps most the most revealing result in the study is that most severe cases of the disease seem to happen in countries in central and eastern Europe. One reason this might be the case is that public healthcare in these countries is not geared towards early detection of the disease, meaning it has time to worsen before being treated.

- Read more in our success story

ERA4TB gives the green light for first in-human trial in an academic centre

One of the goals of the ERA4TB project was to create a tool to validate sites selected for first-time-in-human (FTIH) clinical trials. Up until now, all initial clinical trials for tuberculosis (TB) treatments have been carried out by specialised contract research organisations (CRO), however the costs for running a trial through a CRO can be high, and the waiting times for trials to take place are long because there are a limited number of facilities.

The criteria for carrying out FTIH clinical trials are particularly stringent, because a certain level of quality assurance is required by regulatory bodies, and the risks are high: this is the first step from preclinical or animal studies to human populations.

ERA4TB has developed a feasibility tool for validating FTIH trials and used it to validate five academic centres for clinical trials for TB; the first trial will take place in 2024. Increasing the number of sites that are suitable for phase 1 clinical trials will lower the price that phase 1 clinical trials currently cost and reduce the waiting times for trials, which in turn will accelerate the timeframe that it currently takes for medications to reach the market. The tool and validation process are described in a paper in Clinical and Translational Science.

Clinical trial for TB drug regimen launched by UNITE4TB

Tuberculosis (TB) is the world's second leading killer infectious disease after COVID-19, wiping out 1.3 million people in 2022. Unfortunately, more and more patients with TB are becoming resistant to drugs that are commonly used to treat them. Even when a person's TB responds well to treatment, patients still experience side effects and must undergo a lengthy medication regimen involving 3-4 different drugs over at least 6 months.

Better solutions are needed, and in 2023 IMI project UNITE4TB launched a brand-new clinical trial that will test 14 combinations of 9 existing drugs as well as 2 newly-developed candidate drugs.

The Phase 2B/C clinical trial takes place in Cape Town, South Africa, and tests multiple drug regimens and durations of treatment to find the best results. The research team will be searching for the right combination of drugs and the shortest possible treatment duration.

Developing completely new drugs is essential to overcome the increasing multidrug-resistant TB around the world, so the trial is examining the efficacy of two brand-new agents, GSK-656 and BTZ-043 in combination with bedaquiline and delamanid which represents a totally new combination / regimen.

While TB clinical trials usually focus on developing one drug at a time, a major advantage of the UNITE4TB trial is that it is investigating an entirely new drug regimen. According to the project, this could revolutionise the way TB drug development is done.

- Read more in our success story

TRIC-TB receives orphan drug designation for novel combination treatment for TB

The drug ethionamide (often shortened to Eto) is widely used to treat tuberculosis (TB). However, it can cause severe gastric-related side effects. IMI TB project TRIC-TB has been working to advance the development of novel compounds (boosters) that increase the activity of Eto and overcome resistance. If successful, this would allow clinicians to reduce the dose of Eto (and associated side effects) typically given to patients.

In 2023, the US Food and Drug Administration (FDA) granted orphan-drug designation (ODD) to one of these boosters, alpibectir (BVL-GSK098), and ethionamide in a fixed-dose combination for the treatment of TB. The ODD reflects the urgent need for more research into ways to overcome resistance to TB medicines, and the potential for the alpibectir/ethionamide combination to improve treatment options for patients who have TB.

A phase 1 clinical trial carried out under TRIC-TB showed alpibectir to be safe and well tolerated. Its further development in a Phase 2a clinical trial currently tests the combination in TB patients and is being supported by another EU partnership, EDCTP2, demonstrating the synergies between the two partnerships.

Advancing paediatric research

Developing new treatments for children is particularly challenging – they process, metabolise and excrete medications completely differently to adults. Moreover, the small numbers of children affected by some diseases mean that it is hard to find enough patients to carry out clinical studies and trials. Meanwhile their developing immune systems mean they can be more vulnerable to certain infectious diseases. A number of IMI projects are delivering knowledge, tools and resources that will ultimately help to advance the development of safe, efficient medicines for children of all ages.

RESCEU research sets the stage for the implementation of immunisation strategies for RSV

Respiratory syncytial virus (RSV) is a common respiratory virus that causes cold-like symptoms. Although mild in most older children and adults, infants and older adults can develop severe RSV which can lead to hospitalisation or, in the worst cases, death. Every year, RSV is responsible for more than 100 000 deaths in young children and results in more than 3 million being hospitalised.

Last year, the world's first immunisation products against RSV were approved in the US and Europe. IMI's RESCEU project conducted studies into the impact of RSV, developing tools to better predict RSV outbreaks and making recommendations for future immunisation regimes.

In 2023, the results from a birth cohort study carried out by RESCEU were published in The Lancet Respiratory Medicine. They indicate that vaccinating pregnant women or healthy babies during their first winter season could reduce the healthcare burden caused by RSV.

In an article published by the journal Vaccine, RESCEU studied the cost-effectiveness of employing monoclonal antibodies (mAb) and maternal immunisation (MI) interventions against RSV in six European countries, while another study estimated RSV-associated hospitalisations in children under 5 years in the European Union over the period 2006 to 2018. The results of both studies are now being used to optimise public health responses to RSV and support planning for future RSV immunisation programmes.

Game-changing trial for children with tumours being established thanks to EU-PEARL

IMI project EU-PEARL delivered a range of resources including toolkits and plans to help in the operational planning and development of platform trials. In a platform trial, multiple organisations can test candidate drugs simultaneously against a shared placebo group, and it is relatively easy to add new treatment groups and drop candidate drugs that prove ineffective. The resources developed by EU-PEARL are freely available online.

To guide its work, the project focused on four disease areas: major depressive disorder, tuberculosis, the liver disease non-alcoholic steatohepatitis (NASH), and the rare disease neurofibromatosis. Project partner the Children's Tumor Foundation (CTF) has announced its plans to use the methodology and structure established by EU-PEARL to set up a platform trial for neurofibromatosis 1 (NF-1) and schwannomatosis.

As of the end of 2023, CTF and the Global Coalition for Adaptive Research were working together to select sites and speaking to pharmaceutical companies who could want to test drugs via the trial. According to the CTF, without the funding and the way it brought all stakeholders together, 'the design of this platform trial wouldn't have happened'.

- Read more in our success story

Expert network works towards better drug development for children

Setting up a clinical trial for children comes with a range of challenges. IMI project conect4children (c4c) sought to tackle many of these issues by setting up a Europe-wide network to make clinical trials in children easier to conduct whilst also connecting clinicians, academia, methodology experts and parents to ensure high-quality clinical trials for children's drugs.

One key project output is a pilot expert advice process, through which drug developers can easily access a wide array of important information directly from experts when designing clinical trials. The idea is that drug developers can come to c4c asking for advice in relation to the treatment of a particular childhood disease that they are targeting. An advice group is quickly formed which the drug development company can then consult. The "experts" included not only clinicians, researchers and methodology experts, but also parents and patients themselves. The network is described in a paper in the journal Clinical and Translational Science.

For example, if the experts can propose a trial design that might be innovative, maybe reducing the sample size or reducing the need for a large trial, this could make paediatric drug development more feasible. And if an advice request was around a study design, the patient or parent perspective might say well this is unacceptable, I can't take my child out of school once a week to come for a clinical trial visit. Or they might say there's too many blood tests here. Even on outcome measures, a clinician might find a specific blood value important whereas a patient might say well, I have a terrible headache every day so for me it's more important that my headaches are gone than that my blood value changes.

The c4c network also developed a standardised contractual system for the c4c industry partners and the experts, which greatly reduced the administrative burden for drug development companies.

- Read more in our success story

AIMS-2-TRIALS investigates if sleep disturbance predicts autistic traits

The AIMS-2-TRIALS project tracked babies that were born into families with a history of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) to see whether disturbed sleep in infancy was a predictor of ASD or ADHD onset later. Sleep was assessed according to day/night sleep duration, number of naps in the day, frequency of night awakenings and sleep onset problems, and the infants were assessed at 5-, 10- and 14 months of age.

They found that at 14 months of age, babies with a first-degree relative with ASD, but not ADHD, showed lower night sleep scores than those with no family history of ASD. These lower night sleep scores were also associated with a later ASD diagnosis. The results, published in The Journal of Child Psychology and Psychiatry, indicate that interventions targeting infant sleep might be helpful for families with a history of ASD.

Dealing with data

The discussions on the proposed European Health Data Space (EHDS) mean that health data (and the question of who can access and use it) is rarely out of the headlines. Both the IMI1 and IMI2 programmes launched an extensive portfolio of projects designed to address the multiple challenges of gathering and using diverse types of health data for research, including ethical and legal issues as well as technical problems such as interoperability.

EPND project opens up neurodegenerative disease research

There have been decades of research to find biomarkers relating to neurodegenerative diseases such as Parkinson's or Alzheimer's disease, but the samples and data from this research are spread across laboratories in multiple countries. Each of these may also have different rules and protocols for collecting, storing and sharing samples and data, which further complicates cooperation between researchers, and across borders.

To make things easier the IMI European Platform for Neurodegenerative Diseases (EPND) project aims to bring these disparate sources together in a central hub. In 2023, the project launched the first component of its platform: the cohort catalogue, which covers neurodegeneration research from 12 disease areas. This version already contains over 60 cohort studies, and users can filter them by disease area and the kinds of biological samples, imaging and other data available.

The catalogue also lets researchers filter these cohort studies by certain criteria to suit their own research. Researchers could for instance search for studies on Lewy-body dementia that are collecting serum samples, MRI (magnetic resonance imaging) scans, or a combination of other factors.

- Read more in our success story

An 'app' for biomarkers offers speedier biomedical research

Recent decades have seen a boom in the discovery of biomarkers that are widely used in research and clinical trials. Information on their use in clinical studies can be found in ClinicalTrials.gov, a US-based registry of clinical trials, but the data is 'free text', meaning there is no classification or organisation of the information – only sentences and paragraphs. This means it is difficult for other researchers to further analyse biomarkers for use in other clinical trials.

In a paper published in the Computational and Structural Biotechnology Journal, scientists from IMI project eTRANSAFE describe how they developed a 'natural language processing' machine-learning algorithm to identify, extract and classify the information on biomarkers from ClinicalTrials.gov.

In total, the researchers found over 3 000 biomarkers being used in relation to around 2 600 diseases. The way the biomarkers are classified allows researchers to easily spot patterns in how biomarkers are being used in different therapeutic areas, the type of biomarker (e.g. certain genes being expressed, cell markers, or proteins in the body) and how specific they are to certain diseases.

This information has now been packaged into the Clinical Biomarker App, which the project describes as a 'proof-of-concept tool' to display the data generated by their approach.

- Read more in our success story

IMI projects help bring urology big data hub to life

The clinical guidelines physicians use to treat diseases are often based on randomised clinical trials. Although this data shows the general efficacy of a treatment, it often cannot provide information on the long-term effects of treatments, how they work alongside other drugs, or how they affect certain subgroups in society such as the elderly or those with obesity.

To tackle these gaps in knowledge, a group of experts in urology, health services research, implementation science, artificial intelligence (AI), epidemiology, and data science have launched the UroEvidenceHub platform. The platform aims to better understand real-world urology guidance and practice across all subgroups within and across European countries. This can help optimise the treatment of patients with urological conditions such as prostate cancer, bladder disorders and kidney diseases.

The platform will use urology data from clinical trials alongside information from real world data analytics, including patient feedback. The platform will also see how to best use AI to help develop new guidelines and treatment recommendations, especially where clinical trials do not exist.

The UroEvidenceHub platform was developed by the European Association of Urology and uses similar data techniques to those deployed by the IMI projects PIONEER and OPTIMA. PIONEER aims to format, standardise and integrate data from well-known prostate cancer studies, electronic health records and registries so they could be accessed on a single platform, while OPTIMA project is working to create Europe's first platform for generating oncology data and evidence. Meanwhile IMI project EHDEN is also providing expertise to the platform via its EHDEN Academy, which trains SMEs with the skills and tools needed to map and analyse reports from clinicians and patients about how effective medical treatments are outside the lab, in 'real world' use.

- Read more in our success story

Making data FAIR to all

Ideally, research data would follow four principles: being easy to discover (Findable); easy to obtain (Accessible); possible to combine with other data or systems (Interoperable); and Reusable. Together these are known as the FAIR principles. In reality, much data doesn't match up to these principles. IMI project FAIRplus set out to change that by creating resources and guidance to help organisations and projects to change their data management culture via a 'FAIR transformation'.

A core project result is the FAIRification Framework, a planning process that shows how to use available resources to adopt FAIR principles and expand organisational FAIR data management capabilities. This framework was developed alongside 17 other data-producing IMI projects, which allowed the project to apply the framework to datasets from clinical studies, lab experiments on molecular interactions, and real-world observational data.

The framework means that these and future organisations/projects have a template that is easy to apply, adapt and reproduce within their workflows. However, even these processes may need more specific guidelines to help organisations achieve a FAIR transformation. The project's FAIR Cookbook provides organisations with specific 'recipes' to keep the data FAIR. For example, users of the cookbook can get specific guidelines on search engine optimisation, creating a metadata profile, or data licenses. Although the FAIRplus project has finished, the cookbook is being sustained by project partner ELIXIR as a service currently provided by four ELIXIR Nodes (UK, Luxembourg, Spain, Switzerland).

- Read more in our success story

ConcePTION resource aims to improve collection of data on medicines safety in pregnancy

The ConcePTION project is working to make it easier for people who are pregnant or breastfeeding to find reliable, evidence-based information on which medicines are safe for them and their baby. Today, data on the safety of using medicines during pregnancy is gathered in different ways by different organisations. This makes it much harder for researchers to combine data from different studies for large-scale analyses which could yield useful new results on this important subject.

To address this issue, ConcePTION developed a reference framework of core data elements (CDEs) designed to standardise the collection of data on the benefits and risks of medications used in pregnancy. The framework comprises 98 individual data elements, categorised into 14 tables covering issues ranging from maternal medical history and pregnancy medication exposure to details of the delivery and the longer-term health of the child.

The process through which the CDEs were developed is described in an article in Drug Safety, and the CDEs themselves are publicly accessible on the ENTIS (European Network of Teratology Information Services) website.

IMI projects result in long-lasting collaborations

From the beginning, IMI and now IHI have sought to foster long-term cooperation between industry, academia, patient advocates, and other stakeholders in health research. As the results below demonstrate, the networks formed in our projects often continue to collaborate and deliver results, sometimes several years after the project has ended. This demonstrates the lasting impact of PPPs like IMI and IHI on the health research and innovation ecosystem.

New spin-off set to boost research into childhood cancers

Across the world childhood cancer remains rare, although around 15 000 children and adolescents are diagnosed with cancer in Europe each year. Sadly, around one in four of these patients cannot be cured with existing treatments and do not survive. Roughly two-thirds of those who do survive cancer in childhood will experience long-term side effects because of their treatment.

IMI project ITCC-P4 has developed a platform of over 400 patient-derived models, based on cells and tissues obtained from patients covering more than 20 common childhood cancers such as acute lymphoblastic leukaemia, neuroblastoma, high grade glioma, and osteosarcoma. These models are designed to facilitate research into these diseases and develop much-needed new treatments.

In 2023, the project set up a spin-off company, ITCC-P4 gGmbH, to make the models developed by the project available to the wider research community.

- Read more in the ITCC-P4 press release

Ensuring a future for a paediatric clinical trial network

Conect4children launched in 2018 to set up high-quality paediatric clinical trials for all disease areas and all phases of the clinical drug development process. It has created a pan-European clinical trial network to provide expert advice on all aspects of paediatric clinical trial design. The network also provides support for clinical trial conduct, education and training for researchers on paediatric drug development, and a platform for paediatric multistakeholder meetings.

Now, the project has created the conect4children Stichting, a Dutch non-profit organisation, to sustain the work started by the project.

- Read more in the c4c press release

PREFER Expert Network set to capitalise on pioneering project's output

IMI project PREFER delivered a wealth of resources on when and how patient preferences on benefits and risks should be incorporated into decisions on medicinal products. In 2023, the project set up the PREFER Expert Network to capitalise on the experience and expertise gained through the project and support its sustainability.

The voluntary network includes pharmaceutical companies, academic institutions, consultants, and patient representatives and its goals are to:

- exchange understanding, experience, and implementation practices of patient preference studies and their outcomes;
- discuss policy and methodological questions related to patient preference research;
- develop best practices of patient preference studies and identify knowledge gaps which may lead to new research topics.

Molecules in diabetic patients could help personalise treatments

Although IMI diabetes project RHAPSODY ended in 2021, the academic labs and industry partners of the project continue to collaborate and deliver results. Writing in Nature Communications, the team explain how they carried out extensive analyses of thousands of blood samples to identify new links to molecules that could act as biomarkers for type 2 diabetes progression.

One protein, MIC-1/GDF15, was associated with the highest risk of diabetes progression, confirming previous research on this protein. Another protein called NogoR had the next-largest correlation with disease progression, leading the researchers to try to better understand its method of action. They first injected NogoR into mice fed a high fat/high sugar diet. This improved their glucose tolerance. In contrast, in mice with type 2 diabetes, injecting NogoR worsened their insulin sensitivity; in other words, damaging their ability to regulate blood sugar levels.

This result, says the paper, shows that the effects of NogoR glucose metabolism in animals are complex, and depend on the state of diabetes. In the future, medication might be able to inhibit this protein, thereby preventing it from killing the pancreatic cells responsible for secreting insulin.

A final result from their analysis showed that that the biomarkers identified for diabetes progression are the same as those related to diabetes risk, which suggests that the same biological process happens in both cases.

- Read more in our success story

Creating sub-types of childhood asthma could lead to more targeted treatments

IMI severe asthma project U-BIOPRED ended in 2015, but the partners are still working together, thanks in large part to the strong involvement of patients in the project – this provided the researchers with inspiration and motivation for further collaborations. In 2023 the team published a paper in the American Journal of Respiratory and Critical Care Medicine exploring how the community of microbes living in the sputum (mucus and phlegm) contributes to childhood asthma or wheezing.

They took sputum samples from 131 preschool-age children diagnosed with wheezing and 140 school-age children with asthma and tracked how their condition changed over the following 12-18 months.

They then grouped the children with asthma or wheezing based on their underlying microbiome composition. They found four groups of children with distinct throat microbiome profiles, and these groups were linked to allergies, and how their lungs functioned. In addition, these groups could serve as a predictor for the risk of 'future' lung attacks.

According to the researchers, this could help clinicians to define subgroups among children with asthma or wheezing so they could monitor them more closely or provide personalised treatment options. Furthermore, sampling younger people before they show symptoms could mean that patients get treated even earlier and in a timely manner.

- Read more in our success story

Patients with specific gene could benefit most from certain diabetes drugs

IMI diabetes project DIRECT resulted in biobanks comprising tens of thousands of samples for later use and a strong network of researchers keen to keep working together after the end of the project in 2019. This combination resulted in a 2023 paper in The Lancet Diabetes & Endocrinology that examined why the efficacy of diabetes drugs called GLP-1 agonists varies so much from one patient to another.

GLP-1 agonists work by interacting with the GLP-1 protein in the pancreatic beta cells and so encouraging them to produce more insulin. By studying genetic and clinical data from 4 500 people with type 2 diabetes, the researchers pinpointed two genetic variations acting together in 4 % of their study population who had a 30 % greater reduction in their glucose levels over three months when treated with GLP-1 agonists. Finding this correlation means that these drugs can be better tailored to those with the two genetic variations, where it is most effective.

- Read more in our success story

ABIRISK identifies potential link between development of antibodies and poor response to RA drugs

Biopharmaceuticals (BPs) are drugs based on biological molecules like proteins and monoclonal antibodies. They have revolutionised our ability to treat many serious conditions including some cancers as well as autoimmune diseases like rheumatoid arthritis (RA) and multiple sclerosis (MS). In some patients, BPs can cause the immune system to produce anti-drug antibodies (ADAs), which can change the concentration of the drug in the body or even neutralise it. IMI project ABIRISK, which ended in 2018, shed new light on the causes and consequences of ADAs.

Now, a new paper from the project team, published in JAMA Network Open, sheds new light on the influence of ADAs on how well certain BPs work for patients with RA. The researchers studied 230 people with RA who were starting treatment with a range of BPs and tracked which patients developed ADAs and how well patients responded to their treatment. Their analysis revealed that patients who had developed ADAs were less likely to respond well to their treatment. This suggests that monitoring ADAs could help to improve the management of RA, particularly those who do not respond to biological treatments.

Cross-sector collaborations deliver results

Cross-sector collaboration is embedded in IHI at all levels. However, many IMI projects already include a strong cross-sector component, and their results speak to the added value of this approach.

Revealing an earlier and more effective way to diagnose Alzheimer's disease

One of the clearest ways to help confirm a diagnosis of Alzheimer's disease is to check the brain for a build-up of abnormal proteins called amyloid-β. These amyloid 'plaques' can be detected even in the early stages of the disease, before symptoms start, via a brain scan using positron emission tomography (PET).

IMI project AMYPAD set out to see if PET brain scans could help to diagnose Alzheimer's disease at different stages. In their study, around 800 memory clinic patients underwent a standard baseline consultation and tests to narrow down the possible diseases they might have. They were then assigned randomly into one of three groups. The first group had a PET scan early, i.e. within one month of the baseline visit. The second had a scan 6 to 10 months after the baseline visit. For the third 'free choice' group, the scan was performed at the discretion of the physician at any time in the observation period.

The study, published in JAMA Neurology, shows that access to amyloid PET scans resulted in aetiological diagnoses with very high certainty in 40% of patients within the first three months of the patient's first visit compared to those where the scan was performed 6-10 months later (11%). Additionally knowing the PET scan result also led to changes in diagnosis; for example, if the scan was negative, a diagnosis of Alzheimer's disease could be ruled out.

The scans were also the preferred choice of patients. Another way of detecting amyloid build-up is to extract cerebrospinal fluid from the spine for analysis. In the 'free choice' group, 11% of participants explicitly wanted to undergo an amyloid PET, while another 5% chose the scan because they refused the lumbar puncture procedure.

- Read more in our success story

Study shows how smartphone apps can help monitor effects of depression

For people with major depressive disorder, low moods are just one aspect of the disease. People can also feel their thinking skills such as concentration, attention and memory are also affected. Despite this, few psychiatrists regularly assess thinking skills to help treat or monitor their patients. Asking patients to self-report symptoms can be unreliable, due to inaccurate recall. Patients may be monitored in clinics or laboratories, but these are not real-life settings and so can also skew results.

Using wearable technologies and smartphone apps may overcome these problems, as a study by IMI project RADAR-CNS shows. In a study published in Psychological Medicine, project researchers used an app called THINC-it® to monitor over 500 participants with depression. The study aimed to test if warning signs of a depression episode could be found, which in future could help prevent them having major effects on a person's life.

Every six weeks, the app asked participants to rate their difficulties with organisation, concentration, and forgetfulness on a scale from 0 (never) to 4 (often). The app also measured participants' cognitive performance through in-app tasks. Both measurements were taken for up to two years and then used to calculate how long difficulties in performance lasted.

The researchers found that those who reported persistent thinking difficulties (more than 75% of the time surveyed) were also reporting higher levels of depression compared to those who had less persistent thinking difficulties. Interestingly, some thinking difficulties correlated with certain effects of depressive episodes. For example, those who had difficulties with their processing speed were found to have worse symptoms of depression. The study confirms that using smartphones to self-report and monitor thinking difficulties could help monitor and manage depression.

- Read more in our success story

Wearable technologies can reliably measure fatigue and disturbed sleep in chronic disease

Patients with chronic diseases like Parkinson's disease, inflammatory bowel disease and rheumatoid arthritis often rate fatigue as one of the most disabling symptoms, affecting their daily activities and quality of life. However, monitoring fatigue is rather difficult.

Wearing small devices to monitor key physiological signals throughout the day could provide more accurate and reliable results. To test this, researchers from IMI project IDEA-FAST carried out a study involving both people with chronic diseases and healthy individuals.

The 136 participants wore a small device called VitalPatch, a 12-cm long biosensor that adheres to the skin and is worn on the left side of the chest. It recorded their heart rate, the millisecond intervals between their heartbeats, and their breathing rate, among other things.

Participants were asked to carry on with their regular home life while wearing the biosensor for most of the day, including while sleeping at night. This observation period typically lasted for four weeks; five days of wearing the biosensor, followed by two days of rest. Participants were also asked their perceptions of fatigue and sleep quality four times per day over a survey app.

Writing in Frontiers in Physiology, the researchers note that the biosensor was able to record data that correlated well with what the patients reported in the app. The biosensor also revealed information that participants were unable to record. For example, after six minutes of light exercise (for example going for a walk), biosensor data showed a significant difference in heartrate recovery between healthy people and those with a chronic disease. This can be an important predictor of certain factors that can lead to fatal health events, for example a heart attack.

Meanwhile, the project approached the European Medicines Agency to get the regulatory perspective on novel digital measures of fatigue. The team subsequently shared their experiences and advice for other projects in a paper in Digital Biomarkers.

- Read more in our success story

1.3 Calls for proposals, grant information and other funded actions

Launch and management of calls in 2023

Throughout 2023, the IHI Programme Office continued to develop and refine its call development, evaluation and grant award framework, along with developing and improving relevant templates and guidance documents. These efforts aimed to align with both the regulations of Horizon Europe and the unique requirements of IHI, notably the 45% eligibility criterion. In parallel, the office collaborated with IHI members to formulate the topics, engaging in consultations with the States' Representatives Group (SRG) and the Science and Innovation Panel (SIP).

Thanks to this hard work, IHI was able to launch on 27 July **IHI call 4** (a two-stage call with six topics) and **IHI call 5** (a single-stage call with four topics).

At the end of the year, IHI call 4 was in stage 2, and IHI call 5 was still open for full proposals; the evaluations of both calls will be completed in 2024.

During 2023, the IHI Programme Office also continued the evaluation and GAP (Grant Agreement Preparation) for calls launched in 2022:

- The **IHI call 1** GAP was finalised in May 2023, allowing the first IHI projects to get started.
- The evaluation for **IHI call 2 stage 2** was completed in 2023, the GAP phase started in April, and the Grant Agreements were signed in October.
- The evaluation for **IHI call 3**, was also completed in May, and the Grant Agreement signature phase was completed in November 2023.

The table below provides the key deadlines of the development of the calls that were active in 2023, including the consultations with the SRG, SIP and the European Commission (EC).

Call	SIP/EC/SRG consultation	GB approval of topic text	Call launch	GB approval of evaluation results (stage 1 / single stage)	GB approval of evaluation results (stage 2)	GAP launch	GA signed (deadline)
Call 1 single stage	13/04/2022 to 04/05/2022	17/06/2022	28/06/2022	30/11/2022	NA	01/12/2022	22/05/2023
Call 2 two stage	13/04/2022 to 04/05/2022	17/06/2022	28/06/2022	30/11/2022	26/04/2023	27/04/2023	31/10/2023
Call 3 single stage	03/10/2022 to 24/10/2022	08/12/2022	13/12/2022	15/05/2023	N/A	22/05/2023	15/11/2023
Call 4 two stage	06/06/2023 to 26/06/2023	24/07/2023	27/07/2023	22/01/2024	open	open	open
Call 5 single stage	06/06/2023 to 26/06/2023	24/07/2023	27/07/2023	open	N/A	open	open

Abbreviations:
GA – Grant Agreement.
GAP – Grant Agreement Preparation.
GB – Governing Board.
EC – European Commission.
SRG – States' Representatives Group.
SIP – Science and Innovation Panel

1.4 Evaluation procedures and outcomes

The sections below present, call by call, the progress made on each call in 2023, as well as breakdowns of applicants in eligible proposals and participants in selected proposals where relevant.

In the tables and charts showing the breakdowns by country and by organisation type of applicants / participants, note that the organisation types given are what the applicants declared (self-declarations). For space reasons, the following organisation types are abbreviated in the tables and charts:

- Healthcare = Healthcare professional organisation / healthcare provider
- Large company = Large company (for-profit legal entity)
- Research / education = Research / higher or secondary education organisations (private or public)
- SME = Small & medium enterprise
- Patient / citizen = Patient / citizen organisation
- Mid-cap = Mid-cap (for-profit legal entity)
- HTA = Health technology assessment body
- Regulator = Regulator or regulatory body
- NGO = Non-governmental organisation
- Payer = healthcare payer

IHI call 2 (two stage)

Progress in 2023: from stage 2 submission to signature of the GAs.

IHI call 2 at a glance	
Topics	2 (details here)
Launch date	28/06/2022
Submission deadline (stage 1)	20/09/2022
Proposals received	15
Admissible proposals	15
Eligible proposals (evaluated)	15
Applicants in eligible proposals (stage 1)	274 (251 unique participants)
Proposals above threshold	11
Proposals invited to stage 2	2
Submission deadline (stage 2)	28/02/2023
Applicants in eligible proposals (stage 2)	78
GAs signed in 2023	2

IHI informed the applicants of the outcome of the evaluation **72 days** after the submission deadline, well ahead of the 153-day deadline for sending evaluation result letters.

Ethics evaluation process[5]: The IHI call 2 stage 2 ethics screening was conducted for the two above-threshold proposals. The two proposals were ethically cleared. No proposals were sent to ethics assessment.

Complaints (redress): There were no admissibility/eligibility or evaluation review requests for proposals not selected for funding under IHI call 2.

IHI call 2: participants in selected proposals

45% of the participants are IHI industry partners, and 1% are IHI contributing partners. The table below gives a detailed breakdown of the participants by both country and organisation type.

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	HTA	NGOs	Other	**Total by country**
Austria			1							**1**
Belgium		3	1		1					**5**
Czechia		1								**1**
Denmark	1			1						**2**
France	1	4	1	1				1	1	**9**
Germany		4	5	1						**10**
Ireland			2		1					**3**
Italy	1	1	3	3			1			**9**
Netherlands	2	6	3	3					1	**15**
Norway							1			**1**
Spain	1		1							**2**
Sweden		1								**1**
Switzerland		6				1				**7**
United Kingdom	1	1	2							**4**
United States		8								**8**
Total by org. type	**7**	**35**	**19**	**9**	**2**	**1**	**2**	**1**	**2**	

[5] In addition to the scientific evaluations, the IHI Programme Office organises ethics evaluations for single stage proposals recommended for funding and single stage proposals placed on the main and reserve lists. As per the Horizon Europe Programme Guide, which outlines how the ethics appraisal framework works, the Programme Office independently operates the ethics review procedure and relies on external independent ethics experts.

IHI call 3 (single stage)

Progress in 2023: from single-stage submission to signature of the GAs.

IHI call 3 at a glance	
Topics	5 (details here)
Launch date	13/12/2022
Submission deadline (single stage)	15/03/2023
Proposals received	19
Admissible proposals	19
Eligible proposals (evaluated)	14
Applicants in eligible proposals	348
Proposals above threshold	9
Proposals selected for funding	9
GAs signed in 2023	9

IHI informed the applicants of the outcome of the evaluation **68 days** after the submission deadline, well ahead of the 153-day deadline for sending evaluation result letters.

Ethics evaluation process: The ethics screening was conducted for the 9 above-threshold proposals. Six were cleared while three were conditionally cleared. Those with a conditional clearance have 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. No proposals were sent to ethics assessment.

Complaints (redress): A redress committee was convened to analyse two redress procedures introduced by two different proposals. For one case, no grounds were found to support the complaint. For the other case, the redress committee considered that the complaint was founded, and so a re-evaluation of the specific criterion affected was carried out. The outcome of this re-evaluation had no impact on the final results of the evaluation exercise.

IHI call 3: applicants in eligible proposals

20% of the applicants are IHI industry partners, and 8% are IHI contributing partners. The table below gives a detailed breakdown of the applicants by both country and organisation type.

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	Regulator	NGOs	Payer	Public authority	Charity / foundation	Other	Not declared	**Total by country**
Austria			7										1	**8**
Belgium	2	2	6	3	2			1				1	5	**22**
Canada													1	**1**
Croatia			2											**2**
Czechia			3											**3**
Denmark	2	6	2	3									1	**14**

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	Regulator	NGOs	Payer	Public authority	Charity / foundation	Other	Not declared	**Total by country**
Finland		1	4	1										**6**
France		6	10	3	2	1						1	2	**25**
Germany	3	14	16	6	2	1							4	**46**
Greece			2					1						**3**
Hungary	1			1									1	**3**
India		1												**1**
Ireland		1												**1**
Israel		1	2											**3**
Italy	3	2	7	4	2						1		3	**22**
Lithuania				1										**1**
Luxembourg								1			1			**2**
Netherlands		4	18	5	4			1			1		3	**36**
Norway	1		1											**2**
Poland			2	2										**4**
Portugal	1	1	3					1	1				1	**8**
Romania			1											**1**
Slovakia			1											**1**
Slovenia	3	1	1											**5**
Spain	8	2	14	7					2	1			7	**41**
Sweden	4	1	6	3	1			1						**16**
Switzerland		5	4	1	1		1				1	1	1	**15**
Ukraine				2										**2**
United Kingdom	1	5	13	4	2					1	1		2	**29**
United States	2	9	2	6	1						3	1	1	**25**
Total by org. type	**31**	**62**	**127**	**52**	**17**	**2**	**1**	**6**	**3**	**2**	**8**	**4**	**33**	

IHI call 3: participants in selected proposals

17% of the participants are IHI industry partners, and 12% are IHI contributing partners. The table below gives a detailed breakdown of the participants by both country and organisation type.

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	Regulator	NGO	Public authority	Charity / foundation	Other	Not declared	**Total by country**
Austria			4										**4**
Belgium	1		5	3	1			1					**11**
Croatia			2										**2**
Czechia			2										**2**
Denmark	2	5	2	3									**12**
Finland			3	1									**4**
France		2	5	3		1							**11**
Germany	2	8	9	2									**21**
Greece			2					1					**3**
Hungary				1								1	**2**
India		1											**1**
Israel		1	1										**2**
Italy	2	2	6	3	1					1			**15**
Luxembourg								1		1			**2**
Netherlands		3	14	5	3			1		1			**27**
Norway	1												**1**
Poland			2										**2**
Portugal		1						1					**2**
Romania			1										**1**
Slovakia			1										**1**
Slovenia	3	1	1										**5**
Spain	4	1	11	5									**21**
Sweden	1		4		1			1					**7**
Switzerland		1	2	1			1			1	1		**7**
United Kingdom		2	10	4	2				1	1			**20**
United States		2	1	5	1					3	1		**13**
Total by org. type	**16**	**30**	**88**	**36**	**9**	**1**	**1**	**6**	**1**	**8**	**2**	**1**	

IHI call 4 (two-stage)

Progress in 2023: From call launch to end of stage 1.

IHI call 4 at a glance	
Topics	6 (details below and here)
Launch date	27/07/2023
Submission deadline (stage 1)	08/11/2023
Proposals received	17
Admissible proposals	17
Eligible proposals (evaluated)	15
Applicants in eligible proposals (stage 1)	266
Proposals above threshold	6
Proposals invited to stage 2	6
Submission deadline (stage 2)	23/04/2024
Applicants in eligible proposals (stage 2)	n/a
GAs signed in 2023	n/a

The maximum financial contribution from IHI JU for this call was EUR 83 350 000 million, and the industry / contributing partner contribution was EUR 85 076 000.

The table below highlights how the topics of IHI call 4 are aligned with the specific objectives (SOs) of IHI as described in the legislation creating IHI and the Strategic Research and Innovation Agenda (SRIA).

- **Specific Objective 1 (SO1):** addresses the challenge of unravelling causal factors of disease that are still poorly understood, such as the interplay between genetic and environmental factors, for example the impactof climate change on health.
- **Specific Objective 2 (SO2):** addresses one or more of the barriers for the development of new types of products or services in the health domain that integrate diverse components (such as diagnostics, medicinal products, medical devices, wearables, treatment monitoring, digital solutions), also including the challenge ofenabling the green transition across all aspects of healthcare.
- **Specific Objective 3 (SO3):** addresses the patient-centricity of innovations and the challenge of effectively engaging with all relevant health care actors (patients and civil society, health care professionals, health care providers, regulators, health technology assessment bodies and payers) for the design and development of new and/or integrated health solutions.
- **Specific Objective 4 (SO4):** addresses the issue that currently, data in many countries are hard to gather anddemonstrate limited interoperability.
- **Specific Objective 5 (SO5):** enabling the development of new and improved methodologies and models for a comprehensive assessment of the added value of innovative and integrated healthcare solutions.

Topic	SO1	SO2	SO3	SO4	SO5
Expanding translational knowledge in minipigs: a path to reduce and replace non-human primates in non-clinical safety assessment		x			
Patient-centric blood sample collection to enable decentralised clinical trials and improve access to healthcare	x	x	x		
Inclusive clinical studies for equitable access to clinical research in Europe			x		x
Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases			x		x
Safe & Sustainable by Design (SSbD) packaging and single use device solutions for healthcare products		x			
Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact assessment		x			

The whole stage 1 evaluation process was successful and IHI was on time to inform applicants of the outcome of the evaluation by the end of January 2024.

IHI call 4: applicants in eligible short proposals

1% of the applicants are IHI industry partners, and 15% are IHI contributing partners. Industries appear to be under-represented because the pre-identified industry consortium members will join only in stage 2.
The table below gives a detailed breakdown of the applicants by both country and organisation type.

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	HTA	Regulator	NGOs	Public authority	Charity / foundation	Notified Body	Other	Not declared	**Total by country**
Austria			8	1		1									**10**
Belgium	1		11	5	2	1			1	1		1			**23**
Canada									1						**1**
Czechia			2												**2**
Denmark			3	4									1		**8**
Finland				1											**1**
France	1		6	5					1						**13**
Germany	2		10	2						1	1				**16**
Greece	1		5	3	2				1					1	**14**
Hungary				2		1									**3**
Ireland			1				1				1				**3**
Israel			1										1		**2**
Italy	3		10	10						1			1		**25**
Lithuania				2											**2**
Luxembourg									1						**1**

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	HTA	Regulator	NGOs	Public authority	Charity / foundation	Notified Body	Other	Not declared	**Total by country**
Netherlands	3		11	3	1					2			2	1	**23**
Poland	2		1	3											**6**
Portugal			2	1											**3**
Romania			2	2	2				2					1	**9**
Spain	6	1	16	4	2	1					1		1	1	**33**
Sweden	2		4	4											**10**
Switzerland	1		2	1				1	1						**6**
Ukraine			1	1											**2**
United Kingdom			7	5	2				1						**15**
United States				5											**5**
Kazakhstan			1												**1**
Estonia			2												**2**
Colombia			1												**1**
Moldova (Republic of)				1											**1**
Cyprus			1												**1**
Bulgaria				2					1						**3**
Bosnia and Herzegovina										1					**1**
Albania			1												**1**
Türkiye			1												**1**
Tunisia			1												**1**
Total by org. type	**22**	**1**	**111**	**67**	**11**	**4**	**1**	**1**	**10**	**6**	**3**	**1**	**6**	**4**	

IHI call 4: participants in selected proposals

1% of the applicants are IHI industry partners, and 16% are IHI contributing partners. Industries appear to be under-represented because the pre-identified industry consortium members will join only in stage 2.
The table below gives a detailed breakdown of the applicants by both country and organisation type.

	Healthcare	Large company	Research / education	SME	Patient / citizen	Mid-cap	HTA	Regulator	NGO	Public authority	Charity / foundation	Notified Body	Other	Not declared	**Total**
Austria			6	1		1									**8**
Belgium	1		8	3	2				1	1		1			**17**
Canada									1						**1**
Czechia			2												**2**
Denmark			2	3									1		**6**
France	1		4	5					1						**11**
Germany	2		7							1	1				**11**
Greece			2	3	1				1						**7**
Hungary				1		1									**2**
Ireland							1				1				**2**
Italy	1		4	5						1			1		**12**
Lithuania				2											**2**
Luxembourg									1						**1**
Netherlands	1		5	2						2			2	1	**13**
Poland	1		1												**2**
Portugal				1											**1**
Romania														1	**1**
Spain	6	1	12	3	2	1					1		1	1	**28**
Sweden	1		4	3											**8**
Switzerland			1					1	1						**3**
United Kingdom			5	4	2				1						**12**
United States				3											**3**
Cyprus			1												**1**
Bosnia and Herzegovina										1					**1**
Total by org. type	**14**	**1**	**64**	**39**	**7**	**3**	**1**	**1**	**7**	**6**	**3**	**1**	**5**	**3**	

IHI call 5 (single stage)

Progress in 2023: call launched and still open at the end of the year.

IHI call 5 at a glance	
Topics	4 (details below and here)
Launch date	27/07/2023
Submission deadline (single stage)	16/01/2024
Proposals received	n/a
Admissible proposals	n/a
Eligible proposals (evaluated)	n/a
Applicants in eligible proposals	n/a
Proposals above threshold	n/a
Proposals selected for funding	n/a
GAs signed in 2023	n/a

*The maximum financial contribution from IHI JU for these topics is: EUR 115 million. As this was a single-stage call for proposals, no IHI private member / contributing partner contributions were indicated at call launch in the call topic texts as these contributions depend on the selected proposals. Information on IHI private member / contributing partner contributions to projects funded under IHI single stage calls will be available only once the grants are signed in 2024.

The table below highlights how the topics of IHI call 5 are aligned with the specific objectives (SOs) of IHI as described in the legislation creating IHI and the Strategic Research and Innovation Agenda (SRIA).

Topic	SO1	SO2	SO3	SO4	SO5
Accelerating the implementation of New Approach Methodologies and other innovative non-animal approaches for the development, testing and production of health technologies		x			
Development and proof of principle of new clinical applications of theranostics solutions	x	x	x		
Improved prediction, detection, and treatment approaches for comprehensive stroke management	x	x	x		
Maximising the potential of synthetic data generation in healthcare applications			x	x	

Evaluation and ethics experts

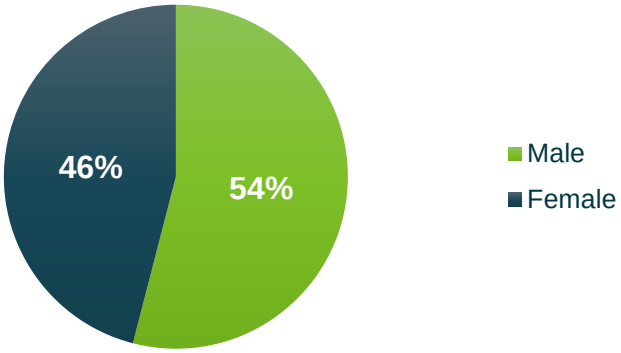
IHI selected 98 experts from 26 countries for the evaluations of call 2 - stage 2, call 3 – single stage, and call 4 - stage 1. Almost half of the experts were female (46%), and most came from the EU and Horizon Europe (HE) associated countries. All experts were selected so as to ensure a high level of skills, experience and knowledge in the areas of the call topics. Special attention was given to achieving an appropriately balanced composition (skills, experience, knowledge, geographical diversity, gender and private-public sector balance) and rotation.

The table below show the number and type of experts allocated per call.

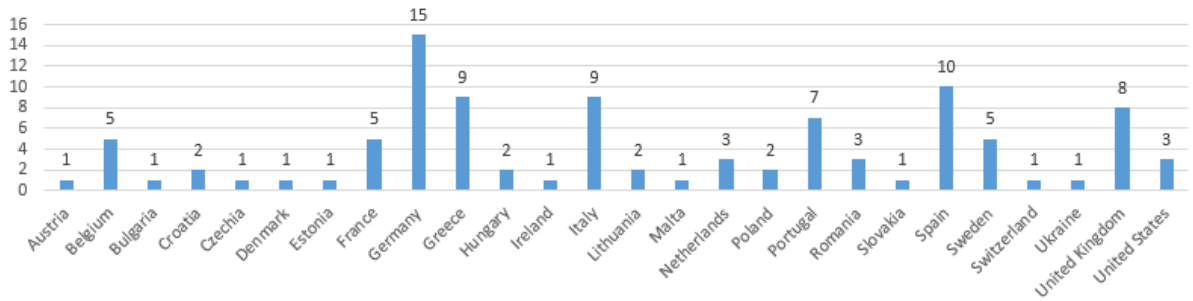
IHI Call	Scientific evaluation experts	Dedicated rapporteurs in scientific evaluation	Ethics screening experts	Observers	Total no. experts
Call 2 – stage 2	11	N/A	2	1	14
Call 3 – single stage	34	2	10	1	47
Call 4- stage 1	35	1	N/A	1	37

Statistics on the selected experts of **Call 2 stage 2, Call 3 and Call 4** can be found in the charts below:

Experts' gender

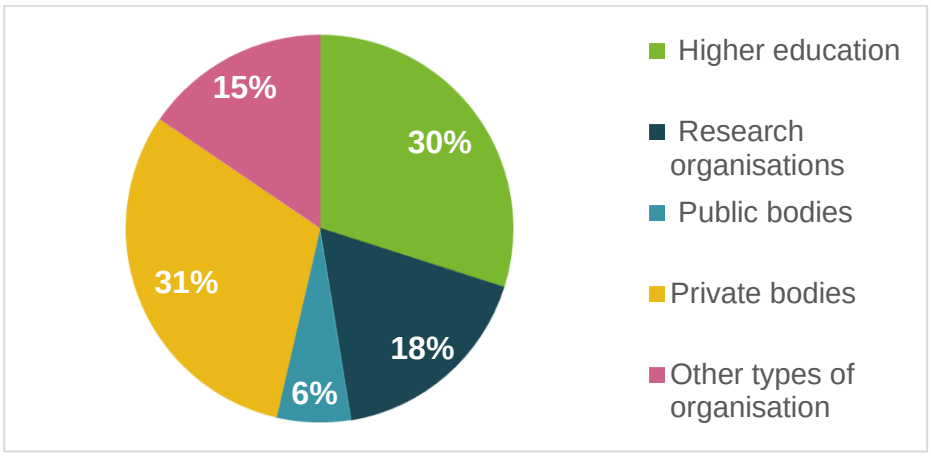


Experts' nationality [6]



[6] Experts with a full signed contract.

Experts' affiliation



1.5 Follow up activities linked to past calls

Interim reviews for IMI projects

In 2023, the Programme Office conducted 15 interim reviews of ongoing IMI2 projects. Each expert reviewer panel consisted of at least three experts.

Project acronym	Call	Full project name	Review date
TRIC-TB	16	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	26/01/2023
PROMISE	22	Preparing for RSV immunisation and surveillance in Europe	08/02/2023
PRISM 2	22	Psychiatric ratings using intermediate stratified markers 2	10/02/2023
SOPHIA	17	Stratification of obese phenotypes to optimize future obesity therapy	09/03/2023
imSAVAR	15	Immune safety avatar: nonclinical mimicking of the immune system effects of immunomodulatory therapies	21/03/2023
SISAQOL-IMI	18	Establishing international standards in the analysis of patient reported outcomes and health-related quality of life data in cancer clinical trials	26/04/2023
ERA4TB	15	European regimen accelerator for tuberculosis	26/04/2023
ImmUniverse	15	Better control and treatment of immune-mediated diseases by exploring the universe of microenvironment imposed tissue signatures and their correlates in liquid biopsies	25 & 26/05/2023
CARDIATEAM	13	Cardiomyopathy in type 2 diabetes mellitus	02/06/2023
ARDAT	18	Accelerating research & development for advanced therapies	29/06/2023
EUbOPEN	17	Enabling and unlocking biology in the OPEN	21/09/2023
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	28/09/2023
IDEA-FAST	15	Identifying digital endpoints to assess fatigue, sleep and activities in daily living in neurodegenerative disorders and immune-mediated inflammatory diseases	03/10/2023
RealHOPE	20	Real world handling of protein drugs - exploration, evaluation and education	09/11/2023
T2EVOLVE	18	Accelerating development and improving access to CAR and TCR-engineered T cell therapy	27 & 28/11/2023

TRIC-TB

TRIC-TB's objective is to advance the development of two molecules that could boost the infection-fighting ability of the anti-TB drug ethionamide. The compounds, BVL-GSK038 and BVL-GSK098, work by interfering with the systems that control gene activity in the TB bacteria. Previous studies have shown that they are able to boost the efficacy of ethionamide three-fold. If the results are confirmed in humans, this could allow doctors to reduce the dose of ethionamide typically given to patients, something that would also reduce the side effects associated with the drug.

During the review meeting, the TRIC-TB consortium presented an up-to date status of the project and the key challenges in the field of tuberculosis treatment. The project has demonstrated outstanding progress until the review meeting and the panel of reviewers stated they were confident that the consortium is well set to continue to out-perform its objectives through the next phase of the funding.

PROMISE

PROMISE aims to build on the IMI2 project RESCEU by increasing further our scientific knowledge on RSV (respiratory syncytial virus). This will be used to inform public health strategies and promote the development and introduction of novel immunisation tools and therapeutics in Europe.

The panel of reviewers was supportive of the project’s work to date but made a series of recommendations to improve project implementation, including improving dissemination and communication activities and strengthening patient involvement in the project.

PRISM 2

The PRISM 2 project aims to determine the reproducibility of the transdiagnostic and pathophysiological relationship between default mode network (DMN) integrity and social dysfunction in schizophrenia and Alzheimer’s disease and its potential to generalise to major depressive disorders (MDD) by running a clinical study. They also aim to test the causality between the quantitative variation in DMN integrity and social dysfunction.

According to the reviewers, the project is progressing as expected, with minor deviations from the original workplan. The project has already brought important scientific discoveries on DMN dysfunction to light. They recommended that the consortium should carefully monitor the subjects' recruitment for the clinical trial to ensure a timely project completion. They also encouraged the project partners to further improve dissemination and communication actions.

SOPHIA

The aim of the SOPHIA project is to improve the ability to predict who will experience which complications, and who will respond best to different obesity treatments. Currently, this is not possible. Part of the project will focus in particular on the relationship between type 1 diabetes and weight, as a large proportion of people with type 1 diabetes is overweight or has obesity.

The reviewers were satisfied with the progress of the project to date and were of the opinion that the successful implementation of the project will result in innovative approaches for diagnosis, patient stratification and for future treatments for obesity. The project's broad design can contribute to improving the effectiveness of obesity treatment and preventing its complications.

imSAVAR

imSAVAR aims to create an integrated nonclinical assessment platform for immunomodulatory therapy safety and efficacy. Current models fall short in representing the immune system's complexity and responses to therapies observed in clinical settings. imSAVAR focuses on refining and developing nonclinical models, with validation goals including assessing their predictive value, incorporating high-throughput assays and physiological systems. The project aims to enhance monitoring approaches, develop new endpoints, and design biomarkers for early detection of adverse effects.

According to the reviewers, the imSAVAR project is generally on schedule and maintains a strong rationale, utilising advanced techniques to mimic the human immune system. Exploitation progress includes advancements in multi-organ-on-chip systems for CAR-T cell therapy, showing potential for patent submission. The reviewers made a number of recommendations, such as improving the reporting of regulatory interactions, increasing patient engagement, boosting the number of articles being published, and intensifying exploitation activities.

SISAQOL-IMI

The aim of SISAQOL-IMI is 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.
To do this, the project will seek to achieve consensus across a range of different, international stakeholder groups on the optimal use of PROs in cancer clinical trials, and gain clarity on the research objectives for the use of PROs in trials.

According to the reviewers, the project progress is excellent and is already demonstrating a solid basis in terms of dissemination, exploitation and overall impact potential. The reviewers highlighted the importance to further engage with HTA bodies and patient organisations.

ERA4TB

ERA4TB aims to drop the sequential approach of drug candidates against tuberculosis and instead adopt a parallel pathway, which will allow the project to investigate the safety and efficacy of combinations of over a dozen drug candidates at the same time. By using a standardised approach and studying multiple molecules in parallel, the project hopes to optimise and speed up the development of new drug regimens needed to stop TB in its tracks. The project will achieve this by creating a world-class 'platform' that brings together the expertise, tools and resources needed to accelerate the development of anti-TB drug combinations.
The hope is that the platform will continue to operate beyond the end of the project.

The panel of reviewers found that the project has demonstrated good progress despite the challenges faced due to the COVID-19 pandemic. Although, the panel of reviewers deemed the consortium well set to

continue to achieve its objectives, they encouraged the consortium to focus its efforts more on the investigation of combinations of drug candidates instead of molecules alone.

ImmUniverse

ImmUniverse is investigating two immune-mediated diseases (ulcerative colitis and atopic dermatitis) using liquid biopsies to detect immune cells circulating in the blood and assessing how they interact with the tissues affected at the microenvironment scale. The work of the project will contribute to improved diagnosis, prognosis and predication of therapy responses in patients.

This was the second interim review of the project as the expert panel wanted to monitor the progress achieved following delays to project implementation resulting principally from impact of the COVID-19 pandemic identified during the first interim review. These delays were due to several factors including the COVID-19 pandemic and an internal reorganisation within the consortium itself.

The panel of reviewers acknowledged that the consortium had taken into account most of the recommendations from the first review and were satisfied with the improvements that had been made in project implementation. However, the panel of reviewers made a number of recommendations to help the consortium continue to improve project implementation in the remaining phase of the project.

CARDIATEAM

The CARDIATEAM project aims to determine how distinct diabetic cardiomyopathy is from other forms of heart failure, and the extent to which type 2 diabetes contributes to its development and progression. The team aims to recruit 1 600 people with a range of cardiometabolic disorders, including people with diabetes, and follow them for 3 years. By studying this group in detail over time, the team hopes to be able to deliver biological markers that would indicate which diabetes patients are at greatest risk of developing diabetic cardiomyopathy, as well as a more detailed understanding of the disease.

While the project has demonstrated progress, there have been delays due to the COVID-19 pandemic that have hindered the recruitment of patients in hospitals into the study. The panel of reviewers deemed that the consortium is progressing well and was satisfied with the mitigation plans and activities to overcome the slow recruitment of patients. In order to ensure that the consortium can reach its ultimate objective the panel has recommended a no-cost-extension.

ARDAT

ARDAT is looking at the currently available clinical data on advanced therapy medicinal products (ATMPs) with the aim of designing preclinical and clinical studies to fill the knowledge gaps in advanced therapies development such as cell and gene therapies.

In the view of the panel of reviewers, the project is progressing as expected and has generated important state-of-the-art data. The panel also made a series of recommendations to improve the implementation of ARDAT in the second half of the project, including the need to accelerate the population of the biobank with material from patients treated with gene therapy products, including patients treated with authorized products.

EUbOPEN

The goal of the EUbOPEN project is to develop high quality chemical tool compounds for 1 000 human proteins. This represents around a third of the ‘druggable’ proteins in the human body. The project will test the new tools in the areas of immunology, oncology and neuroscience.

The review panel was highly impressed with the accelerated progress and impressive output of the project so far, and only made minor recommendations to help maximise the utility of the project outputs and further increase community awareness to ensure sustainability of these outputs beyond the lifetime of the project.

RespiriTB

The aim of RespiriTB is to find new drug candidates as potential components of a new, more efficient combination drug regimen against tuberculosis (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.

Following a first review of the RespiriTB project, an additional review was requested to assess a new action plan put forward by the consortium that included the testing of a new compound against TB. The panel of reviewers supported the action plan proposed by the consortium.

IDEA-FAST

The aim of IDEA-FAST is to identify digital endpoints for fatigue and sleep disturbances that will provide a more sensitive, reliable measure of the severity and impact of these symptoms in a real-life setting.

The panel of reviewers highlighted the importance of the results coming from the IDEA-FAST feasibility study which evaluated the feasibility, acceptability, utility, and performance of a range of digital technologies for their ability to capture sleep problems and fatigue symptoms. The panel of reviewers made a number of recommendations focussed on ensuring efficient and timely recruitment for the recently started clinical observational study and maximising the impact of the resulting data.

RealHOPE

RealHOPE is a project that aims to improve our understanding of how protein drugs are handled in the real world, and the effect this has on product quality.

According to the panel of reviewers the partnership is working well, and the project is progressing in line with the project workplan. The panel made a number of recommendations to the consortium with the view to further maximise the impact of the project results.

T2EVOLVE

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 range of cancer treatments based on T cells, but their efforts are hampered by several 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 the IMI T2EVOLVE project is to develop an innovation ecosystem that will accelerate the development of engineered T cell therapies in the EU.

The panel of reviewers found that the project has made substantial progress to date and the consortium is well set to achieve its objectives with emerging plans to develop the work of the consortium beyond the end of the currently funded project.

1.6 Openness, cooperation, synergies and cross-cutting themes and activities

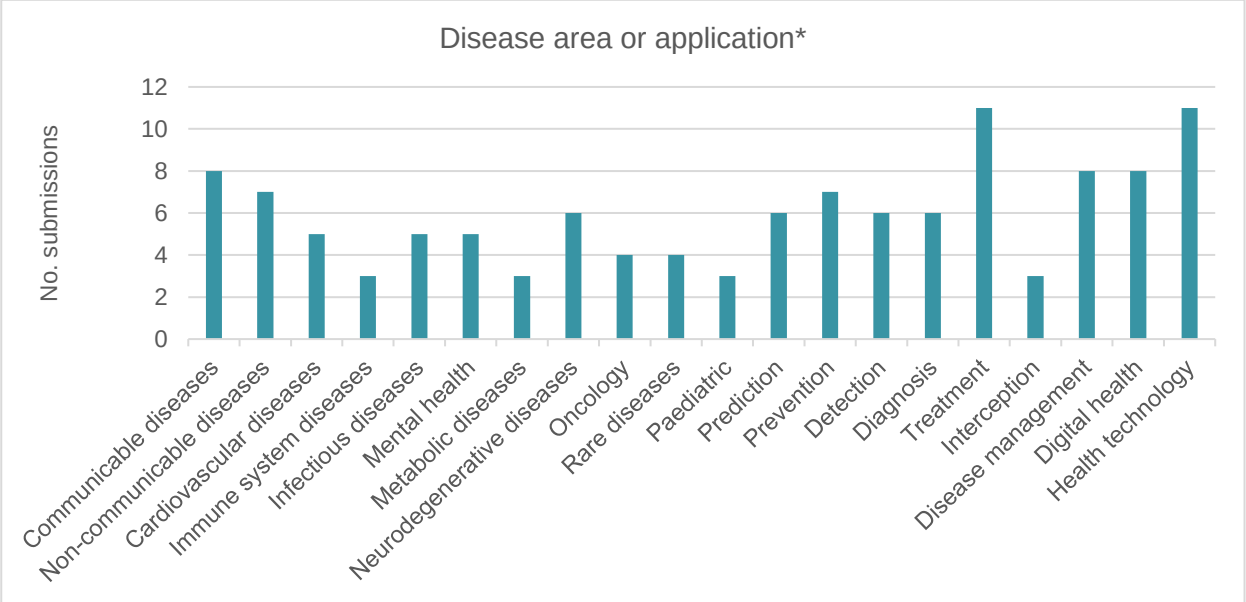
Collecting ideas to support the definition of IHI's annual priorities and areas for calls for proposals

In line with the Council Regulation establishing IHI[7] , in 2022 the Programme Office developed a process for the collection of ideas from a wide range of stakeholders to help IHI define its annual scientific priorities and areas for future calls for proposals. While the online form and the platform for the collection of ideas were launched in July 2022, in 2023 efforts were made to increase the number of high-quality ideas submitted. The "Ideas Incubator" web page including the guidance for submitters was updated based on experience gathered so far to help increase the quality of ideas collected. In November 2023, the Programme Office launched the "Ideas Incubator" awareness-raising campaign which was translated into several languages and is discussed in more detail in the chapter on communications.

In 2023, 16 ideas were collected, of which 6 passed the completeness and quality check and were reviewed by the SIP. Since the creation of the Ideas Incubator platform, 36 ideas have been collected, of which 12 passed the completeness and quality check and were reviewed by the SIP.

Most of the ideas (56%) received in 2023 were submitted in the personal capacity of the submitter. For those ideas submitted on behalf of an organisation, a large part came from small and medium-sized enterprises, while ideas were also submitted by patient, research and healthcare professional organisations. The ideas came from several countries, namely the Netherlands (3 ideas); India, Spain, and Turkey (2 ideas each); and Austria, France, Germany, Iran, Israel, Switzerland, and the United Kingdom (1 idea each).

The collected ideas covered a wide range of areas, as shown in the chart below, with the most popular being treatment and health technology (*people submitting ideas can select more than one disease area or application per idea).



[7] Council Regulation (EU) 2021/2085 of 19 November 2021 establishing the Joint Undertakings under Horizon Europe and repealing Regulations (EC) No 219/2007 (EU) No 557/2014 (EU) No 558/2014 (EU) No 559/2014 (EU) No 560/2014 (EU) No 561/2014 and (EU) No 642/2014.

As of the end of 2023, in total 7 SIP opinions on the collected ideas had been published on the IHI JU website, of which 3 were viewed as meriting further consideration. One of them, *Novel nuclear theranostics for personalised cancer diagnosis and care* (ref. 001173). was further taken on board in the IHI call 5 *topic 2: Development and proof of principle of new clinical applications of theranostics solutions* launched in July 2023.

Synergies

IHI has the potential to trigger EU-wide transformations by contributing to two key European objectives: pushing the digital transformation and gaining more resilience in the health domain. Addressing these challenges requires the development of close collaborations and synergies with relevant EU funding instruments, both within Horizon Europe and with other Union programmes, particularly with those supporting the deployment of innovative solutions in the fields of education and regional development. Moreover, implementing synergies and complementarities should help to avoid duplications when identifying priorities covered by collaborative research.

In order to explore all possible types of synergies, IHI regularly sought the advice of its three governance bodies: The Governing Board for strategic orientation regarding collaboration with other European partnerships, the SRG for information on synergies between IHI and national or regional initiatives and the Science and Innovation Panel for advice on synergies with other Horizon Europe activities, including other European partnerships, as well as other Union and national funding programmes. In parallel, IHI JU reported back to the governance bodies on the activities carried out during the year.

Moreover, the Programme Office followed up on the activities initiated by its internal task force set up in 2022 with representatives from the Programme Office, the EC and industry partners. The group continued to map existing and planned EU strategies, programmes, initiatives and policies of potential relevance. To complete this strategic exercise, representatives of relevant initiatives were invited to present their work and identify areas where complementary or shared activities would be of interest to address common challenges, avoid overlaps, align activities and ensure access to results and other relevant means of knowledge exchange. The Programme Office also sought opportunities to involve representatives of the other European partnerships in discussions during the drafting of IHI call topic texts.

At policy level, IHI held exchanges with the different EC teams leading key European political priorities such as the EU4Health programme (HERA, EHDS pilot action) and the Digital Europe programme to strengthen the design and planning of our calls. In the area of implementation, IHI JU regularly interacted with sister Joint Undertakings, notably Chips JU and GH EDCTP 3 JU, and with other European health-oriented initiatives such as the Cancer Mission, the Rare Diseases partnership, the partnership on Transforming Health and Care Systems and the EIT Health. We also established contacts with the Member States driven initiative Important Project of Common European Interest (IPCEI) on Health and international organisations such as the World Health Organisation.

Of note, in 2023, IHI JU signed a memorandum of understanding with EIT Health. In this context, IHI JU organised a joint workshop with EIT Health to promote the activities of both organisations across their networks (including the States' Representatives Group), supporting cross-pollination of their communities and mutual dissemination of their opportunities. It also showcased projects that have journeyed from IMI programmes onto EIT Health initiatives.

1.7 Progress against Key Impact Pathways and Key Performance Indicators

1.7.1 Progress against IMI2 / H2020 KPIs

The Programme Office continues to monitor the performance of the IMI2 programme towards its objectives since there are many projects that are still ongoing. KPIs track IMI's activities in the following strategic areas:

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

The Programme Office gathers data on these points via a dedicated web platform through which project coordinators can submit their project's results. The platform also allows the Programme Office 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. Annex 6 outlines these key performance indicators.

The analysis of the data collected up to 31 December 2023 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 439 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 IMI projects have reached 590 assets that completed a significant milestone so far. The definitions of 'project assets and achievements' and 'significant milestones' 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 delivered assets that have an impact on the regulatory framework and received acceptance by regulatory authorities: in IMI2 there are 29 completed procedures (versus a target of 10) and if we look at both IMI1 and IMI2 programmes together there are 51 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 (standard operating procedures), use of screening platforms, clinical trial networks, etc.). The data shows 642 implementation results in IMI2 (versus a target of 50) and 956 implementation results if we consider both IMI1 and IMI2 programmes together.

Additionally, more than half of IMI2 projects (63.33%) 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 numerous 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 cross-sector collaborative research in the healthcare space.

In addition, the Programme Office collects data to report against the relevant standard Horizon 2020 (H2020) KPIs, 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. More information on the progress towards the IMI2 specific KPIs as well as towards the H2020 objectives can be found in Annex 6.

1.7.2 Progress against JU-specific (IHI) KPIs

The IHI Governing Board adopted the IHI-specific key performance indicators (KPIs) in March 2022. The Programme Office will track IHI's activities in the following strategic areas:

1. Resources (input), processes and activities
- 1.1 Involvement of multiple healthcare stakeholders
- 1.2 Cross-sectoriality of the partnership
- 1.3. Engagement of regulators

2. Outcomes
- 2.1. Cross-stakeholders' collaboration
- 2.2. Public-private collaboration
- 2.3. Project outputs for use in clinical practice and health research development and innovation (R&D&I)
- 2.4. Integrated health care solutions considering end-users' needs
- 2.5. Methodologies for value assessment of integrated solutions
- 2.6. New or improved clinical guidelines
- 2.7. Management of health data
- 2.8. Demonstration of data integration
- 2.9. Demonstration of AI in health care

3. Impacts
- 3.1. Creation of sustainable resources and infrastructures that facilitate translation of the knowledge to innovations
- 3.2. Development of preventive or therapeutic strategies in different therapeutic areas to address unmet public health needs
- 3.3. Cross-sector activities established by the partnership that will help contribute to a globally competitive EU health care industry

Up to 31 December 2023 there were 16 IHI Grant Agreements signed. These projects will have their first reporting period in 2024, therefore there is minimal progress to report against the IHI specific KPIs at the moment.

Despite this early stage, some aspects related to IHI performance are already visible. IHI projects demonstrate the ability to involve multiple healthcare stakeholders and generate cross-sectorial collaboration. Analysing the composition of the IHI consortia, all IHI projects (100%) involve more than two types of healthcare stakeholders as project participants and almost all of them (94%) bring together private members and/or contributing partners (or their affiliated or constituent entities) from two or more technology sectors.

In addition, all IHI projects (100%) aim to develop new or improved existing methodologies also across disciplines addressing public health needs included in the list of the WHO Europe Health 2020 priority areas. Out of the 16 projects, 7 (44%) focus on “burden of disease” (specifically communicable diseases); 8 projects (50%) focus on “health systems” (specifically on digital health systems governance, health technology and medicines”); and 6% focus on ‘life-course approaches” (specifically “health aging”).

The Programme Office will report on the full set of IHI-specific KPIs in future reports, as soon as data becomes available.

1.7.3 Progress against general Horizon Europe Key Impact Pathways (KIPs) indicators

The Horizon Europe Key Impact Pathways (KIPs) mirror three complementary impact categories reflecting the non-linear nature of R&I investments: scientific, societal and technological or economic impact. For each of the impact categories, proxy indicators are used to track progress distinguishing between the short, medium and longer terms, as outlined in Annex 7.

The first IHI projects started in 2023, therefore it is too early to see any impacts on the scientific, societal, and technological/economic pathways. The European Commission IT central service is developing a centrally managed dashboard to collect the micro-data behind the KIP indicators for all parts of the Programme. So far, the dashboard could only capture limited data concerning the KIPS. IHI will report on the full set of KIP indicators as soon as data becomes available for IHI in the central dashboard.

1.7.4 Progress against common Horizon Europe KPIs for JUs

An expert group was appointed by the European Commission to support the strategic coordinating process for partnerships and provided a framework for current and future reports on the performance of European partnerships. The list of key performance indicators common to all European Partnerships is outlined in Annex 8 and covers aspects such as additionality, directionality, transparency and openness, coherence and synergies, international visibility and positioning.

Summary of IHI performance relative to these indicators

The total budget committed by the partners other than the Union for IHI projects for the whole duration of the partnership is EUR 1 200 million (EUR 1 000 million from funding industrial partners and EUR 200 million from contributing partners). By the end of 2023, IHI had signed grant agreements for 16 projects representing a total committed budget of EUR 189.8 million.

IHI projects have the potential to trigger EU-wide transformations by contributing to two key European objectives: pushing the digital transformation and gaining more resilience in the health domain. As a result, IHI project budgets to date is mobilised towards the Digital EU priority (95%) in the field of healthcare and the Resilience EU priority (95%) in the healthcare space.

To accomplish its mission, IHI established synergies with other European Partnerships, EU Missions, and other EU Programmes and funding instruments, particularly with those supporting the deployment of innovative solutions, education and regional developments, and other relevant programmes and policies at the international, national and regional levels. IHI, since its start, has carried out 9 collaborative initiatives with other European Partnerships and EU Missions and 9 cooperative initiatives with other EU Programmes, in the forms of strategic support, operational exchanges, promotion and communication activities and the

signature of one Memorandum of Understanding with the EIT Health (more details on synergies are provided in chapter 1.6).

IHI aspires to be an open partnership and serve the interests of all relevant stakeholders. Consequently, the implementation of IHI is open to new players to enter, participate in and benefit from its activities. IHI Calls attracted 820 applicants, coming from 42 countries. In funded projects there were 160 newcomer beneficiaries (beneficiary organizations that have never participated in a project funded by the predecessor partnership), coming from 24 countries. IHI projects also involved 10 international actors (Contributing Partners coming from third countries).

To increase the visibility of the programme and support its implementation, IHI has been supported by significant communication efforts. Since it started, IHI organised and supported diverse dissemination and communication activities including 32 webinars, 44 news articles and 24 newsletters.

1.8 Dissemination and information about project results

The IHI office encourages its project consortia to make their results available to the people that can best make use of them e.g. the scientific community, industry, other commercial players, policymakers, and more. IHI also encourages its consortia to ensure that the results they have generated are taken up and used, translating research concepts into concrete solutions that have a positive impact on the public's quality of life.

This section describes how project results are disseminated by both the project partners and the Programme Office.

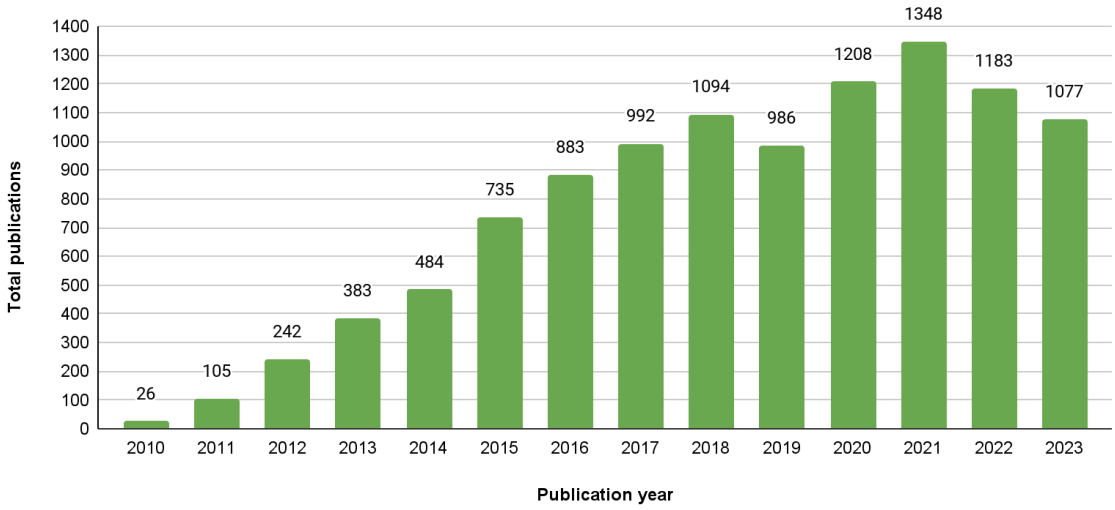
Publications in peer-reviewed journals.

IMI projects regularly publish articles in peer-reviewed journals as a key way of disseminating their results and activities. Links to these articles can be found on the projects' factsheets on CORDIS (see e.g. for EHDEN) and on the projects' own websites.

To gain a broader overview of the publications produced by its projects, the Programme Office has been monitoring and analysing the papers coming out of its projects since 2012. The analyses, now carried out by Nature Research Intelligence, demonstrate both the sheer volume and high quality of research taking place in IMI projects.

IMI projects have produced more than 10 000 publications to date

IMI-funded projects continue to produce a large number of publications, reaching 10 746 publications to date. In 2023, IMI projects generated 1 077 publications. In the past 5 years IMI publications have averaged 1 160 publications per year.

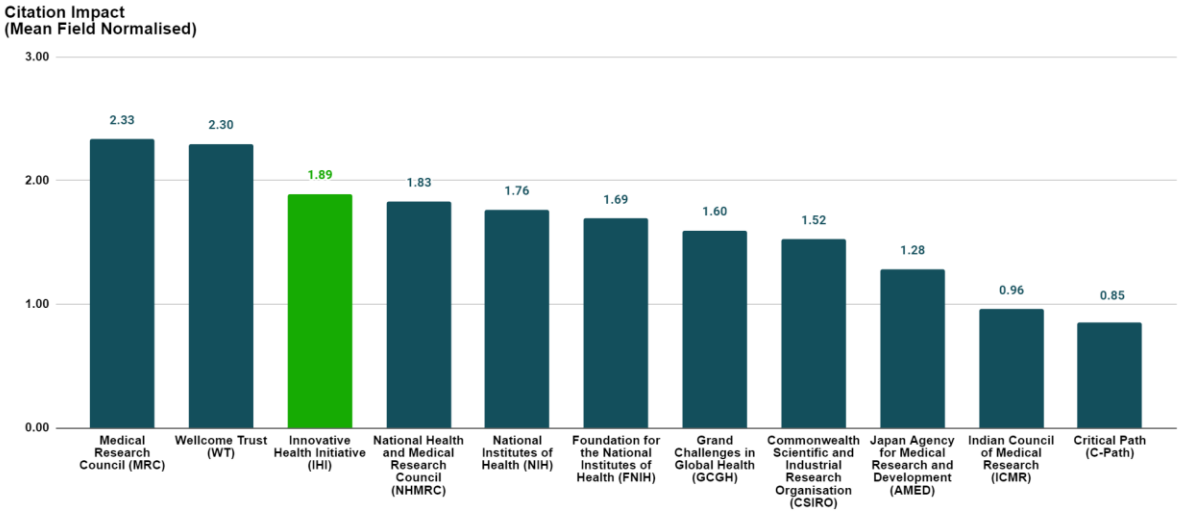


The citation impact of IMI research is higher than EU and world averages

The field-normalised citation impact for all IMI papers is 1.89 (compared to 1.37 for the EU[8] and the baseline of 1 for the world). IMI also compares favourably with similar organisations such as the Medical Research Council (MRC), the Wellcome Trust, and the National Health and Medical Research Council (NHMRC) and

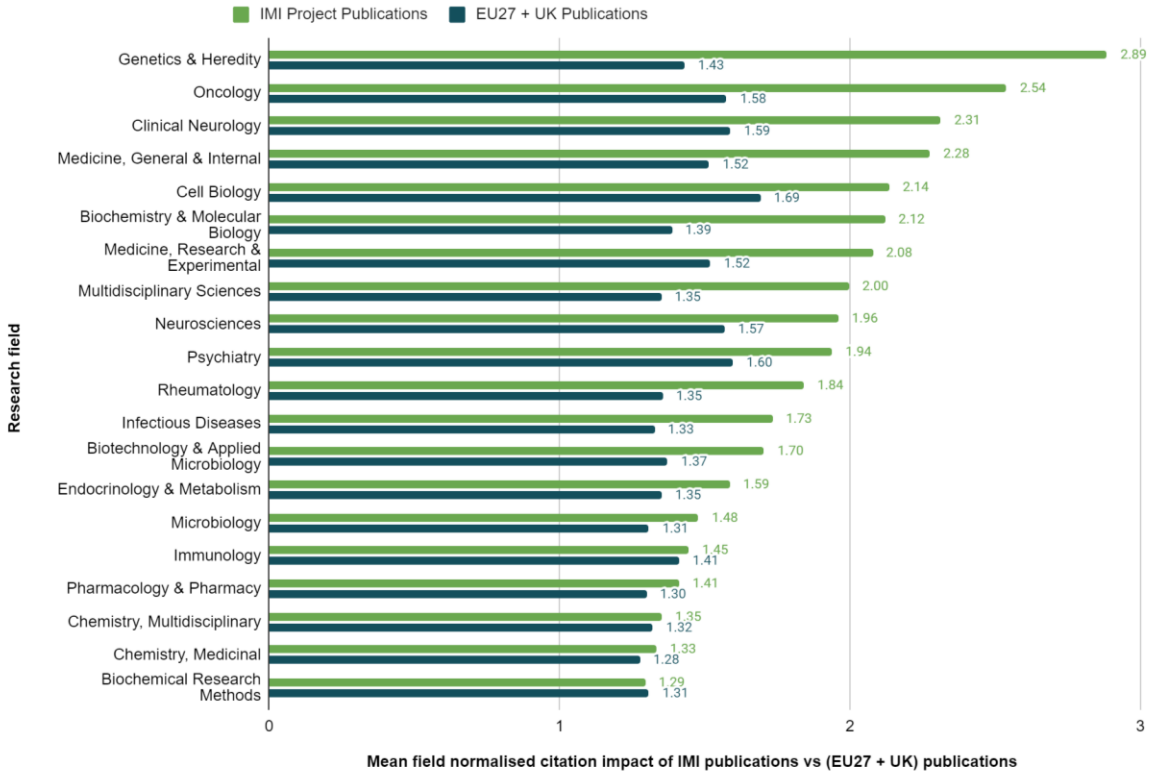
[8] I.e. research output with at least one EU (EU27 countries + UK) affiliation assigned to the paper.

positions third in the overall competitor set. 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 almost all fields, IMI research has a higher citation impact than the EU average. This is most notable in the fields of genetics and heredity, oncology, clinical neurology and medicine, general and internal where the IMI citation impact is between 2.89 and 2.28.

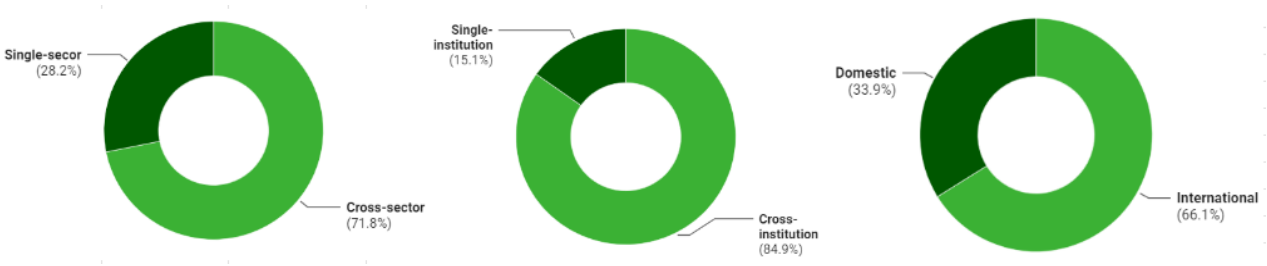


Other key facts and figures revealed by the latest analysis include the following.

- The internationally collaborative nature of IMI is reflected in the authorship of the papers, with almost two thirds of publications recording authors from more than one country.
- 27.9% (n=2 993) 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 been published in 1 803 journals to date, and the average journal impact factor for IMI research is 7.52. The average journal impact factor for 2023 across 491 journals is 10.37.
- Journals with a particularly high impact factor that have published IMI research include The Lancet, New England Journal of Medicine, Journal of the American Medical Association (JAMA), Nature journals (e.g. Nature Drug Discovery. Nature Molecular Cell Biology, Nature Reviews Immunology, Nature Reviews Microbiology, Nature Medicine and Nature Reviews Disease Primers), and British Medical Journal (BMJ).

IMI research is highly collaborative

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



- More than two-thirds of (72%) of all IMI project papers were published by co-authors working in different sectors.
- The majority (85%) of IMI project papers involved collaboration between different institutions.
- More than half (66%) of all IMI project papers involved international collaboration.

Project snapshot – top 10 projects by number of publications

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 mean normalised citation impacts range between 1.62 and 2.78.

Rank	Project	Total publications	Mean field-normalised citation impact
1	BTCure	730	1.62
2	EU-AIMS	629	1.78
3	ULTRA-DD	461	1.62
4	AIMS-2-TRIALS	366	2.28
5	EMIF	358	2.22
6	BigData@Heart	280	2.47
7	EUbOPEN	279	1.46
8	INNODIA	256	1.63
9	NEWMEDS	227	1.90
10	CANCER-ID	215	2.78

Journal snapshot – top 10 journals by number of publications and journal impact factor (JIF)

Between 2010 and 2023, IMI projects published papers in 1 803 different journals.

The following table shows the top 10 journals by number of IMI publications.

Rank	Journal	JIF	Total publications	Total citations
1	Scientific Reports	4.6	232	6 173
2	Annals of the Rheumatic Diseases	27.4	221	8 353
3	PLoS One	3.7	213	5 423
4	Diabetologia	8.2	190	3 122
5	Nature Communications	16.6	165	11 308
6	Frontiers in Immunology	7.3	136	1 983
7	Journal of Medicinal Chemistry	7.3	109	2 205
8	Diabetes	7.7	98	2 193
9	International Journal of Molecular Sciences	5.6	86	1 591
10	Arthritis & Rheumatology	13.3	78	2 573

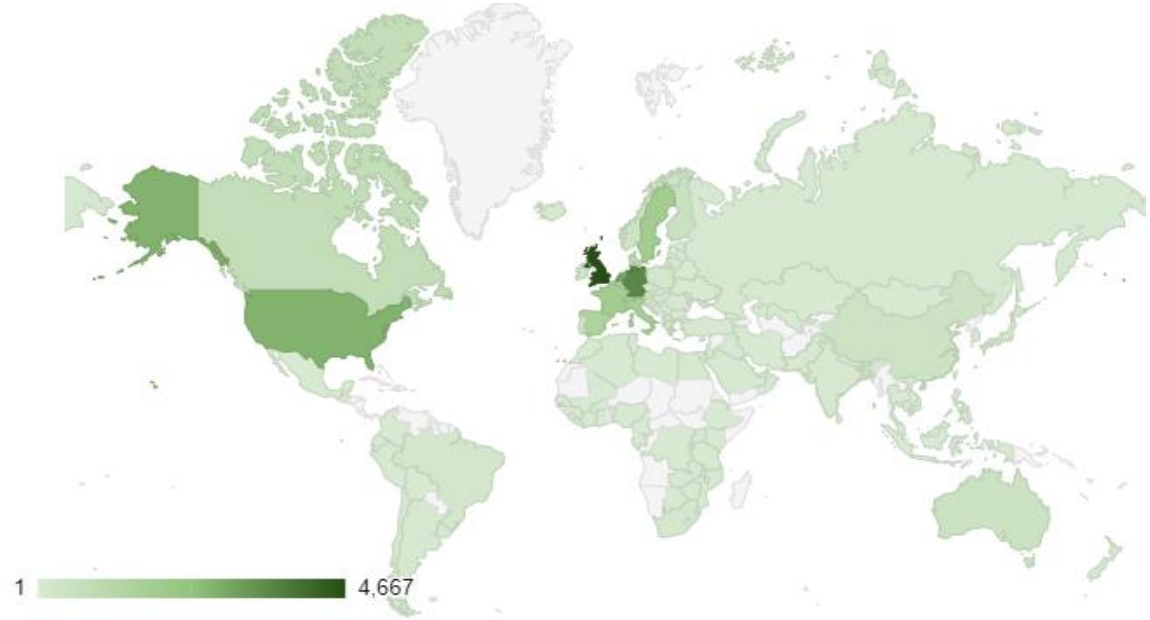
The following table shows the top 10 journals by JIF in which IMI projects have published.

Rank	Journal	JIF	Total publications	Total citations
1	Lancet	168.9	10	2 816
2	New England Journal of Medicine	158.5	3	177
3	JAMA - Journal of the American Medical Association	120.7	9	2 398
4	Nature Reviews Drug Discovery	120.1	17	2 142
5	Nature Reviews Molecular Cell Biology	112.7	2	391
6	BMJ - British Medical Journal	107.7	14	994
7	Nature Reviews Immunology	100.3	4	880
8	Nature Reviews Microbiology	88.1	2	530
9	Nature Medicine	82.9	28	3 009
10	Nature Reviews Disease Primers	81.5	3	2 290

Countries with at least 1 paper funded by IMI

The analysis also reveals the global reach of IMI's research activities. In total, **125 countries** have at least one paper funded by IMI. There are **66 countries** which have 10 or more publications funded by IMI.

The graph below shows countries having from 1 publication to 4 253 publications. The top 5 countries based on publication output include UK (4 667); Germany (3 527); Netherlands (2 768); United States (2 674) and France (1 772).



Note: China mainland, Macau, Hong Kong are combined into one unit.

Spreading the word further – how the IHI Programme Office disseminates results to a wider audience

The Programme Office uses scientific publications from projects as the basis for the news articles published on our own website – these are discussed in the communications section of this report.

In 2023, the IHI Programme Office finalised a special issue of the journal Frontiers in Neurology showcasing how public-private collaborative research through IMI and now IHI is making a difference in the Alzheimer's disease field.

The special issue comprises 12 articles which cover issues including the impacts and added value of the IMI and IHI neurodegeneration portfolio; experiences and best practice on data sharing; the use of digital technologies in Alzheimer's disease research; the importance of involving people with Alzheimer's disease in research; platform trials for Alzheimer's prevention; and the use of amyloid imaging to follow disease progression. The special issue closes with a presentation of PROMINENT, the first IHI project in this field.

The IHI office requires its consortia to report on their dissemination and exploitation of results activities in their periodic reporting, and to inform the IHI office when important dissemination events occur or when significant progress is made in exploiting project results. These are important elements of the interim review of IHI projects as well as the close out meetings. Consortia are also directed to use the EC's free tailor-made dissemination and exploitation support services, such as the Horizon Results Platform (HRP) and the Horizon Results Booster (HRB). In addition, the Innovation Radar, a policy tool that helps to identify high potential innovations and innovators in EU-funded research and innovation projects was included in many interim reviews.

When communicating about project results, IHI has taken a portfolio approach to better illustrate how the research we fund is having a real impact in tackling a particular global health challenges. We do so by combining two activities, the thematic health spotlight webpages and the IMI impact series events, where IMI projects are invited to discuss the relevance of their research. In 2023, the following new topics were added to the collection: vaccines, clinical trials and Ebola.

The impact event on vaccines and associated health spotlight page explore how IMI projects are facilitating innovations in vaccine development and effectiveness assessment.

The impact event on clinical trials showcased how IMI projects are delivering results that will improve how clinical trials are run. This event was also an opportunity to feature some of the IMI project results that will contribute to the Accelerating Clinical Trials in the EU (ACT EU) initiative launched by the European Commission, the Heads of Medicines Agencies and the European Medicines Agency. Again, additional information on this subject is presented via the health spotlight pages.

The impact event on Ebola focused in particular on how IMI projects are delivering results to advance the development and uptake of Ebola vaccines. In addition to detailing IMI projects' work on vaccines, the related health spotlight page provides additional information on IMI's work on diagnostics for Ebola and related diseases.

In addition, the Programme Office organised an event to demonstrate how IMI projects contribute to early career researchers' development by providing them the opportunity to gain practical experience of working in multidisciplinary teams with people from diverse backgrounds, such as government agencies, non-profit organisations, and industry.

In 2023, the IHI Programme Office took the decision to open to the public the internal close-out meetings with projects that have concluded. The meetings were rebranded as "In conversation with…", and the first event in the series featured IMI project iConsensus. The project partners discussed how the project drew on the agility and specialist knowledge of SMEs and the know-how of academic experts to make biological drug development faster, cheaper, and more efficient. They showcased some of the new tools that had been developed such as the new "Sensor Sticks" made by PreSens which measure dissolved oxygen, partial pressure of carbon dioxide and pH levels rapidly and accurately within bioreactors; new and improved glycan assay tests developed by PAIA Biotech using special microplates for high throughput assays; a new cell density quantification tool put forward by IpraSense that gives automated high throughput cell count and viability determination; and monitoring methods by Kantisto to better quantify various components of the cell culture and of the media used to grow the cells.

Prior to the decision to open up close-out meetings to the public, IHI held three close-out meetings under the old, internal model. As usual, the IHI Programme Office used the information presented during the close-out, and interviews with the project coordinators, to update the project factsheets on the IHI website so that they reflect the results, impacts and legacy of the projects.

- TRANS-QST delivered models, knowledge and resources to improve pre-clinical safety testing of potential medicines.
- PREFER produced recommendations on integrating patient preferences into drug development. The recommendations were endorsed by the European Medicines Agency, and the project's work is being carried forwards by the PREFER Expert Network.
- PHAGO shed new light on the role of the TREM2 and CD33/SIGLEC33 genes in Alzheimer's disease and developed a series of tools to support future therapy development.

The main goal of the PharmaLedger project is to develop a blockchain-based platform with reference use cases in supply chain, clinical trials and health data designed to foster wider adoption of blockchain within the pharma industry. During the IHI-organised dissemination event, project representatives presented two of their seven flagship use cases: the electronic Product Information (ePI) capabilities, which allow patients, healthcare providers, and other stakeholders to access the most recently updated information directly from the manufacturer, and the clinical trial electronic Consent (auditable, version-controlled, real-time and immutable informed consent forms management). They also presented the not-for-profit PharmaLedger Association created to ensure the sustainability of the project's results.

With an emphasis on exploitation and sustainability, IHI and the EIT Health organised jointly a workshop for IMI projects to showcase projects that have journeyed from IMI/IHI programmes onto EIT Health initiatives, demonstrating how participations in programmes run by the two organisations enable continued maturation of best-in-class activities in the network.

The table below shows the number of participants who joined these important dissemination events.

Event	Participants
IMI Impact on Ebola Part of the Health Spotlight series	132
IMI Impact on Clinical trials Part of the Health Spotlight series	215
IMI Impact on Vaccines Part of the Health Spotlight series	65
Impact on early career researchers Part of the Health Spotlight series	100
In conversation with iConsensus First of our public close out meetings	48
PharmaLedger dissemination event Showcasing the results and impacts of the project	128
Joint IHI - EIT Health workshop - Bridging the gap Internal meeting for IMI projects	70

2 Support to operations

2.1 Communication activities

IHI's communication activities support the organisation's strategic goals and are guided by the IHI Communications Policy which was approved by the Governing Board on 8 December 2022. The Policy is split into six key objectives and progress against these is outlined below.

1. Establishing the brand and raising awareness of IHI's core identity

During 2023, IHI launched two week-long awareness campaigns in collaboration with our founding members and the SRG. Based on social media posts, the campaigns addressed different aspects of IHI's core identity, featuring powerful visuals that made them attractive to share.

The **#IHITransformingHealth** campaign, launched to mark the second birthday of IHI, focused on raising awareness about who we are, what we do, and why we do it in a concise, impactful way with different visuals and messages per day.

The social media campaign was complemented by a POLITICO Pro Morning Health Care newsletter take over (which earned 175 total clicks vis à vis the 2022 Politico benchmark of 106 clicks), together with an advertising banner campaign on the Politico website (with 88K impressions on POLITICO.eu and 87.77% viewability vis à vis the industry benchmark of 57%).

Altogether, we experienced a marked increase in IHI website page views over the course of the campaign, with a peak of 3 331 page views, 2 896 unique page views and 1 737 entries on 27 November. Regarding social media, the campaign earned 201 LinkedIn reactions and 42 LinkedIn reposts, as well as 25 reactions, 2 580 impressions and 15 retweets in X, confirming the increasing weight of LinkedIn among our social media channels.

In the same vein, IHI launched the **#IdeasIncubator** campaign. This time we sought the collaboration of the SRG, targeting their wider national health and research communities. We provided social media content – visual and text – in 29 languages with the goal of increasing submissions to the Ideas Incubator, IHI's tool for submitting suggestions for potential new call topics.

The best performing LinkedIn post was published by Vinnova using the Swedish language version – their post received 91 reactions, 4 comments and 6 reposts, showing the potential for the campaign reach. On X, a post by the Health NCP N3 cluster achieved the most success (5 likes and 4 reposts).

Ensuring that there is clarity on the new rules under IHI and the different ways that stakeholders can get involved in the programme has been a priority for the communications team. To that end, several events have been organised to inform stakeholders about the role of contributing partners, the financial aspects of proposals for single stage calls and on how to prepare an expression of interest to participate in the IHI Patient Pool.

Targeted info sessions on the new IHI features	Participants
Single stage calls - Preparing the financial part of the proposal	60
Single stage calls - rules and procedures	105
Two - stage calls - rules and procedures	104
IHI contributing partners - who, why and how	152
How to apply to the IHI Patient Pool	39

These events had a positive impact on attendees. Following the sessions, IHI ran a survey among participants and 85.4% of the respondents totally agreed and 9.8% tended to agree with the statement "the IHI Call Days has improved my understanding of the IHI call process". Moreover, the webinars left a positive perception of IHI on most participants, with 34.1% feeling more positive and 29.3% feeling slightly more positive about us.

Along with the anniversary celebration, IHI marked each 2023 milestone achieved during the year with the publication of 11 articles on call topics, call launches, the IHI Patient Pool, the signing of the IHI-EIT Memorandum of Understanding, and the appointment of IHI's new Executive Director.

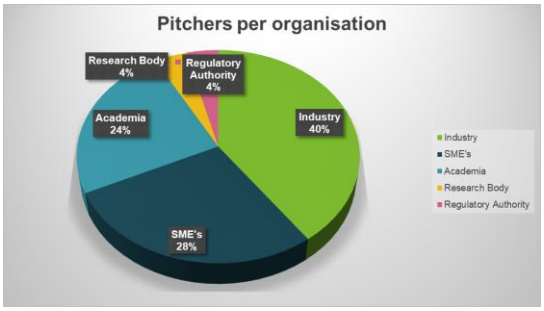
2. Engaging stakeholders in calls for proposals

IHI's goal is to reach researchers from all over the EU by making our events accessible to all interested stakeholders. Consequently, IHI events are open, free of charge and can be followed online.

In 2023 the Programme Office organised the IHI Call Days for Calls 4 and 5. Over 595 participants attended the different sessions.

27 participants pitched for Call 5, while 165 participants attended the pitching sessions.

In parallel, all registered stakeholders were provided with the option of organising matchmaking meetings through our dedicated online platform, the IHI Events Platform.



In response to IHI's post-event surveys, a vast majority of participants (95%) said that they would be likely to attend other IHI events and webinars, indicating a positive interest in future events.

The IHI Office contributed to external events by sending speakers to promote the programme and IHI's calls for proposals. In the case of key sectoral events such as the MedTech Forum or BIO-Europe, IHI was also present at their exhibitions with a booth, where the communications team was on hand to answer questions about the programme including current and future funding opportunities. The list of external info sessions is summarised in the table below.

Date	Organiser	Event name	Location
06.03.2023	French Minister of Finances & EIT Health	IPCEI match-making event and info session	Brussels, BE
31.05.2023	MedTech Europe	The MedTech Forum - One year in: IHI leads to its first successful and collaborative European projects	Dublin, IE
29.06.2023	Catalan industry association for Biotech and HealthTech	EU projects day	Barcelona, ES
03.07.2023	SOST-CDTI	Partenariados en el Clúster 1 de Horizonte Europa (Innovative Health Initiative)	Online
05.09.2023	Swiss Eurosearch	IHI webinar	Online
21.09.2023	CDTI/SRG	Iniciativa de Salud Innovadora – Convocatorias 4 y 5	Madrid, ES
27.09.2023	The German National Contact Point (NCP) Health	Information session on calls 4 and 5 of IHI	Online
10.10.2023	MedFIT	What's new in grant financing across Europe and how to prepare for it?	Strasbourg, FR
23.10.2023	French Ministry of Research/ SRG	IHI Call 5 info session	Online
24.10.2023	APRE associazione per la ricerca europea	IHI Italian info day	Online

27.10.2023	European Brain Council	Brain Innovation Days	Brussels, BE
06-08.11.2023	BIO-Europe	BIO-Europe exhibition	Munich, DE
08.11.2023	Johnson & Johnson	Introduction to the IHI	Online
21-22.11.2023	Polish NCP Horizon Europe	Horizon4Poland 23	Warsaw, PL
15.12.2023	East and North Finland Region	IHI Info session	Brussels, BE

In an effort to maximise the time available for potential applicants to start forming consortia early, which is key to receiving a robust number of submissions to IHI calls, the communications team ensured the early publication and continuous promotion of draft call topics through the newsroom section of the IHI website, IHI's social media, and the monthly newsletter.

3. Highlighting project successes

To maximise visibility for successful results from our projects, we drafted news items and created project factsheets for the new IHI projects, which will be regularly updated along the lifetime of the projects.

From January to December 2023, we published 41 new articles on IMI project results. All articles were published in the newsroom section of the IHI website, were promoted on IHI´s social media, and featured in the monthly newsletter.

IHI continued its media partnership with *Science Business*. This allowed us to promote 12 articles via the *Science Business* website, newsletter and social media accounts (i.e. posts on Science Business's Twitter, LinkedIn, and Facebook). Each article was promoted for a week. In total, these resulted in the following:

- Home page views while our articles were live: 114 138
- Social media impressions: 11 919
- Social media engagements: 481
- Newsletter impressions (opened): 68 076
- Clicks on article in newsletter: 2 368

The three most visited articles in the IHI web on project success stories were:

- New treatment shows promise for combating dangerous drug-resistant bacteria
- Wearable technologies can reliably measure fatigue and disturbed sleep in chronic disease
- IMI project provides world's first preclinical drug tests for children with cancer

IHI also contributed to the European Commission's efforts to explain the growing body of results yielded by our projects. Project stories from VHFMoDRAD, VITAL, PIONEER, BigData@Heart, BIOMAP, HIPPOCRATES, EU-AIMS, AIMS-2-TRIALS, PRIMAVERA and UNITE4TB were published either in the *Horizon Magazine* or in *Cordis*, under the "scientific advances" section.

IHI's strategy for the promotion of project results is based on a seamless combination of communication and dissemination activities, however for the purpose of this report, the dissemination activities are reported separately in section 1.8.

4. Demonstrating IHI's alignment with its purpose

Continuing with the series inaugurated last year, we produced a brochure based on the 2022 CAAR, highlighting the impact of the programme in tackling today's health challenges in fields as diverse as cancer, COVID-19, antimicrobial resistance, drug discovery and digital health. With short project stories and simple infographics on KPIs we aim to demonstrate the programme's progress in delivering the IHI Strategic Research and Innovation Agenda. The report was electronically distributed to all Budgetary Control Committee members of the European Parliament on the day of the JU's discharge hearing.

Demonstrating IHI's alignment with its purpose starts with active participation in the fora where debates take place. In 2023, IHI staff contributed to the global discussion in the events summarised in the table below.

Date	Organiser	Event name	Location
17-18.02.2023	ICPerMed and Navarra region	ICPerMed Workshop Preparing the future in personalised medicine (EP PerMed)	Pamplona, ES
07-08.03.2023	EASI-Genomics	Key Areas of the SRIA discussion: the personalised medicine innovation system and industrial collaboration	Stockholm, SE
23-24.03.2023	Drug Information Association	DIA Europe 2023	Basel, CH
01-03.05.2023	National Multiple Sclerosis Society	Pathways to Cures Global Summit	New York, USA
20-21.09.2023	The Economist's 9th annual World Cancer Series Europe	Strategy session: Innovations in diagnosis	Brussels, BE
17-18.10.2023	The European Forum for Good Clinical Practice	EFGCP Annual Paediatric Conference	Amsterdam, NL
19.10.2023	Global AMR R&D Hub	Annual Stakeholder Group / Joint Meeting	Berlin, DE
26.10.2023	Representation of the State of Rhineland-Palatinate	Discussion on the Future of Health and Research in Europe	Brussels, BE
27.10.2023	European Brain Council	Brain Innovation Days	Brussels, BE
22-23.11.2023	Lyonbiopôle and Mabdesign (member of EuropaBio)	7th edition of the Immunotherapies & Innovations for Infectious Diseases Congress	Lyon, FR
24.11.2023	HSI/Europe multi-stakeholder Roundtable	Identification and prioritisation of the most relevant public health issues and unmet biomedical needs?	Brussels, BE
29.11.2023	Women Brain Project	Enhancing care in Parkinson's	Online
30.11.2023	Inspire2Live Annual Congress	Session: "'If about us not without us"	Amsterdam, NL
05.12.2023	HERA Conference	Is the EU better prepared?	Brussels, BE
05-06.12.2023	European Commission	European Partnership Stakeholder Forum	Brussels, BE

5. Anticipating and countering criticism

In 2023 we formalised IHI´s communication policy following the approval of the *IHI strategy for crisis management and communication*. This document sets out IHI's approach to crisis management, understood as the process designed to prevent or lessen the damage a crisis can inflict on the organisation and its stakeholders by ensuring that IHI gets factual information to the right people with maximum speed, minimising the risk of misinformation.

Crisis management starts with early identification and continuous monitoring, and the communications team remained alert to issues that could damage IHI's reputation. As in previous years, we performed a content analysis to measure the tone of both news coverage and Twitter engagement. For the press, the tonality for mentions of IMI was neutral in 76% of news items, while the content of around 24% of the pieces was positive. As for IHI, the tonality was recorded as neutral in 77% of news items and positive in 24%. Neither of the two Programmes attracted negative coverage. On Twitter more than half of all posts about IHI were positive in tone, with the rest being largely neutral and just a small proportion having a negative tonality.

6. Unlocking IHI partners' potential as multipliers

At a strategic level, the IHI Office worked in close cooperation with its founding partners through regular discussions within the IHI Comms Task Force. We also created opportunities to leverage the partners' extensive communication channels. For instance, IHI's social media material was shared widely by the accounts of Horizon Europe (EC), COCIR, MedTech Europe and EFPIA. In addition, IHI staff regularly participated in the different events organised by our partners with the aim of mobilising their communities to either participate in the design of our calls or to apply to IHI calls.

Similarly, IHI staff participated in the various info days organised by the SRG and launched the #IdeasIncubator multilingual campaign together with the SRG.

2.2 Stakeholder engagement

2.2.1 Patient engagement

Patient engagement has been a priority for the organisation throughout the IMI1 and IMI2 programmes, and it remains a priority under the new IHI programme. Thanks to efforts to promote patient engagement in projects, as of the end of 2023, 59% of all IMI1 and IMI2 projects have patient organisations either as partners in the consortium or represented in advisory boards, ethics advisory boards, or being consulted for topics of relevance.

IHI continued throughout 2023 the systematic involvement of patients and carers at all levels of its activities, mainly through the establishment of the IHI Patient Pool aiming to provide in a rigorous and systematic way, patients' perspectives, needs and priorities within IHI. Specifically, in April 2023, the IHI Programme Office launched a new call for expressions of interest. The purpose was to set up a new and wider IHI Patient Pool, confirming the interest of IMI Patient Pool members and allowing other patients/caregivers to become members of the pool and provide their perspectives within IHI activities, at both strategic and operational level.

The pool has 120 people – 87 patients and 33 caregivers. The members come from 25 countries and have direct experience as patients / caregivers in rare diseases, cancer, neurodegenerative diseases, inflammatory/immune diseases, diabetes, musculoskeletal disorders, and more. A majority have knowledge or experience in patient reported experience, preference, and outcomes, in patient engagement and involvement, in using telemedicine applications as well as digital, remote and wearable technologies in medical healthcare, in research and innovation activities, in health industries, and ethics and regulatory processes.

In 2023 the IHI Programme Office invited patients from the IHI Patient Pool to perform a variety of roles and tasks. These include:

- Evaluation of proposals submitted to IHI calls for proposals – two members of the IHI Patient Pool participated as patient experts in the evaluation panel for the proposals submitted to IHI - call 2 (stage 2) topic 2, and call 4 (single stage) topic 3, respectively.
- Review of IMI projects – one member of the IHI Patient Pool participated as patient expert in the panel for the review of one IMI2 project.

To deploy the full potential of the IHI Patient Pool, the IHI 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, the IHI Programme Office invited patients and carers from the IHI Patient Pool to attend project close-out meetings where they 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, learn first-hand about the project outcomes, identify patient relevant results, and 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 IHI. Throughout 2023, IHI provided detailed updates on its activities to patients with news of IHI activities, calls and events, and highlights from IMI/IHI projects.
IHI also participated in external high-profile events, webinars, and meetings to raise awareness of IHI's goals and achievements while contributing to patient-centred discussions and debates.

2.2.2 SMEs

The involvement of small and medium-sized enterprises (SMEs) in IHI activities is crucial as SMEs can act as a key interface between the latest academic discoveries and implementation in industry, can drive projects to achieve high impact results, and can help ensure the results of IHI projects are widely available after the funding ends. Therefore, IHI aims to create a favourable ecosystem for SME innovation and growth.

Several of the newly launched IHI projects are supporting the growth of SMEs, for example, HEU-EFS, which is working on developing a harmonised framework for early feasibility studies for medical devices in the European Union. The consortium contains health technology developer SMEs which should benefit from the results of the project.

Several IMI projects also significantly supported SMEs in 2023. The EHDEN project has selected, trained and certified 63 SMEs from 23 countries in data harmonisation. Many of these SMEs are actively mapping the EHDEN data partners' data and have also gained contracts outside of the EHDEN project, for example, EdenceHealth have worked on the LAISDAR project to harmonise COVID-19 data from 15 Rwandan hospitals & health centres to the OMOP CDM (Observational Medical Outcomes Partnership common data model). The European Lead Factory project came to a close. During the project approximately 30% of the crowdsourced drug screening proposals were submitted by SMEs, and four start-up companies were initiated based on project results.

2.2.3 Regulators

The regulatory environment is key to ensuring that safe and effective health innovations are developed to address public health needs. The regulators' perspective is embedded in the scientific priorities and calls for proposals, most notably through the representation of regulators in the SIP. To ensure that the science generated by IMI and IHI projects is translated into people-centred healthcare solutions, IHI JU has continued to engage with all relevant regulatory authorities. IHI Programme Office has continued successful collaboration with the European Medicines Agency (EMA), including through contribution to the EMA multi-stakeholder workshop on qualification of novel methodologies held in April 2023. Furthermore, IHI JU has started engaging more broadly with the national competent authorities (NCA) and the Medical Device Coordination Group (MDCG) to reflect the cross-sectoral nature of the partnership.

Building on the successful IMI-EMA-FDA regulatory science summits held within IMI, the Programme Office has also initiated the organisation of the first IHI Regulatory Science Summit scheduled to take place in February 2024. This meeting gathering representatives from medicinal products and medical devices regulatory agencies from Europe and US, notified bodies, industry, the European Commission, the IHI SIP aims to be a forum for discussing strategic research areas of common interests between founding members and medicines/devices regulators, and identifying challenges and gaps where IHI could be ideally placed to be at the forefront of generating actionable solutions. This will inform proposed ideas for IHI topics that contribute to regulatory science.

IHI JU continued to increase the awareness of applicants and project consortia about regulatory needs to be considered when relevant. In particular, in line with the action plan developed by the Programme Office to implement the recommendations elaborated by the Critical Path Institute Limited through the framework contract for services to support the regulatory acceptance of IMI results report the Programme Office has reviewed the topic text template and has updated the guidance document ''raising awareness of regulatory requirements'' which will be released in 2024.

2.3 Legal and financial framework

During 2023, IHI implemented the Council Regulation establishing IHI (Council Regulation (EU) 2021/2085), while continuing to manage projects launched under the IMI1 and IMI2 programmes (Council Regulations (EC) 73/2008 and (EU) 557/2014 respectively).

2.4 Budgetary and financial management

2.4.1 Total budget 2023

IHI JU's total budget for 2023 was EUR **223 231 575** in commitment appropriations (CA) and EUR **225 848 975** in payment appropriations (PA). The budget execution of the commitment appropriations and the payment appropriations reached **92.65%** and **90.29%** respectively.

The IHI JU's 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 IHI such as renting of premises, IT needs, meetings, expenses related to external communication and costs of ex-post audits.

Titles 1 and 2 together form the administrative expenditure.

- Title 3 covers IHI's operational activities.

The IHI JU Governing Board approved the 2023 budget on 22 December 2022. The budget approved was EUR 215.3 million in commitment appropriations and EUR 219.5 million in payment appropriations. The budget was subsequently amended during 2023.

The budget amendment was approved by the Governing Board on 24 July 2023. The commitment appropriations were adjusted to include the carry overs from the previous year, of EUR 1.6 million. The total budget approved was EUR 216.9 million in commitment appropriations and EUR 219.5 million in payment appropriations.

2.4.2 Operational expenditure

IHI JU's operational budget (Title 3) reflects expenses linked to the implementation of the IHI JU research agenda. Here it should be noted that, since November 2021, IHI JU has managed three programmes in parallel:

IHI JU (under Horizon Europe, HE)

Starting from 30 November 2021, IHI JU manages a third programme, Horizon Europe.

As set out in the 2021 Council Regulation establishing IHI JU, the EU has committed to contribute EUR 1.170 billion from Horizon Europe to the IHI programme, for operational activities. The IHI JU industry partners have committed up to EUR 1 billion to IHI JU, and furthermore up to EUR 200 million can be committed by other organisations that decide to support the objectives of IHI in specific areas of research, by becoming contributing partners.

Regarding the commitment appropriations, in 2023 IHI JU launched the fourth and the fifth calls for proposals under the Horizon Europe programme. The committed amounts were EUR 83.4 million for IHI call 4 and EUR 115 million for IHI call 5.

IMI2 (under Horizon 2020, H2020)

As initially set out in the 2014 Council Regulation, the European Union has committed to contribute EUR 1.595 billion from H2020 to the IMI2 programme, for operational activities. At the end of 2021, the total EU commitments available at programme level over the lifetime of the IMI2 JU (2014-2021) for operational activities amount to EUR 1.4566 billion:

EUR 1.595 billion	(as initially set out in Council Regulation 557/2014)
- EUR 139 million	(reduction in 2019)
- EUR 6.7 million	(redeployment to climate related activities under Horizon 2020)
+ EUR 7.3 million	(50% of unused commitments since 2014, transferred from the administrative budget to the operational budget)
= EUR1.4566 billion	total EU commitments available at programme level over the lifetime of the IMI2 JU (2014-2021) for operational activities at the end of 2021

In 2023, payments related to H2020 projects amounted to EUR 118.3 million. The payment appropriations related to H2020 were mainly used by interim and final payments for projects of IMI2 - Calls 3-23.

IMI1 (under the Seventh Framework Programme, FP7)

FP7 was the EU's research and innovation funding programme for 2007-2013. Through FP7, the EU contributed EUR 966 million to the IMI1 research programme.

In 2023, payments related to FP7 projects amounted to EUR 7.3 million. The payment appropriations related to FP7 were used by payments for periodic or final reports for projects of IMI1 - Calls 6 and 8.

2.4.3 Administrative expenditure

The administrative budget implementation of the commitment and payment appropriations reached a level of 81.3% and 80.1% respectively.

At the end of 2023, the administrative budget was EUR 9.7 million in commitment appropriations and equal amount in payment appropriations. The implementation rates show a good achievement for administrative expenditure (Titles 1 and 2) in 2023, as a result of continuous actions in planning and monitoring the administrative budget.

Regarding Title 1, the budget implementation of the commitment and payment appropriations reached a level of 87.5% and 86.4% respectively.

Regarding Title 2, the budget implementation of the commitment and payment appropriations reached a level of 68.7% and 67.3% respectively.

A significant part of the Title 2 budget was used for expenditure linked to rent, IT, meetings, workshops, communication and studies, as support provided in managing the three programmes running.

The execution of budget related to formal meetings, expenditure in connection with operational activities and communication costs was impacted by meetings and events taking place mainly virtually.

IHI JU continued to execute its budget applying the principles of sound financial management, which resulted in several budget transfers between budget chapters, in line with operational needs. In 2023, there were no budget transfers between titles.

2.4.4 Overview of the total budget 2023 in EUR

IHI JU statement of revenue 2023 (EUR)

The table below shows the statement of revenue, per nature of revenue, indicating EFTA contributions on individual lines. The EFTA percentage used for 2023 was 2.89% for Horizon Europe and 2.45% for H2020.

CA = commitment appropriations PA = payment appropriations

Heading	Voted budget 2023		Amended budget 2023	
	CA	PA	CA	PA
EU contribution excl. EFTA	204 709 810	209 283 412	204 709 810	209 283 412
of which Administrative	4 709 810	4 630 031	4 709 810	4 630 031
of which Operational	200 000 000	204 653 381	200 000 000	204 653 381
Third countries contribution including EFTA	5 820 190	5 466 588	5 820 190	5 466 588
of which Administrative	40 190	119 969	40 190	119 969
of which Administrative third countries excluding EFTA	-	-	-	-
of which Operational	5 780 000	5 346 619	5 780 000	5 346 619
Industry financial contribution	4 750 000	4 750 000	4 750 000	4 750 000
of which Administrative	4 750 000	4 750 000	4 750 000	4 750 000
of which Operational				
Other revenue (assigned revenues - amounts recovered from beneficiaries)			6 348 975	6 348 975
SUB-TOTAL REVENUES	215 280 000	219 500 000	221 628 975	225 848 975
Reactivation of unused appropriations from administrative expenditure			825 232	
Of which from 2022			*825 232*	

Reactivation of unused appropriations from operational expenditure			777 368	
Of which from 2022			*777 368*	
TOTAL	**215 280 000**	**219 500 000**	**223 231 576**	**225 848 975**

IHI JU statement of revenue per member in 2023 (EUR)

For a complete overview, the table below shows the statement of revenue per Members' contributions, indicating the evolution of the budget approved, through budget amendments during 2023, per fund sources, current year, carry overs (reactivation) and assigned revenue, balancing the expenditure per titles.

CA = commitment appropriations. PA = payment appropriations

Chapter/line	Heading	Budget 2023.1		Budget 2023 Amendment 1		Assigned revenue		Final Amended Budget 2023.1	
		CA	PA	CA	PA	CA	PA	CA	PA
10	**European Commission contribution**								
1000	European Commission contribution (including EFTA contribution) for current year out of IMI2 budget	3 325 000	137 325 000		-4 000 000			3 325 000	133 325 000
1002	European Commission contribution (including EFTA contribution) for current year out of IHI JU budget	207 205 000	77 425 000		4 000 000			207 205 000	81 425 000
1001	European Commission - appropriations carried over from previous years			1 602 600				1 602 600	-
European Commission contribution - total		**210 530 000**	**214 750 000**	**1 602 600**	**-**			**212 132 600**	**214 750 000**
20	**JU members other than the Union contribution**								
2000	EFPIA contribution for current year out of IMI2 budget	3 325 000	3 325 000					3 325 000	3 325 000
2002	EFPIA contribution for current year out of IHI budget	697 500	697 500					697 500	697 500

2001	EFPIA - appropriations carried over from previous years							-	-
EFPIA contribution - total		**4 022 500**	**4 022 500**	**-**	**-**			**4 022 500**	**4 022 500**
2010	EuropaBio contribution for IHI current year	15 000	15 000					15 000	15 000
2011	EuropaBio - appropriations carried over from previous years							-	-
EuropaBio contribution - total		**15 000**	**15 000**	**-**	**-**			**15 000**	**15,000**
2020	COCIR contribution for IHI current year	356 250	356 250					356 250	356 250
2021	COCIR - appropriations carried over from previous years							-	-
COCIR contribution - total		**356 250**	**356 250**	**-**	**-**			**356 250**	**356 250**
2030	MedTech Europe contribution for IHI current year	356 250	356 250					356 250	56 250
2031	MedTech Europe - appropriations carried over from previous years							-	-
MedTech Europe contribution - total		**356 250**	**356 250**	**-**	**-**			**356 250**	**356 250**
20	**JU members other than the Union contribution - total**	**4 750 000**	**4 750 000**	**-**	**-**			**4 750 000**	**4 750 000**
	Assigned revenue (amounts recovered during the year from suppliers and projects)					6 348 975	6 348 975	6 348 975	6 348 975
	Total revenue	**215,280,000**	**219 500 000**	**1 602 600**	**-**	**-**	**-**	**223 231 575**	**225 848 975**
	Expenditure								
Title 1	Staff expenditure	6 488 000	6 488 000	-	-	-	-	6 488 000	6 488 000
Title 2	Infrastructure expenditure	3 012 000	3 012 000	-		152 799	152 799	3 164 799	3 164 799
Title 3	Operational expenditure	205 780 000	210 000 000	1 602 600		6 196 176	6 196 176	213 578 776	216 196 176
	Total expenditure	**215,280,000**	**219 500 000**	**1 602 600**	**-**	**6 348 975**	**6 348 975**	**223 231 575**	**225 848 975**

IHI JU statement of expenditure 2023 in commitment appropriations (EUR)

The table below shows the **commitment appropriations (CA) implementation** for the financial year 2023, reflecting the following fund sources: current year credits, recoveries from beneficiaries and re-activation of appropriations from preceding financial years.

In line with article 174.14 of the Single Basic Act and article 6 of the Commission Delegated Regulation (EU) 2019/887, the unused appropriations may be carried over up to the following three financial years. The unused appropriations shown in the table below, to be carried over, are estimated, being subject to Governing Board approval.

In line with article 26 of the Single Basic Act, any unused part of the contribution for administrative costs may be made available to cover the operational costs of the Joint Undertaking. As such, 50% of the 2023 unused administrative appropriations (EC part) is available to be carried over to operational expenditure in 2025. These appropriations are planned to be used for new calls under the programme Horizon Europe.

	Chapter	Amended budget 2023	Amended budget 2023 after transfers	Executed Budget 2023	%	Unused commitment appropriations 2023	Estimated to be carried over to 2024	Estimated Available for future use (N+3 rule)
Title 1 - Staff expenditure		**6 488 000**	**6 488 000**	**5 674 330**	**87%**	**813 670**	**406 835**	**-**
11	Staff in active employment	5 922 000	5 850 876	5 196 230	89%	654 646	327 323	
12	Miscellaneous expenditure on staff recruitment	5 000	6 800	6 800	100%	-	-	
13	Missions	144 000	144 000	33 296	23%	110 704	55 352	
14	Socio-medical structure	232 000	241 562	197 361	82%	44 201	22 100	
15	External staff	175 000	234 762	234 762	100%	-	-	
17	Representation expenses	10 000	10 000	5 880	59%	4 120	2 060	
Title 2 - Infrastructure expenditure		**3 012 000**	**3 164 799**	**2 173 337**	**69%**	**991 463**	**495 731**	**-**
20	Rent and related expenditures	698 000	853 074	653 250	77%	199 825	99 912	

21	IT (hardware and software)	1 090 000	1 095 230	869 382	79%	225 848	112 924	
22	Office equipment	5 000	2 680	-	0%	2 680	1 340	
23	Current administrative expenditure	124 000	144 000	89 650	62%	54 350	27 175	
24	Postage and telecommunications	40 000	40 045	11 416	29%	28 629	14 315	
25	Meetings	80 000	80 000	41 781	52%	38 219	19 110	
26	Expenditure in connection with operational activities	250 000	260 000	141 450	54%	118 550	59 275	
27	External communication information and publicity	300 000	300 000	202 408	67%	97 592	48 796	
28	Service contracts	425 000	389 770	164 000	42%	225 770	112 885	
Administrative expenditure Total Title 1+ Title 2		**9 500 000**	**9 652 799**	**7 847 666**	**81%**	**1 805 133**	**902 567**	**-**
Title 3 - Operational expenditure		**207 382 600**	**213 578 776**	**198 983 171**	**93%**	**14 595 605**	**638 071**	**-**
Previous years' calls		1 602 600	1 602 600	1 484 529	93%	118 071	118 071	-
Current year's calls		205 780 000	211 976 176	197 498 642	93%	14 477 534	520 000	-
GRAND TOTAL (Title 1 + Title 2 + Title3)		**216 882 600**	**223 231 575**	**206 830 838**	**93%**	**16 400 738**	**1 540 637**	**-**

IHI JU statement of expenditure – commitments carried forward (EUR)

For a complete overview of the unused appropriations, the table below shows the implementation of fund source C8 (representing the commitments carried forward from 2022).

Chapter	Appropriations 2023 carried forward	Appropriations Consumed	Unused commitment appropriations 2023	Estimated to be carried over to 2024	Estimated available for future use (N+3 rule)
Administrative expenditure Total Title 1+ Title 2	1 100 861	978 558	122 303	61 152	-
Title 3 - Operational expenditure					
GRAND TOTAL (Title 1 + Title 2 + Title3)	**1 100 861**	**978 558**	**122 303**	**61 152**	**-**

In terms of total commitment appropriations, the first estimate of the 2023 surplus that remains within the Joint Undertaking is EUR 16 523 041 in commitment appropriations with the following breakdown:

- EUR 8 282 600 unused commitment appropriations of operational activities related to programme Horizon Europe, to be carried over to financial year 2025.
- EUR 6 313 005 unused commitment appropriations stemming from recoveries related to closed programmes, FP7 and H2020. Of this, it is estimated to be carried over the amount of EUR 291 992 to financial year 2024, for potential ex-post audits' regularisations or interest on late payments.
- EUR 1 927 436 unused commitment appropriations of administrative activities. Of this, the amount of EUR 963 400, representing 50% of the EC part, it is envisaged to be carried over to financial year 2025.

IHI JU statement of expenditure 2023 payment appropriations (EUR)

The table below shows the **payment appropriations (PA) implementation** for financial year 2023, reflecting the following fund sources: current year credits, recoveries from beneficiaries and re-activation of appropriations from preceding financial years.

Chapter		Amended budget 2023	Amended budget 2023 after transfers	Executed Budget 2023	%	Unused commitment appropriations 2023	Estimated to be carried over to 2024	Estimated Available for future use (N+3 rule)
Title 1 - Staff expenditure		**6 488 000**	**6 488 000**	**5 602 300**	**86%**	**885 700**	**-**	**885 700**
11	Staff in active employment	5 922 000	5 850 876	5 196 230	89%	654 646		654 646
12	Miscellaneous expenditure on staff recruitment	5 000	6 800	4 974	73%	1 826		1 826
13	Missions	144 000	144 000	33 413	23%	110 587		110 587
14	Socio-medical structure	232 000	241 562	186 954	77%	54 609		54 609
15	External staff	175 000	234 762	174 850	74%	59 912		59 912
17	Representation expenses	10 000	10 000	5 880	59%	4 120		4 120
Title 2 - Infrastructure expenditure		**3 012 000**	**3 164 799**	**2 129 790**	**67%**	**1 035 010**	**-**	**1 035 010**
20	Rent and related expenditures	698 000	853 074	641 791	75%	211 283		211 283
21	IT (hardware and software)	1 090 000	1 095 230	930 430	85%	164 800		164 800
22	Office equipment	5 000	2 680	-	0%	2 680		2 680
23	Current administrative expenditure	124 000	144 000	79 326	55%	64 674		64 674
24	Postage and telecommunicat-ions	40 000	40 045	6 657	17%	33 388		33 388

25	Meetings	80 000	80 000	41 781	52%	38 219		38 219
26	Expenditure in connection with operational activities	250 000	260 000	96 075	37%	163 925		163 925
27	External communication information and publicity	300 000	300 000	106 711	36%	193 289		193 289
28	Service contracts	425 000	389 770	227 020	58%	162 750		162 750
Administrative expenditure Total Title 1+ Title 2		**9 500 000**	**9 652 799**	**7 732 090**	**80%**	**1 920 710**	**-**	**1 920 710**
Title 3 - Operational expenditure		**210 000 000**	**216 196 176**	**196 185 496**	**91%**	**20 010 680**	**20 010 680**	**-**
Previous years' calls			-	-		-		-
Current year's calls		210 000 000	216 196 176	196 185 496	91%	20 010 680	20 010 680	-
GRAND TOTAL		**219 500 000**	**225 848 975**	**203 917 585**	**90%**	**21 931 390**	**20 010 680**	**1 920 710**

In terms of total payment appropriations, the first estimate of the 2023 surplus that remains within the Joint Undertaking is EUR 21 931 390 in payment appropriations, with the following breakdown:

- EUR 20 010 680 unused payment appropriations of operational activities to be carried over to financial year 2025.
- EUR 1 920 710 unused payment appropriations of administrative activities. Out of it, the amount of EUR 1 094 135 is related to administrative commitments carried forward to 2024. These appropriations will be carried over to financial year 2024 depending on operational needs.

2.4.5 Budget transfers

In 2023, there were no budget transfers between titles. Budget transfers between chapters were authorised in 2023, which led to the following changes in commitment appropriations:

Chapter		Budget approved and assigned revenue (EUR)	Budget transfers (EUR)	Budget after transfers (EUR)
		Commitment Appropriations	Commitment Appropriations	Commitment Appropriations
11	Staff in active employment	5 922 000	-71 124	5 850 876
12	Staff recruitments - miscellaneous expenditure	5 000	1 800	6 800
13	Missions expenses	144 000		144 000
14	Socio-medical structure	232 000	9 562	241 562
15	External staff services	175 000	59 762	234 762
17	Representation	10 000	-	10 000
20	Office building and associated costs	850 754	2 320	853 074
21	Information technology (hardware and software)	1 090 000	5 230	1 095 230
22	Office equipment	5 000	-2 320	2 680
23	Current administrative expenditure	124 000	20 000	144 000
24	Telecommunication and postal expenses	40 045	-	40 045
25	Formal meetings	80 000		80 000
26	Administrative expenditure in connection with operational activities	250 000	10 000	260 000
27	External communication information and publicity	300 000	-	300 000
28	Service contracts	425 000	-35 230	389 770
	Total	**9 652 799**	**0**	**9 652 799**

2.4.6 Overview of total commitments outstanding

The summary of commitments outstanding at the end of 2023, for administrative and operational expenditure, was as follows:

	EUR
Commitments carried from previous year	787 966 178
De-commitments (-)	-87 948 419
Payments made during 2023 related to commitments carried forward (-)	-196 955 259
Commitments made during 2023	206 830 838
Payments made during 2023 related to commitments made during 2023 (-)	-6 962 326
Total commitments outstanding at the end of 2023	**702 931 011**

De-commitments made during 2023 were related to FP7 and H2020, and to Horizon Europe, related to call 1, call 2 and call 3, that were launched in 2022.

Commitments made during 2023 were EUR 206.8 million, of which operational commitments EUR 199.0 million and administrative commitments EUR 7.8 million. The operational commitments were related to Call 4 (EUR 83.4 million) and Call 5 (EUR 115 million) under Horizon Europe programme. In addition, the amount of EUR 0.5 million was committed for evaluation experts.

The payments made during 2023, related to commitments carried forward and commitments made during 2023, were operational payments of EUR 196.2 million and administrative payments of EUR 7.7 million. The operational payments were related to pre-financing payments under Horizon Europe and interim and final payments of projects under the FP7 and H2020 programmes.

2.4.7 Operational budget per programme

IHI JU's operational budget (Title 3) reflects expenses linked to the implementation of the IHI JU. It should be noted that since November 2021, IHI JU has been managing three programmes in parallel:

- IHI (under Horizon Europe)
- IMI2 (under H2020)
- IMI1 (under FP7)

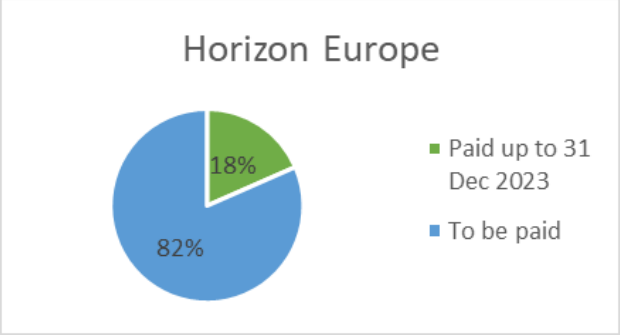
IHI (under Horizon Europe)

The table below outlines the breakdown per call of EU committed funds for IHI JU (Horizon Europe).

EUR '000

IHI JU (HE)	Committed EU (level 1)	De-committed	Paid up to 31/12/2023	To be paid
	1	2	3	4=1-2-3
Call 1	95 000	19 146	30 494	45 360
Call 2	21 929	1 454	8 190	12 285
Call 3	138 000	50 491	31 808	55 701
Call 4	83 350	-	-	83 350
Call 5	115 000	-	-	115 000
Total HE (IHI JU)	**453 279**	**71 092**	**70 491**	**311 696**

At the end of 2023, 18 % 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 Horizon Europe.



IMI2 (under Horizon 2020)

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

EUR '000

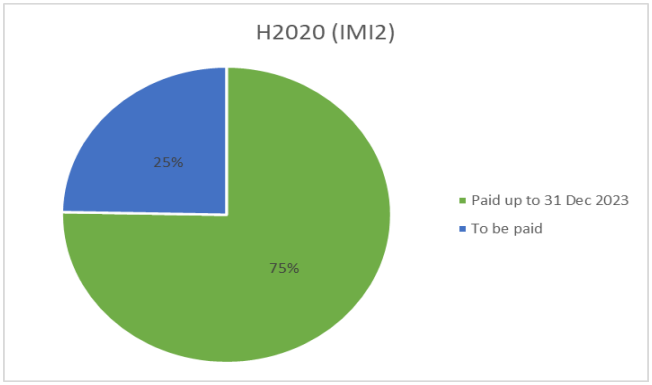
H2020 (IMI2)	Committed EU (level 1)	Committed AP and other members	De-committed	Paid up to 31/12/2023	To be paid
	1	2	3	4	5=1+2-3-4
Call 1	17 630			15 867	1 763
Call 2	114 090		10 051	104 040	-
Call 3	49 060	7 000		56 060	-
Call 4	1 130		52	1 078	-
Call 5	47 477			45 026	2 451
Call 6	46 496	200	153	43 264	3 278
Call 7	46 795		366	42 722	3 706
Call 8	47 462		3 089	41 102	3 271
Call 9	53 606	4 000		53 494	4 112
Call 10	173 874		262	151 433	22 179
Call 11	3 284		18	3 092	175
Call 12	64 052		25	56 777	7 249
Call 13	114 152		306	98 800	15 046
Call 14	82 310			49 817	32 493
Call 15	165 608			98 077	67 531
Call 16	35 184			28 288	6 896
Call 17	40 786			30 508	10 278
Call 18	74 866		6	38 036	36 824
Call 19	12 715			10 494	2 221
Call 20	133 009			39 978	93 031
Call 21	72 000		2	57 477	14 521
Call 22	11 427		2 702	7 806	919
Call 23	47 790		3	19 276	28 512
Total H2020 (IMI2)	**1 454 803**	**11 200**	**17 035**	**1 092 513**	**356 455**

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

In addition to the total amount to be paid, at the end of 2023, in ABAC there is the amount of EUR 2.1 million representing the open amount of the PERISCOPE project.

At the end of 2023, the total EU commitments available at programme level over the lifetime of the IMI2 programme (2014-2021) for operational activities amounted to EUR 1.4566 billion. Compared with the total EU committed at the end of 2023, the difference was EUR 18.8 million. This difference comes from the total de-committed amount of EUR 17.1 million, administrative carry overs to operational expenditure of EUR 1.6 million, and unused commitment appropriations of EUR 0.1 million, which could not be carried over as the programme was closed.

At the end of 2023, 75% 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).


H2020 (IMI2)
25%
75%
Paid up to 31 Dec 2023
To be paid

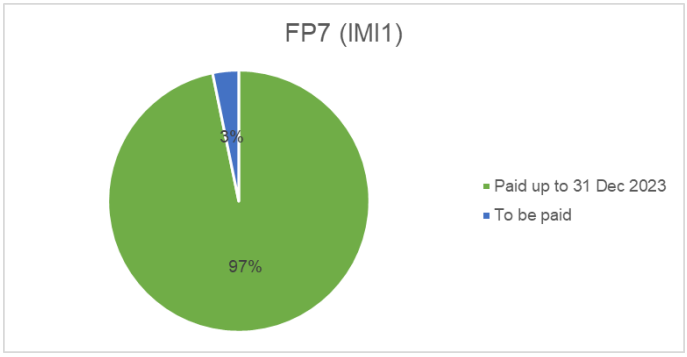
IMI1 (under FP7)

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

EUR '000

FP7 (IMI1)	Committed (level 1)	De-committed 2023	Committed amount updated at 31/12/2023	Paid up to 31/12/2023	To be paid
	1	2		3	4=1-2-3
Call 1	116 082	1 475	114 607	114 607	-
Call 2	85 765	549	85 216	85 216	-
Call 3	112 854	306	112 547	112 548	-
Call 4	97 944	776	97 168	97 168	-
Call 5	80 021	644	79 377	79 377	-
Call 6	125 417		125 417	119 295	6 122
Call 7	13 000	936	12 064	12 064	-
Call 8	98 774	5 911	92 863	85 064	7 799
Call 9	56 441		56 441	50 571	5 870
Call 10	6 100	501	5 599	5 599	-
Call 11	173 410	21 192	152 218	140 932	11 286
Total FP7 (IMI1)	**965 808**	**32 291**	**933 517**	**902 440**	**31 076**

At the end of 2023, 97% 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).



2.5 Financial and in-kind contributions from Members other than the Union

This chapter presents the contributions of members other than the Union for the three different programmes IHI JU is managing in parallel (IMI1, IMI2, IHI).

IHI JU is a public-private partnership between the EU (represented by the European Commission) and life science industries represented by COCIR, EFPIA (also representing Vaccines Europe), EuropaBio and MedTech Europe (hereafter 'the members other than the Union'). IHI JU's prior initiatives, the IMI1 and IMI2 programmes, were public-private partnerships between the EU and the European pharmaceutical industry represented by EFPIA.

All IMI and IHI projects are based on the same co-funding principle between public and private funds:

- In each IMI/IHI project, legal entities eligible for JU funding receive financial support from IMI/IHI to fund their project activities.
- Members other than the Union contribute their own resources to the projects. Some projects also include the own resources of contributing partners (for IHI projects) or Associated Partners (for IMI2 projects). These contributions consist of in-kind and financial contributions as explained below in the respective sections of each programme.

This chapter presents the commitments made by members other than the Union as well as Associated Partners / contributing partners (when applicable) at call and project launch, and actual contributions made during the lifetime of the projects. The equivalent EU commitments / actual contributions are also provided throughout this chapter to facilitate the comparison between public and private contributions, which should match by the end of each respective programme.

Members other than the Union and Associated Partners / contributing partners are contractually obliged to report to the Programme Office all costs that they incur in IMI and IHI projects. The Programme Office controls the eligibility and regularity of the contributions and carefully monitors the development of the total contributions to the three programmes.

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

2.5.1 IMI1 programme

IMI1 EU and EFPIA commitments

This section highlights the commitments pledged by EFPIA companies to the 59 projects in the IMI1 portfolio. These commitments are made up of:

- in-kind contributions[9], i.e. costs incurred by EFPIA companies in the implementation of the IMI1 projects for researchers, research equipment, and materials;
- financial contributions at project level to beneficiaries receiving JU funding.

The table below shows the EU and EFPIA commitments to IMI1 at the end of 2023.

IMI1 million EUR	EU commitment	EFPIA commitment
Number of projects	59	
Total on 31/12/2023	933.5	914.1

IMI1 EU and EFPIA validated contributions - comparison by year

As of 31 December 2023, EFPIA contributions of EUR 816.3 million had been formally validated (checked by IHI staff and / or audited by external auditors). The table below gives an overview of validated IMI1 contributions, in EUR millions, 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	112.4	103.5
2019	62.3	55.2
2020	62.1	49.0
2021	23.2	29.1
2022	43.6	42.2
2023	7.3	7.5
Total	**851.4**	**816.3**

[9] In-kind contribution is defined as follows: 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'.

(*) excluding pre-financing

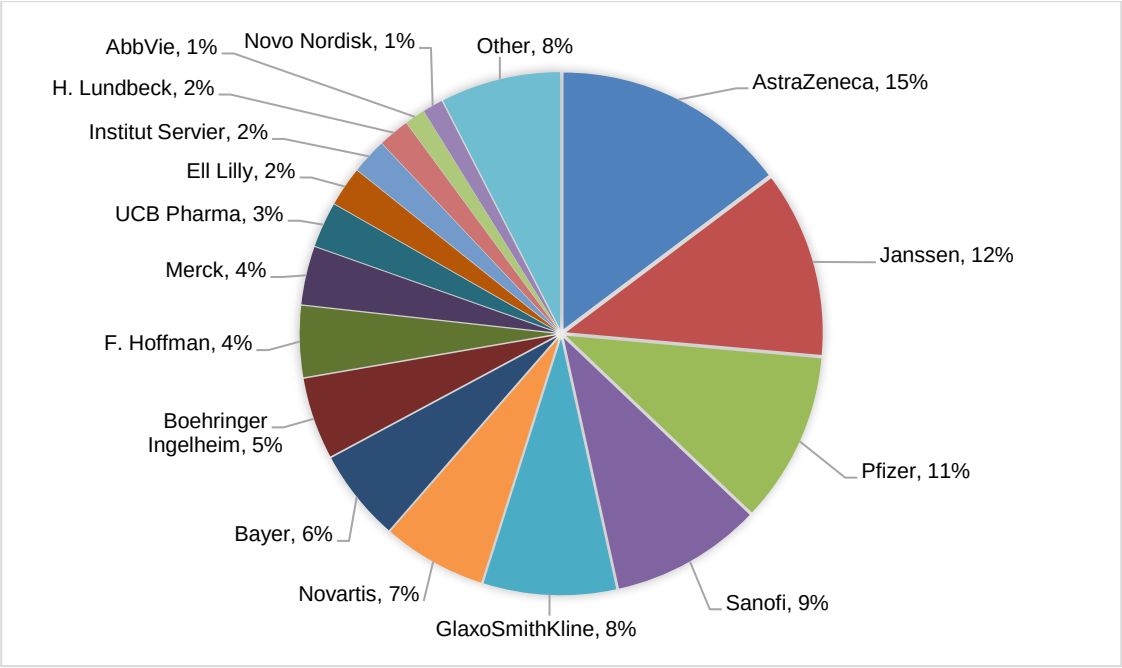
The difference between validated EU cost claims and EFPIA contributions results from the fact that, in some projects, tasks for the different consortium partners do not run in parallel but are often sequential.

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 2023, there was 1 project still running out of the initial 59 IMI1 projects, as well as 3 projects that ended but were not yet closed.

In 2023, the IHI Programme Office continued to closely monitor the overall commitments of EFPIA participants. The outstanding contributions should be reported by 2025 as the last IMI1 (FP7) project is foreseen to end in 2024.

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, Amgen, Astellas, Aridis, Alaxia, Almirall, Basilea Pharmaceutica, Biogen, Bristol-Myers, Chiesi Farmaceutici, Da Volterra, Eisai, Employers' Union, Evotec, Farmaindustria, Genzyme, Grünenthal, Ipsen, Islensk, Laboratorios del Dr. Esteve, The Medicines Company, Merck Sharp & Dohme, Orion, Polyphor, Seqirus, Sigma-Tau, Silicon Biosystems, Spexis, Takeda, Teva Pharmaceuticals Europe, Verband forschender Arzneimittelhersteller, Vifor.

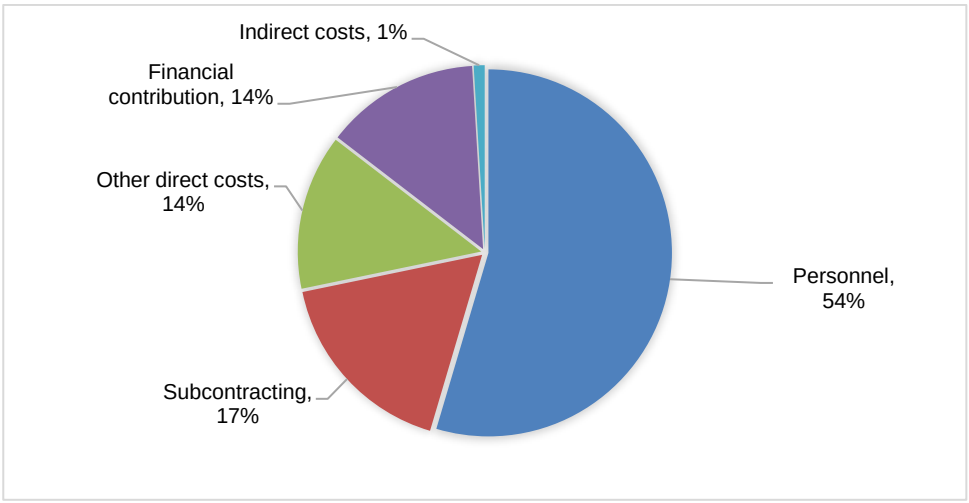
IMI1 EFPIA contributions - by cost category

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.



2.5.2 IMI2 programme

IMI2 EU, EFPIA and Associated Partner commitments

This section highlights the commitments pledged by EFPIA companies and Associated Partners (APs) in IMI2 projects. Both EFPIA and Associated Partner commitments include in-kind contributions, as well as financial contributions directly to the IMI2 programme's operational costs, or at project level to beneficiaries receiving JU funding.

The last IMI2 Grant Agreements were signed in 2021, bringing the total number of IMI2 projects to 123. At the end of 2023, the total commitments to the IMI2 programme were:

- EUR 1 452.1 million in EU funding.
- EUR 1 506.1 million commitments from EFPIA companies (EUR 1 302.6 million) and Associated Partners (EUR 203.5 million).

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

IMI2 million EUR	EFPIA commitment	AP commitment	Total EFPIA + AP commitment	EU commitment
Number of signed projects	123			
Up to 31.12.2022	1 296.7	202.7	1 499.4	1 452.1
2023	+5.9	+0.8	+6.7	00
Total on 31/12/2023	**1 302.6**	**203.5**	**1 506.1**	**1 452.1**

Compared to 2022, the EU commitment remained at EUR 1 452.1 million while the commitment from EFPIA and APs increased from EUR 1 499.4 million to EUR 1 506.1 million, mainly following the amendment of an ongoing IMI2 project (3TR) where a new EFPIA company joined and committed additional in-kind contribution to the project.

Out of the overall commitment of EUR 1 452.1 million from the EU over the programme lifetime, at least 70% - which is EUR 1 016.4 million - should be matched by industry contributions incurred in the EU and H2020 Associated Countries, by the end of the IMI2 programme. At the end of 2023, from the total committed by EFPIA and Associated Partners, EUR 1 044.1 million was from the EU and H2020 Associated Countries, thus fulfilling the minimum requirement of 70%.

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

In 2023, EFPIA companies and APs had contributed EUR 218.3 million to the IMI2 programme (amount certified by external auditors and validated by IHI). For comparison, accepted cost claims for JU funding from beneficiaries stood at EUR 190.04 million for the same period. The following table shows the validated EFPIA and Associated Partner contributions as well as validated cost claims from beneficiaries receiving EU funding.

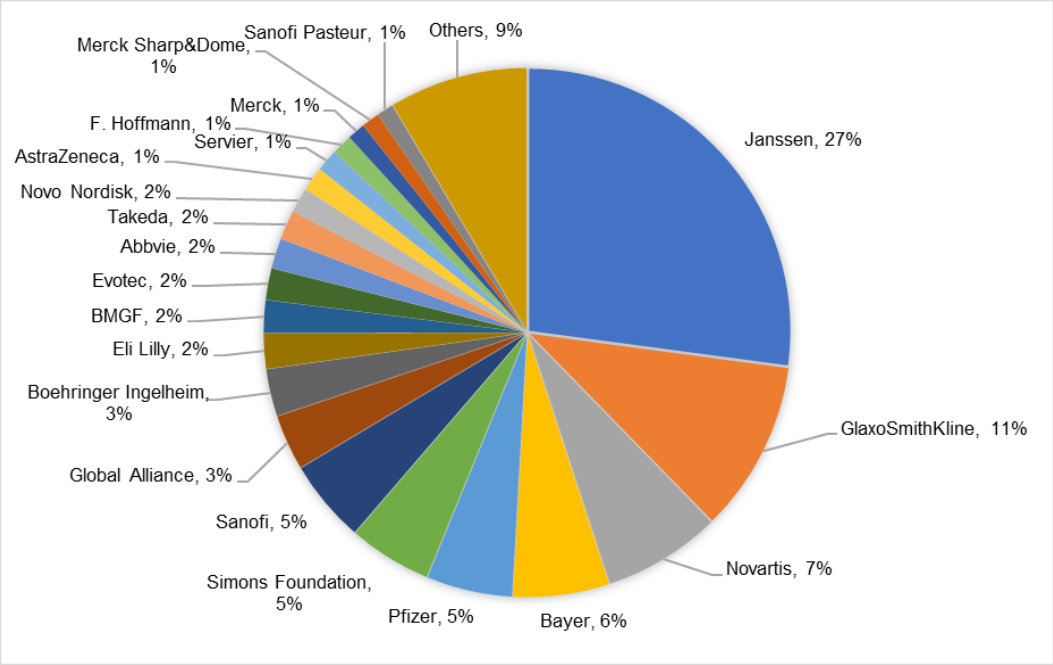
	EFPIA contributions	Associated Partner contributions	Total validated EFPIA and Associated Partner contributions (1)	Validated cost claims from beneficiaries receiving EU funding (2)
2016	47.3	2.9	50.2	13.0
2017	35.3	1.0	36.3	26.3
2018	47.7	1.3	49.0	50.4
2019	75.5	8.7	84.2	80.7
2020	115.6	28.2	143.8	128.3
2021	201.6	52.4	254.0	161.7
2022	223.2	24.5	247.7	180.0
2023	198.6	19.7	218.3	190.0
Total	**944.8**	**138.7**	**1 083.5**	**830.5**

(1) Includes EUR 11.2 million paid directly by EFPIA and AP to IMI for projects PERISCOPE, DRIVE and HARMONY

(2) excluding pre-financing

IMI2 EFPIA and Associated Partner contributions - by organisation

Up to the end of 2023, there were more than 80 EFPIA companies and Associated Partners contributing to IMI2 projects. As the organisational breakdown below shows, 27 % of the IMI2 contribution is provided by Janssen. This is because Janssen has a high involvement in IMI2 projects (more than 50 projects). The remaining 73 % contribution comes from other EFPIA companies and Associated Partners. 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 1 083.5 million certified by external auditors and validated by IHI.



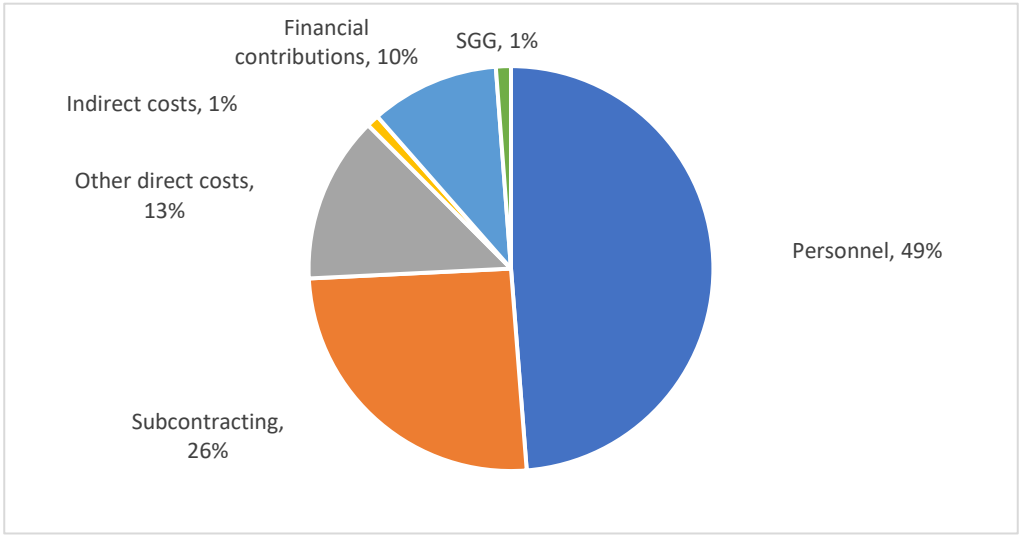
Organisations under 'other' include Abbott, AC Immune, Actelion, Amgen, Asociacion national empresarial, Biogen, bioMérieux, Bristol-Myers, Celgene, Cepheid, Charles River, Children's Tumor Foundation, Coalition for Epidemic Preparedness Innovation, Cohen veterans bioscience, CSL Behring GmbH, CureVac, Da Volterra, Deutsches Zentrum fur Infektionsforschung, Diamond Light Source, EFPIA, Ellegaard Gottingen, Esteve Pharmaceuticals, Gates Ventures LLC, GE Healthcare, Grünenthal, H. Lundbeck, Helmsley Charitable Trust, Icon Clinical Research, Illumina Cambridge, Imcyse, Institut Pierre Fabre, Intercept Pharma Europe, Intervet, Ipsen, JDRF, JLP Health, Kungliga, Labcorp Clinical Development, Labcorp early development, Leo Pharma, Life Molecular Imaging, Link2Trials, Lonza, Ludwig-Maximilians-Universitaet Muenchen, Menarini, MSD, MMV Medicines, Ontario Institute for Cancer Research, Orion, Otsuka Novel Products, Pharma Mar, Psychogenics, Rentschler, Roche, Seqirus, Spark Therapeutics, Teva, Helmsley Charitable Trust, Association of British Pharmaceutical Industry, Transgene, UCB, VFA, Vifor, Viscofan, Zoetis.

IMI2 EFPIA and Associated Partner 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 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.

2.5.3 IHI programme

Contributions from JU Members other than the Union in 2023

This section highlights the commitments pledged by COCIR, EFPIA (also representing Vaccines Europe), EuropaBio and MedTech Europe (hereafter the IHI private members) as well as contributing partners to the IHI programme. These commitments are made up of:

- in-kind contributions to operational activities (IKOP)[10], i.e. costs incurred by IHI private members and contributing partners in the implementation of IHI projects for researchers, research equipment, and materials;
- financial contributions (FC) made by IHI private members and contributing partners to IHI project beneficiaries eligible to receive funding;
- in-kind contributions to additional activities (IKAA)[11], i.e. costs incurred by IHI private members in the implementation of additional activities, either contributing to IHI projects specifically (project-specific IKAA) or to the IHI JU Programme more generally (programme-specific IKAA). (not applicable for contributing partners).

While IHI private members can contribute all types of contributions (IKOP, IKAA, FC), contributing partners can only contribute IKOP and FC, not IKAA.

During 2023, the first grant agreements were signed for IHI calls 1, 2 and 3, bringing the total number of IHI projects to 16. The table below shows the commitments to the IHI programme (to projects and programme-level IKAA) from the EU, private members, and contributing partners as of the end of 2023.

IHI programme million EUR	Private members (PM) commitment	Contributing partners (CP) commitment	Total PM + CP commitment	EU commitment
Signed projects	139.8	50	189.8	183.8
IKAA (programme level)	26.4		26.4	
TOTAL on 31/12/2023	**166.2**	**50**	**216.2**	**183.8**

At the end of 2023, the total commitments to the IHI programme were:

- EUR 183.8 million in EU funding to IHI signed projects;

[10] In-kind contributions to operational activities ('IKOP') is defined in Article 2.8 of the Council Regulation (EU) 2021/2085 as follows: 'contributions made by private members and contributing partners, their constituent or affiliated entities consisting of the eligible costs incurred by them in implementing indirect actions less the contribution of the IHI JU and of the participating states of that JU to those costs'.

[11] In-kind contributions to additional activities ('IKAA') is defined in Article 2.10 of the Council Regulation (EU) 2021/2085 as follows: 'contributions made by the private members, their constituent or affiliated entities consisting of the costs incurred by them in implementing additional activities less any contribution to those costs from the Union and from the participating states of the IHI JU'. More information on IKAA can be found in the IHI JU Guidelines for in-kind contribution to additional activities (IKAA).

- EUR 216.2 million commitments from IHI private members (EUR 166.2 million) and contributing partners (EUR 50 million), consisting of
  - EUR 189.8 million commitment to IHI signed projects from IHI private members (EUR 139.8 million) and contributing partners (EUR 50 million); and
  - EUR 26.4 million commitment from IHI private members as IKAA to the IHI JU Programme[12].

The commitment of EUR 139.8 million to signed projects from IHI private members includes EUR 57.9 million from EFPIA (also representing Vaccines Europe), EUR 42.3 million from MedTech Europe, EUR 36.6 million from COCIR and EUR 3 million from EuropaBio. The total commitment of EUR 189.8 million from IHI private members and contributing partners to IHI projects is composed of in-kind contributions to operational activities (IKOP), financial contributions (FC) and in-kind contributions to additional activities (IKAA).

The following table provides an overview per IHI call of the commitment composition from IHI private members and contributing partners to IHI signed projects.

IHI million EUR	IKOP	FC	IKAA	Total commitment (PM + CP)
Call 1	47.9	5.1	15.0	68.0
Call 2	16.7	2.2	1.0	19.9
Call 3	82.7	13.6	5.6	101.9
Total	**147.2**	**20.9**	**21.7**	**189.8**

In each IHI project, at least 45% of the project's eligible costs and costs for additional activities must be provided by contributions from IHI private members and/or contributing partners.

Values of IKOP and IKAA

There was no IKOP to report by IHI Private Members and contributing partners in 2023. The first IHI grants were signed in 2023 and as a result, the first contributions in terms of IKOP and FC will be reported in 2024 together with the first project periodic reports.

IKAA can be of two types:

- Project-specific additional activities contribute towards the achievement of objectives of the IHI JU funded projects, or the dissemination, sustainability, or exploitation of IHI JU project results.
- Programme-specific additional activities contribute to the uptake of results from funded projects (by IHI JU or its preceding initiatives, i.e. IMI1 JU or IMI2 JU) or have a significant added value for the Union.

The first reporting of IKAA took place in 2023.

In 2023, IHI private members contributed EUR 129 615 to the IHI programme in term of in-kind contribution to additional activities (amount certified by external auditors and validated by the GB).

Annex 10 provides details on the reported and validated IKAA until end 2023.

[12] See the IKAA Plan in the WP 2024 adopted on 14 December 2023.

2.6 Administrative procurement and contracts

The majority of IHI's contractual commitments in 2023 were concluded on the basis of multiannual framework contracts (FWCs). In terms of volume, the FWCs were most used in the field of IT, human resources, 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 2023 outside existing FWCs with a value exceeding EUR 15 000.

Subject of the contract	Type of contract[13]	Contractor	Tender procedure	Signature date	Amount (EUR)
Analysis of Bibliometric Data and Other IMI/IHI Project Output Indicators	Multiannual framework contract	Nature Customer Service Centre GmbH	Open procedure	27/10/2023	508 000.00

In 2023, IHI concluded the following service level agreement (SLA):

Subject of the contract	Type of contract[14]	Parties	Signature date
BOA Procurement	SLA	Clean Aviation, Circular Bio-based Europe, Europe's Rail, Clean Hydrogen, Innovative Health Initiative, Key Digital Technologies, Single European Sky ATM Research 3, European Smart Networks and Services, EuroHPC and Global Health EDCTP3 Joint Undertakings	21/11/2023

[13] Framework Contract, SLA, others.

[14] Framework Contract, SLA, others.

2.7 IT and logistics

IT activities in 2023 were mainly focused on improving inter-JU collaboration in the scope of back-office arrangements (BOA), the migration of the IT infrastructure to the new FWC supplier, and the further development of appropriate and secure IT and business support tools, including their evolution towards IHI JU.

Management of the common IT infrastructure and BOA

IHI JU shares a common IT infrastructure and facilities with seven other joint undertakings and participates in the common IT governance. Following the common annual work plan, the most notable achievements in 2023 are:

- Onboarding of the awarded contractor of the JUs' common call for tenders for IT managed services. Two new Joint undertakings (SNS and ECDTP3) co-located in the White Atrium building and EuroHPC (Luxemburg) are now part of the shared services as well.
- Migration of the common and IHI-specific IT infrastructure to the Cloud II DPS as successor of EFSA FWC for IaaS.
- Back-office arrangements

As co-lead of BOA IT, IHI JU participated actively in consultations and preparations for formalising the BOA, including in the identification of potential areas for enhanced collaboration and synergies and the definition of the IT service catalogue, structured in six service groups:

1. Inter-JU IT Governance: this service group coordinates common ICT activities and services, planning, effort allocation, decision-making and reporting.
2. Management of shared ICT infrastructure: this service group ensures the provision of ICT infrastructure (servers, networks, IT security infrastructure, cloud services, teleconferencing systems, Wi-Fi provision, landlines and Internet infrastructure) and related services to the JUs.
3. Management of ICT tools, services and contracts: this service group is related to the management of services (tools, systems, contracts) provided by the European Commission.
4. Workplace services provision: this service group ensures the provision of configured JUs specific ICT hardware, licenses, workplace services and end user support.
5. Security and compliance management.
6. ICT activities specific per JU: can include development of specific software in relation with the JU's mission and objectives.

Enhancements of in-house applications

IHI JU's in-house applications were continuously maintained, updated, and further developed to serve the evolving business needs. Major new enhancements and change requests were as follows:

- SOFIA (Submission of Information Application) will continue to complement IHI JU's main grant management software suite "eGrants", provided by the European Commission. Following a gap analysis, in 2023 we initiated development of two new modules:
- "Project profile" covering the need to gather IHI-specific participants and stakeholder types and affiliations, as well as the core and secondary public health need that will be addressed by the project (listed as WHO priority areas).
- Project outputs collection – a new KPI survey tool, designed to collect the data for IHI-specific KPIs. The KPI reporting will be enforced by making it part of the periodic and final reports templates. All the important lessons learned from the similar IMI2 tool were considered during this implementation (final implementation is due in 2024).

In parallel with the new developments, IHI JU continued with the standard maintenance, including checks and updates of all underling packages and libraries. A number of change requests were implemented as well, mainly linked to improvements in IMI2 in-kind reporting and processing front-end user interfaces.

- Data Warehouse and Qlik sense reporting
- Combining all available data in a central repository, serving the organisation as a single point of truth facilitates a lot the work for the call coordination team, science and financial officers.
- The IHI data warehouse merges data from SOFIA, the SEP datastore, the EC eGrants data warehouse, the website content management system (CMS), publications data from Clarivate, projects results from all previous AARs, IHI applicants' affiliation (Excel files filled by the proposal coordinators and uploaded in SEP as PART B, Section 4), topic ideas from the new respective tool, and some other reference files with data not available in IHI operational application.
- The data warehouse facilitates data synchronisation of IHI and IM2 grant agreements from eGrants to SOFIA.
- All existing Qlik sense reports were redesigned to accommodate the IHI proposals and projects data. A separate Qlik sense channel was created to serve the data needs of IHI industry partners.

Business support tools

In 2023 a new tool for the annual appraisal exercise was developed under the lead of HR. As of 2024, the appraisal exercise will be handled in a completely new in-house developed software tool eCDR (electronic Career Development Report), based on the modern PowerApps platform.

It complements the main HR system, SYSPER (owned by EC, DG HR) and covers the complete process from staff self-assessment, appraisal report, setting the objectives etc.

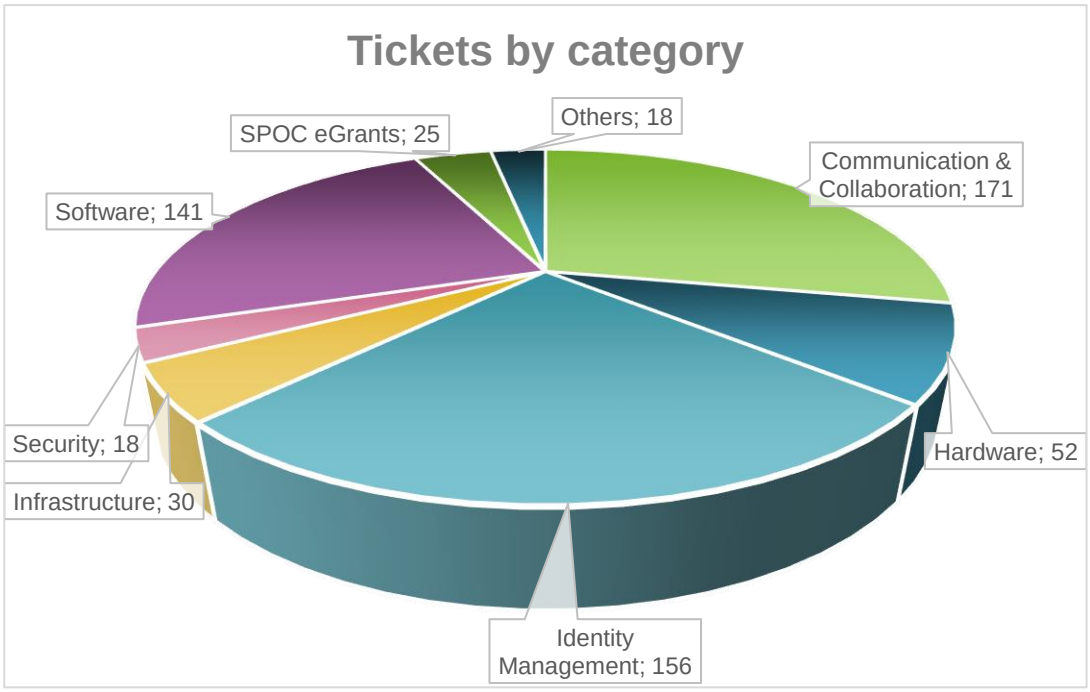
Cybersecurity and collaboration with Computer Emergency Response Team for the Institutions, Bodies and Agencies of the European Union (CERT-EU)

The main areas of collaboration with CERT-EU in 2023, coordinated by IHI on behalf of the JUs, were: 1) a security assessment on IHI M365 tenant, 2) IHI official website penetration test, 3) external assessment on our compliance with CERT-EU logging guidance and 4) end-users phishing awareness exercise.

The resulting reports provided valuable input on IHI's cybersecurity maturity level and recommendations for further improvements. After detailed technical analysis, supported by the external contractors for IT managed services and software development, the Programme Office created action plans in order to monitor the implementation of the suggested measures.

Service desk requests

In 2023, a total of 611 requests were handled by the IHI IT Helpdesk. The following graph depicts the various categories assigned to the tickets:


Tickets by category
Others; 18
SPOC eGrants; 25
Communication & Collaboration; 171
Software; 141
Security; 18
Infrastructure; 30
Hardware; 52
Identity Management; 156

2.8 Human resources

2.8.1 HR management

Staff selection and recruitment

The IHI JU staff establishment plan (SEP) allows for 39 temporary agents and 15 contract agents, in total 54 staff members. On 31 December 2023 there were 44 positions occupied: 34 out of 39 temporary agents (87%), and 10 out of 15 contract agents (67%).

The table below provides a summary of the staff planning:

	Positions planned in SEP	Positions filled on 01.01.2023	Resignations / end of service in 2023	Recruitment / appointment in 2023	Positions filled on 31.12.2023
Temporary agents	39	36	4	3	34
Contract agents	15	13	6	2	10
SNEs	N/A	N/A	N/A	N/A	N/A
Total	54	49	10	5	44

Five new staff members joined IHI in 2023.They were recruited either via existing reserve lists or via new selection procedures.

In 2023, IHI JU launched and organised three new selection procedures and completed one selection procedure launched at the end of 2022, as follows:

- 1 Financial Officer (temporary agent);
- 1 Programme Officer – Call coordinator (temporary agent);
- 1 Financial Assistant (contract agent);
- 1 Human Resources Support Officer (contract agent).

The financial officer position was filled in June 2023, and the last three mentioned positions will be filled in the first trimester 2024.

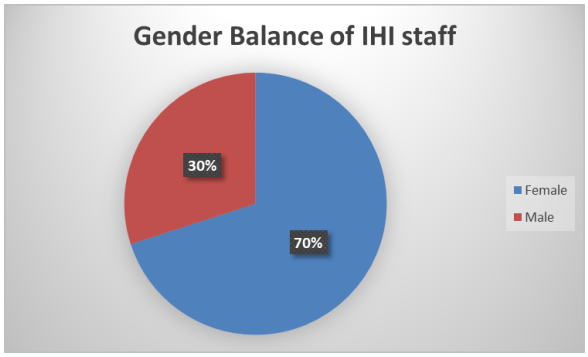
The IHI JU traineeship programme 2023 was launched in November 2022 and finalised in January 2023, which gave the opportunity to a trainee to join the organisation in February 2023 for a period of 6 months. The traineeship provided the opportunity for the trainee to gain hands-on professional experience and to develop and strengthen skills and competences.

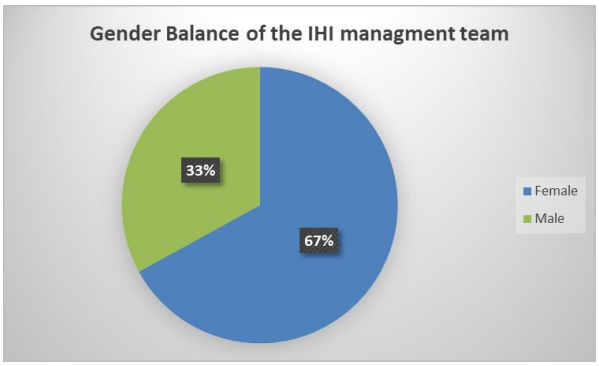
Staff turnover in 2023 was 18.52% (10 staff members), mainly due to the Programme Office staff moving to the Executive Agencies or the European Commission as officials.

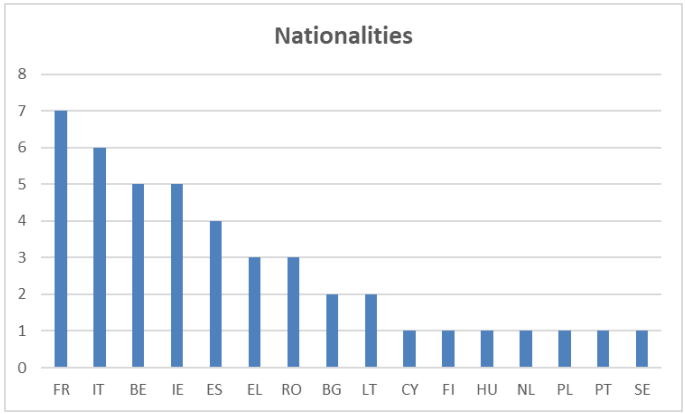
To cope with the peak period of workload, and vacant positions, IHI JU concluded – via the EC framework contract for interim services – three short-term interim contracts to address specific needs of the Programme Office.

The two graphs below show the gender and geographical balance within IHI JU on 31 December 2023. In detail, 70% of the staff are women, whereas 30% are men; and 2/3 of IHI JU management team are women.

Regarding the geographical balance, IHI JU ensures a wide representation of EU countries among its staff. In 2023, 16 EU nationalities were represented in IHI JU.







Learning and professional development

The IHI JU promotes the continuous development of its staff, and to this end organises training activities to (i) support the personal and professional growth of IHI staff, and (ii) to keep their knowledge up to date. In 2023, the HR team, in collaboration with its staff, organised several training activities, as follows:

- Operational and legal framework: staff followed general training on IKAA, IHI contribution types, the new SOFIA user interface to track project participants and healthcare priorities, Horizon Europe and IHI performance monitoring framework, and Horizon Europe - GAP training.
- Data protection: two training sessions were organised to raise awareness on the importance and legal obligations on the protection of data. One session focused on data protection rules in practice, and a second one focused on the management of personal data breaches.
- In-house soft skills and specific training courses were organised by IHI on different subjects, such as: the appraisal exercise, performance management, and reclassification to enhance IHI staff awareness and understanding of HR procedures and processes; as well as sessions on the role of confidential counsellors and induction training sessions for newcomers. In addition, some in-house training courses were organised by IHI JU and delivered in cooperation with other joint undertakings, for example: ethics and integrity trainings, anti-fraud courses and prevention of psychological and sexual harassment training for managers.

- Online ‘soft’ and ‘hard’ skills courses, language training and lunchtime well-being conferences and courses were followed using the ‘EU Learn’ catalogue which helped IHI staff in the selection of the trainings according to their learning needs.

Staff well-being and new ways of working

To promote and guarantee staff well-being, IHI fully implemented the European Commission’s decision on working time and hybrid working and conducted a staff survey to assess the impact of the new ways of working. The survey showed that IHI staff is very satisfied with the new ways of working (overall satisfaction rate 4.15 out of 5). In detail, the survey results showed that IHI staff felt that the organisation cared about their physical and mental well-being. The staff also welcomed the flexibility provided by the teleworking policy which improved their work-life balance and wellbeing.

In the second semester of 2023, the first IHI Staff Engagement survey was launched to measure IHI JU staff engagement, well-being, communication and cooperation. Overall respondents expressed a high satisfaction rate; they declared being quite satisfied and committed to work for IHI JU and they appreciated the recognition of their work and accomplishments. Nevertheless, some actions are needed in order to further improve IHI staff work-life balance and to balance the workload.

Reclassification exercise

The reclassification exercise is a valuable tool to recognise and promote the performance of highly qualified staff members. In accordance with the Staff Regulations the reclassification exercises for temporary and contract agents successfully took place in 2023. As a result, four staff members (two temporary agents and two contract agents) were reclassified to the immediate higher grade.

2.8.2 Legal framework

Staff implementing rules (SIR) implemented in 2023

In 2023, IHI HR continued strengthening the legal framework of the IHI JU and implemented the General Implementing Provisions (GIP) on the conduct of administrative inquiries and disciplinary proceedings.

Title of the SIR	Reference of the GB decision
GIP on the conduct of administrative inquiries and disciplinary proceedings	IHI-GB-DEC-2023-05

2.8.3 Efficiency gains and synergies

The Council Regulation establishing IHI and the other Joint Undertakings (SBA) states that the JUs shall achieve synergies via the establishment of back-office arrangements (BOA), operating in some identified areas. The Regulation also underlines that these synergies should be implemented where screening of resources has proved to be efficient and cost effective, while respecting the autonomy and the responsibility of each Authorising Officer.

The JUs jointly commissioned an independent analysis (provided by an external contractor in June 2022) to identify the areas most appropriate for the establishment of formal back-office arrangements.
The study concluded that the estimated efficiency gains in terms of full time equivalent (FTE) savings were modest for most synergies, but there were potential benefits in terms of harmonisation of current practices, standardisation of procedures, establishment of critical mass for effective negotiation, coordination and cost savings. The largely preferred model for the BOA among JUs is a setup with one JU taking the lead in coordinating tasks with one backup JU, organising the work among staff of several JUs and having a clear scope and decision-making power.

In 2023 back-office arrangements were followed up and further developed.

BOA Procurement

This BOA was established with the objective of centralising administrative procurement capability and processes to maximise open tenders for award of inter-JU FWCs and middle value negotiated procedures.

The concept note was approved by the GB and the SLA was signed by the ED in November 2023.
IHI has joined the following common procurements in 2023:

- Building rental
- Managed IT services
- Audit & accounting support services
- Catering services in the White Atrium
- Coffee machine rental for the common meeting rooms

BOA ICT

Clean Hydrogen JU is the lead JU and IHI JU is the co-lead for the BOA ICT. IHI JU participated actively in consultations and preparations for formalising the BOA, including in identification of potential areas for enhanced collaboration and synergies and definition of the IT service catalogue[15]:

The BOA ICT concept note was prepared and is under the approval by the IHI JU GB. The concept note covers the following service areas:

- Inter-JU IT governance
- Management of shared ICT infrastructure
- Management of ICT tools, services and contract
- Workplace services (e.g. IT helpdesk)
- Security and compliance management (incl. cybersecurity)

These activities or services are either provided within the JU and/or with the support of external service provider, or fully delivered by others (e.g. EC services).

HR synergies and BOA HR support services

Due to the increased complexity of IHI projects and the necessity to manage the large and complex legacy from IMI1 and IMI2 projects, the Programme Office paid particular attention to the efficiency and cost-effective management of its resources. During 2023, IHI proceeded with the reshuffling of its internal resources in order to back up some functions and strengthen the collaboration with other Joint Undertakings through arrangements and mechanisms of pooling expertise for specific time-bound tasks.

[15] See IT section 2.7 above for details.

In detail, in 2023, IHI optimised efficiency gains and synergies with the other JUs by (i) sharing reserve lists to shorten time to recruit; (ii) providing expertise and resources (e.g. IHI staff were panel members in several selection procedures of other JUs); (iii) supporting new Joint Undertakings during their on-boarding/start-up phase by providing guidance, advice and templates; (iv) organising training courses of general interest for all JUs (e.g. ethics and integrity, respect and dignity at work place for JUs managers, etc); (v) contributing to the development of a common legal framework among JUs by sharing ED and GB decisions on diverse regulatory topics; and (vi) supporting the communication campaign on the role of confidential counsellors (CCs) and presentation of the newly appointed CCs to all JU staff members.

IHI JU kept exercising the back-up role for the HR back-office arrangements and supports the lead JU, CBE JU. In addition, in 2023 the JUs continued sharing the human-resource IT tools, for example the e-recruitment tool SYSTAL whose use was granted to two other JUs; Chips JU and EDCTP3 JU, resulting in a total of 7 JU's using the same e-recruitment platform; SYSPER, etc; sharing information and best practices with the different JUs e.g. through weekly HR officer meetings, and adopted a common approach to implementing rules of the EU staff regulations.

BOA HR will implement services in three main areas of HR Support: recruitment, HR legal framework and HR digitalisation[16].

BOA Accounting

BOA Accounting Services is in place since 1 December 2022. Accounting officer services are provided by three JUs: Clean Aviation (CA) JU, SESAR JU and EU-Rail JU. The three accounting officers deliver the services to one or more JUs and are responsible for the accounts they sign off on, while counting on the support and coordination by EU-Rail JU who is the lead JU for the accounting services. The IHI JU accounting officer is a staff member of SESAR JU and was appointed by the IHI JU GB in November 2022.

In 2023 BOA Accounting services issued the first deliverables – IHI JU provisional and final accounts 2022 - which received a clean audit opinion from independent financial auditors.

[16] The Service Level Agreement for HR BOA was signed on 6 March 2024.

2.9 Data protection

Throughout 2023 the JU pursued its efforts to render its processes and working methods fully compliant with Regulation (EU) 2018/1725. Foremost among these efforts were the updating and improving the JU's online register of processing operations, data protection documentation for use by the Programme Office, updating/implementing data protection measures for IHI's new electronic platforms and tools, and ensuring that IHI JU staff were kept informed of data protection issues.

The JU participated in various interinstitutional data protection activities, including events held by the European Data Protection Supervisor (EDPS).

In March 2023, a staff training was held on the general principles of data protection Regulation (EU) 2018/1725 to continue acquainting staff with data protection principles and terminology, and obligations arising under the data protection rules.

In August 2023, IHI JU suffered a data breach. The breach was managed in accordance with the provisions of Regulation (EU) 2018/1725 and the published breach guidelines from the European Data Protection Supervisor. The IHI JU's online breach register was updated to reflect this event and the data protection team liaised closely with the EDPS in the management of the breach. In September and October 2023, additional mandatory staff trainings were held on the principles and practices surrounding data breaches.

3 Governance

3.1 Major developments

2023 was a normal year with no major developments.

3.2 Phasing-out plan monitoring

In accordance with the SBA, the Programme Office drafted a plan for the phasing-out of the joint undertaking from Horizon Europe funding. This plan was adopted by the GB in December 2023. The plan focused on the main administrative and operational adaptations needed and main tasks that the new legal entity managing the legacy activities of IHI JU should be able to perform during the necessary period. The other elements of the phasing-out plan related to e.g. short and long-terms targets and future financial stability will be further completed during 2024.

3.3 Governing Board

The Governing Board (GB) is the main decision-making body of IHI JU and is composed of eight members (four from the EC and four from the industry trade associations).

Until 15 December 2023, the Chairperson was Salah-Dine Chibout (EFPIA / Novartis) and the Vice-Chairperson was Irene Norstedt (EC). As of 16 December 2023, Irene Norstedt and Nathalie Virag (Medtronic Global Technology and Innovation (MedTech Europe) were appointed respectively for the positions of Chairperson and Vice-Chairperson for a period of one year. Information on GB membership, including CVs and declarations of interest, can be found on the IHI website.

2023 corresponded to the second year of full operation activity for the GB. In 2023, the GB met three times in March, June and December. The GB amended its rules of procedure by decision of 14 August 2023 (IHI-GB-DEC-2023-21).

The Programme Office ensured a smooth and effective communication with the GB, notably through the GB platform where all GB meetings documents and draft decisions that undergo written procedure are posted.

Several decisions were adopted by the GB, either during the meetings or by means of a written procedure. Key decisions are those adopting the amended Work Programmes for 2023, the Work Programme 2024, the list of proposals selected under calls 2 and 3, a range of contributing partners in specific call topics, the back-office arrangements on IT and HR as required by the Council Regulation, the IHI JU phasing-out plan as required by the Council Regulation, the establishment of a candidates list for the selection procedure for the position of the IHI JU Executive Director, and the designation of the new Executive Director. The full list of decisions adopted is available on the IHI website.

3.4 Executive Director

From 16 September 2022 Dr Hugh Laverty was appointed by the GB as Executive Director ad interim and on 16 September 2023 was renewed as acting Executive Director until 15 January 2024. He was responsible for the day-to-day running of IHI JU activities and leading the organisation.

In 2023, IHI announced that Dr Niklas Blomberg had been appointed as the next Executive Director of the organisation, with a start date of 16 January 2024.

3.5 States Representatives Group

The States' Representatives Group (SRG) is composed of up to 2 representatives and up to 2 alternates from EU Member States and countries associated to Horizon Europe. A description of the role and duties of the SRG, meeting agendas, and information on the members can be found on the IHI website.

In 2023, the Chairperson was Martha Cahill (Ireland), and the Vice-Chairperson was Jan Skriwanek (Germany). Towards the end of the year, the election process for the new Chairperson and Vice-Chairperson was launched. The SRG met in April and October, and the meetings included discussions on IHI activities and future plans, and feedback from the SRG on IHI's first calls and best practices regarding promoting IHI and identifying potential synergies with national programmes.

During 2023, the SRG was consulted on the IHI corporate documents such as the CAAR 2022, the amendment to the Work Programme 2023, and the Work Programme 2024. Moreover, in compliance with the Council Regulation, the SRG provided its annual report to the Governing Board and this was published on the IHI website.

The Programme Office continued to ensure a smooth, effective and transparent communication with the SRG via the dedicated SRG private site. There were also regular interactions between the Programme Office and the Chairperson and Vice-Chairperson. In addition, the QlikSense business intelligence platform provides SRG members with information and data concerning IHI calls and projects. Additionally, preliminary information on topic generation was shared with the SRG.

As new States' Representatives regularly joined the SRG, the Programme Office organised dedicated workshops to facilitate the rapid integration of new members into the group. SRG members were also invited to several other workshops organised by the Programme Office.

3.6 Science and Innovation Panel

The Science and Innovation Panel (SIP) is an advisory body to the GB which has been set up to gain input from a wider range of health and research stakeholders much earlier in the call topic design process.
The 18 members come from the European Commission, the industry members of IHI, the SRG, the scientific community, and the wider healthcare community. Information on the members and the role of the SIP as well as agendas and reports from meetings can be found on the IHI website.

Anna Chioti and Ralf Herold were Chairperson and Vice Chairperson respectively throughout 2023.
In 2023, the SIP met in January, March, July and September. The agendas of the meetings are available on the IHI website.

During the year, the SIP focused mainly on discussing and providing opinions on the annual scientific priorities, ideas submitted by the wider health and research community (the SIP outcomes on the ideas that passed the completeness check are available on the IHI website), and draft topic texts proposed by the IHI JU founding members. The SIP was also consulted on whether to review the process for collecting ideas, the amendment to the Work Programme 2023, the Work Programme 2024, the IKAA planning, and how to best create synergies with other Horizon Europe activities, including other European partnerships as well as other EU and national programmes. The SIP is also kept updated on engagements with contributing partners.
More strategic discussions were also initiated about optimising IHI's relevance for and impact on healthcare.

After each meeting, the SIP issued a report to the Governing Board that includes its opinion and recommendations on the matters discussed. The reports are available on the IHI website.

In order to maximise the communication with the SIP, the Programme Office further developed the secured IT environment that ensures adequate sharing of data and information between IHI JU and the SIP panellists.

Promoting interactions between the governance bodies

Regular interactions between the SRG and the SIP are enabled by the fact that the SRG Chairperson and Vice-Chairperson are panellists of the SIP, while the Chairperson of the SIP is invited to the SRG meetings. Regular interactions between the SRG and SIP and the GB were enabled by the fact that the SRG and SIP Chairs participated as observers in the GB meetings and reported to the GB on their activities. Finally, the agendas and minutes of the meetings of each governance body are shared with the others.

3.7 Contributing partners

The ‘contributing partner’ category was created with the goal of opening up IHI to a wide range of stakeholders who may want to invest in IHI without becoming full members. Contributing partners invest their own resources (which can be researchers’ time, laboratories, data) or cash in a specific IHI project or projects. Any country, international organisation or legal entity that wants to contribute to the IHI objectives can apply to become an IHI contributing partner, provided they are not a member of IHI or an affiliate or a constituent entity of an IHI member. Furthermore, in the application process an applicant contributing partner needs to demonstrate the relevance and potential added value of the proposed contribution (scientific relevance, activities in the context of a public private partnership, duration and nature of contributions) to the achievement of the proposal objectives but also to the overall objectives of IHI JU.

In 2023, IHI worked further on improving its procedures related to receiving and reviewing applications from legal entities interested in becoming IHI contributing partners. The IHI published on its website an updated version of guide for contributing partners, a comprehensive source of information for entities interested in applying to become a contributing partner. Further, IHI developed additional resources for applicant contributing partners, including updated communication on the website; new templates for application letters in single-stage and two-stage calls, and a checklist for single-stage call applications. In October 2023, the IHI legal and financial officers hosted a webinar for existing and potential contributing partners.

In 2023 the Governing Board of IHI accepted 24 applications coming from 21 legal entities who became IHI’s contributing partners. Three legal entities were accepted by the Governing Board as contributing partners in more than one project.

List of contributing partners in IHI grant agreements signed in 2023

- AB Science SA: CLAIMS
- Altoida Inc.: PREDICTOM
- ALZpath, Inc.: PREDICTOM
- BrainCheck Inc.: PREDICTOM
- C2N Diagnostics, LLC: AD-RIDDLE
- Cambridge Cognition Limited: AD-RIDDLE
- Combinostics Oy: PROMINENT, AD-RIDDLE

- Davos Alzheimer's Collaborative: AD-RIDDLE
- FSHD Society: PaLaDIn
- GN Hearing A/S: PREDICTOM
- icoMetrix N.V.: CLAIMS, PREDICTOM
- JDRF: iCARE4CVD, EDENT1FI
- Julius Clinical Research BV: GRIPonMASH
- LGC Clinical Diagnostics, Inc: GUIDE.MRD
- Mercodia AB: GRIPonMASH
- Metadeq, Ltd.: GRIPonMASH
- Muhdo Health Ltd.: PREDICTOM
- neotiv GmbH: AD-RIDDLE
- Pharmacoidea Ltd.: PREDICTOM
- The Leona M. and Harry B. Helmsley Charitable Trust: EDENT1FI
- TREAT-NMD Services Ltd: PaLaDIn

4 Financial management and internal control

4.1 Control results

IHI JU implements an internal control framework applicable at all levels of management which is designed to provide reasonable assurance that operations are effective and efficient, but also that the financial reporting is reliable, and that the JU complies with applicable laws and regulations.

This section explains how the results described in the previous sections have been achieved by the JU[17]. It focuses on the results generated by the whole internal control system and presents other relevant information that supports management assurance on the achievement of the financial management and internal control objectives[18].

Moreover, following the transition from the Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) to the Innovative Health Initiative (IHI JU), a revised guidance[19] for the implementation and measurement of the IHI JU internal control framework defining new internal control indicators and targets was adopted and is used as a basis for the internal control self-assessment 2023.

4.1.1 Effectiveness of controls (ex-ante and ex-post)

To assure the effective and efficient implementation of expenditure, IHI JU has set out an internal control framework[20] embedded across its organisational structure, which relies on a combination of ex-ante and ex-post controls as summarised in the following table.

	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 gives 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 the 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.

[17] Including both IMI2 JU up to 29.11.2021 and then the IHI JU as explained above.

[18] According to Art 36.2 FR those objectives are: 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.

[19] IHI JU ED decision No 43 of 22.12.2022 on the Guidance for the implementation and measurement of the IHI JU Internal Control Framework.

[20] The Internal Control Framework of IHI JU adopted by the Governing Board on the 16 December 2021 (IHI-GB-DEC-2021-03) as amended by GB decision No 14/2023.

In order to prevent errors and irregularities before the authorisation of operations, and to mitigate risks of non-achievement of objectives, each operation is subject, at least, to an ex-ante control. This type of control relates to the operational and financial aspects of the operation, on the basis of a multiannual control strategy which takes risk into account. The purpose of the ex-ante controls is to ascertain that:

- the expenditure is correct and complies with the applicable provisions;
- the principle of sound financial management set out in Article 13 of the IHI Financial Rules[21] has been properly applied.

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 the costs paid is provided by ex-post audits carried out at the beneficiaries' premises, after the costs have been incurred and declared.

Ex-post audits can be carried out up to two years after the payment of the balance for the HE and H2020 programmes. For the FP7 programme, an audit can be carried out up to five years after the project is closed. In case of findings, they can also be implemented as part of the project management cycle.

Ex-ante controls on operational and administrative expenditure

In order to support the statement of assurance on the achievement of the internal control objectives, this section covers reporting on and assessing various kinds of expenditure, i.e. operational and administrative, with references to the budget coverage and the indicators set out.

The JU's annual budget is implemented through the administrative expenditure (i.e. related to staff and day-to-day activities – Titles 1 and 2 of the budget) and the operational expenditure (i.e. related to the research programme and payments to the beneficiaries - Title 3 of the budget)[22].

IHI JU has developed and continues to apply comprehensive procedures defining the controls to be performed by scientific project and financial officers for every commitment, payment of financial claim, payment of invoice, and recovery order, taking into account risk-based and cost-effectiveness considerations.

For operational expenditure, the processing and recording of transactions in the IT accounting system (ABAC) are performed via the corporate Horizon 2020 IT tools (SyGMa/COMPASS) for H2020 grants and evaluation experts, which ensures a high degree of automation as the controls are embedded in each workflow.

A pivotal element of this control system is the implementation of the horizontal guidance on H2020 and HE ex-ante controls for interim and final payments. This allows a consistent, simplified and trust-based approach to beneficiary controls with risk-based considerations.

[21] Decision of the Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking Adopting the Financial Rules of the Innovative Medicines initiative 2 Joint Undertaking on 27.05.2020 (IMI2-GB-DEC-2020-16) and readopted by IHI JU GB decision on 16.12.2021 (IHI-GB-DEC-2021-03).

[22] See Section 2.4 'Budget and financial management'.

Overview and ex-ante control results on operational expenditure

The tables below show the balance between the actions implemented under the IMI1/FP7, IMI2/H2020 and IHI/HE programmes in terms of project portfolio and the value of operational expenditure at the cut-off date of 31 December 2023.

As shown in the table below, a total of 59 projects were funded under IMI1 programme. At the end of 2023, there was one on-going project foreseen to end in 2024.

In the course of 2023, EUR 7 288 133 of interim and final payments were made to the beneficiaries for IMI1 projects.

IMI1 (FP7) project portfolio			Pre-financing payments	Interim & final payments[23]
59	Running on 01/01/2023	3	0	7 288 133
	Ended[24] during 2023 (-)	-2		
Total IMI1 projects running on 31/12/2023		1		

As shown in the table below, a total of 123 projects were funded under the IMI2 programme. 59 projects continue to run on 31.12.2023. In 2023, a total of EUR 118 292 421 was paid to the beneficiaries. Note that the last grant agreements for IMI2 projects were signed in 2021, with the last project having an expected end date in 2028.

IMI2 (H2020) project portfolio			Pre-financing payments	Interim & final payments[25]
123	Running on 01/01/2023	78	0	118 292 421
	Ended during 2023 (-)	-19		
	Signed during 2023	0		
Total IMI2 projects running on 31/12/2023		59		

As shown in the table below, a total of 16 Grant Agreements s were signed under the IHI programme during 2023 for a value of EUR 70 491 271 paid, as pre-financing, to the beneficiaries.

[23] 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).

[24] IMI1 projects which have ended their activities and submitted or are due to submit the final report.

[25] 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).

IHI (HE) project portfolio			Pre-financing payments	Interim & final payments[26]
	Running on 01/01/2023	0		
	Ended during 2023 (-)	0		
	Signed and pre-financed during 2023	15[27]	70 491 271	0
Total IHI projects running on 31/12/2023		13		

Total IMI1, IMI2 and IHI total project portfolio		Pre-financing payments	Interim & final payments[28]
Running on 01/01/2023	81		
Ended during 2023 (-)	-21	70,491,271	125,580,554
Started[29] during 2023	13		
Total running IMI1 + IMI2 + IHI projects on 31/12/2023	73	70,491,271	125,580,554

Volume and value of operational transactions

The following table provides a multiannual overview of operational transactions[30], including pre-financing payments (new projects) as well as interim and final payments made to ongoing projects funded under FP7, H2020 and HE programmes, and shows the evolution of the programmes' implementation.

[26] 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).

[27] Ibid.

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

[29] In total, 16 grant agreements were signed in 2023, of which 3 start their activities in 2024. 15 projects received pre-financing in 2023. Of the 3 starting in 2024, 2 projects started in January 2024 and were pre-financed in December 2023.

[30] 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 IHI. In technical terms, the clearing is the recognition of costs incurred against the pre-financing paid to projects.

Number of operational transactions (project payments)	*2023*	2022	2021
Pre-financing payments	*15*[31]	0[32]	16
Interim and final payments	*80*	94[33]	83
Recoveries on final payments[34]	*4*		
Volume of EU transactions	**99**	**94**	**99**

Value of operational transactions	2023	2022	2021
Value of all EU transactions, in million EUR	**267.8**	**224.2**	**242.1**
Value of all validated in kind, in million EUR	**225.6**	**289.9**	**283.1**
Total value validated EU and in kind, in million EUR	**493.4**	**514.1**	**525.2**

With regards to the value of validated transactions, it amounts to almost half a billion euro (EUR 493.4 million in 2023). This represents a significant effort for validation of both EU payments and in-kind contributions.

The breakdown of the costs accepted and paid in 2023 is presented in the tables below.

In 2023, the value of payments reached EUR 267 826 509 of which EUR 196 185 496 were actually paid to beneficiaries as interim/final payments, while EUR 71 754 683 are the result of full and partial clearing made against pre-financing paid at the beginning of the project.

The interim and final payments are related to IMI2 projects. Also, the clearing payments of EUR 71 754 683 relate to IMI2 projects.

EUR 70 491 271 were pre-financing payments of IHI projects launched in 2023.

[31] In total, 16 grant agreements were signed in 2023, of which 3 start their activities in 2024. 15 projects received pre-financing in 2023. Of the 3 starting in 2024, 2 projects started in January 2024 and were pre-financed in December 2023.

[32] No pre-financing was paid in 2022 as there were no grants signed.

[33] 94 = 9 IMI1 + 80 IMI 2 + 5 Recovery Orders (final cost claim).

[34] In some cases, instead of a final payment after the acceptance of the final report, there is a recovery. This happens when the consortium has underspent and IHI is recovering unspent pre-financing from the Consortium.

IMI1 (FP7)		No of transactions	Value of payments in EUR	Value of clearings in EUR	Value of all transactions in EUR
	Interim payments (1)	1	7 288 133	0	7 288 133
	Final payments (2)	0			
	Full Clearing (3)	0			
	Total (1) + (2) + (3)	1	7 288 133	0	7 288 133

IMI2 (H2020)		No of transactions	Value of payments in EUR	Value of clearings in EUR	Value of all transactions in EUR
	Interim payments (1)	44	118 292 421	71 754 683	**190 047 105**
	Final payments (2)	20			
	Recoveries for ended projects (4)[35]	4			
	Full Clearing (3)	11			
	Total (1) + (2) + (3) + (4)	**79**	**118 292 421**	**71 754 683**	**190 047 105**

IHI (HE)		No of transactions	Value of payments in EUR	Value of clearings in EUR	Value of all transactions in EUR
	Pre-financing payments (0)	15[36]	70 491 271		**70 491 271**
	Interim payments (1)	0	0	0	
	Final payments (2)	0			
	Full Clearing (3)	0			
	Total (1) + (2) + (3)	**15**	**70 491 271**	**0**	**70 491 271**

Expert payments		**113 670**		
TOTAL	**95 (1+79+15)**	**196 185 496**	**71 754 683**	**267 826 509**
Annual approved budget 2023 - TITLE 3		**210 000 000**		
Annual budget after recoveries		**216 196 176**		
Budget execution % - TITLE 3		**90.74%**		

The budget execution rate for project payments has increased from 86% in 2022 to 91% in 2023. Hence the budget execution rate is calculated on the increased budget of EUR 216 million (91%) instead of the initially forecast budget 210 million (93%).

[35] In some cases, instead of a final payment after the acceptance of the final report, there is a recovery. This happens when the consortium has underspent and then IHI is recovering unspent pre-financing from the Consortium.

[36] In total, 16 grant agreements were signed in 2023 but 3 of them only start their activities in 2024. 15 projects received pre-financing in 2023. Out of the 3 starting in 2024, 2 projects started in January 2024 and were thus pre-financed in 2023.

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 IHI. As shown in the below table, the rejection rate of IMI1 and IMI2 are in line with the rates of the previous years.

	Reported costs in EUR	Accepted costs in EUR	Rejected costs in EUR	Accepted costs in %	Rejection rate in %
IMI1	7 564 214	7 288 133	276 081	96.4%	3.6%
IMI2	187 272 542	182 640 862	4 631 680	97.5%	2.5%
IHI[37]	-	-	-	-	-
TOTAL	**194 836 756**	**189 928 995**	**4 907 761**		

Overview and ex-ante control results on administrative transactions

The following table shows the number and amount of all administrative transactions in 2023, including experts for project monitoring under Title 2. Regarding administrative expenditure, the time to pay (TTP) indicators presented further refer to all transactions (excluding budget Title 1 salary-related costs).

Administrative transactions made in 2023 - Title I and Title II	No	%	TTP average in days
Total # payments (including experts)	414	100%	11
# payments on time (within 30 days)	411	99%	
No. late payments	3	1%	

Administrative transactions made in 2023 - Title I Title II	Amount paid in EUR	%
Total # payments (including experts under Title 2)	3 764 655	100%
# payments on time (within 30 days)	3 761 987	99.9%
Late payments	2 667	0.1%

37 IHI projects related costs have not yet been declared.

The rate of payments on time reached 99.9% in 2023 which is an excellent rate and has further improved in comparison to the 2022 rate which amounted to 99.8%. This demonstrates efficient implementation of the workflows and monitoring in place.

Ex-post controls of operational expenditure and error rates identified

Ex-post controls are the final stage of IHI'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.

Since the legal basis and the budgetary frameworks are different, IHI reports separately on the IM1 programme under FP7 and the IMI2 programme under Horizon 2020.

Ex-post control: audit and corrective actions

Ex-post audits have three main objectives:

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

IHI 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 IHI 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 IHI 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 IHI contributions on completion of the audits, but does not take into account the corrections and follow-up undertaken by IHI. The formula for the calculation of the representative error rate is presented in Annex 12 – Materiality Criteria.

- The ***residual error rate*** (**ResER**) is the level of error remaining in the population after deducting corrections and recoveries made by IHI. This includes the extension of audit results to non-audited financial statements of the audited beneficiaries to correct systemic errors. The formula for the calculation of the residual error rate is presented in Annex 12 – 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 IHI and the fact that IHI extrapolates the systemic 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, IHI 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

IHI Programme Office remains responsible for the management of ex-post audits under FP7 operational expenditures, 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) in terms of the number of beneficiaries and projects as well as the accepted IHI contributions.

	Total population	Audited	Audit coverage
Beneficiaries	681	254	37 %
Projects	59	58	98 %
Contributions accepted by IHI (EUR, cumulative)	**852 003 798**[38]	**149 877 115**	**17.57 %**

The following table gives an overview of the status of individual audit assignments as of 31 December 2023.

	Total audits	Audits finalised[39]	Audits ongoing
Representative	279	279	-
Risk-Based	23	23	-
Total	**302**	**302**	**-**

[38] Figure as of 31/12/2023.

[39] 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 IHI 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 2023, 6 audits were finalised in total. No new samples were drawn during the year.

Representative and residual error rates as of 31 December 2023

At this point, the **cumulative Representative Error Rate** (RepER) resulting from all representative audits finalised by 31 December 2023 is 2.07 % in terms of IHI contribution.

The **cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.79 % in terms of IHI contribution. The residual error rate is thus below the 2 % materiality threshold established in Annex 12 of this report.

Implementation of audit results

When an audit report concludes that any amount has been unduly paid to a beneficiary, IHI launches the necessary corrective actions. Where the project is ongoing, the amount is offset against subsequent claims. Where the project is already closed, IHI 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 2023.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
229	225	98 %	3 796 671

Extension of audit findings

When an audit detects findings of a systemic nature, IHI 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 systemic findings	Beneficiaries
Audits finalised	302
Pre-information letters / letters of conclusion sent	302
Of which affected by systemic errors[40]	71
Extrapolation feedback received from beneficiary	71
Of which implemented	71
Amount implemented (EUR)	1 046 622

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

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

As regards the operational expenditure under H2020, IHI's ex-post controls of grants are aligned with the harmonised strategy adopted for the entire H2020 programme[41]. The Common Implementation Centre (CIC) 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 IHI. IHI works closely with the 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.

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

The IMI2 Regulation[42] establishes a requirement for an individual discharge procedure, therefore 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 2023

The Horizon 2020 audit campaign started in 2016. At this stage, four Common Representative Samples with a total of 788 expected results were selected. By the end of 2023, cost claims amounting to EUR 49.2 billion had been submitted by the beneficiaries to the services. The error rates on the H2020 programme level on 31 December 2023 are:

- Cumulative representative detected error rate**:** 2.57%[43],
- Cumulative residual error rate for the R&I Family of DGs: 1.55 % (1.64 % for DG R&I).

Since Horizon 2020 is a multi-annual programme, the error rates, and the residual error rate in particular, should be considered within 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.

These error rates are calculated on the basis of the audit results available when drafting the Consolidated Annual Activity Report. They should be treated with caution as they may change subject to the availability of additional data from audit results. The effectiveness of the control strategy of the R&I Family can only be measured and assessed fully in the final stages of the EU Framework Programme, once the ex-post audit strategy has been fully implemented, and errors, including those of a systemic nature, have been detected and corrected.

41 Horizon 2020 Ex-post Audit Strategy (2016 – 2025).

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

43 Based on the 581 representative results out of the 788 expected in the four Common Representative Samples.

Ex-post control specific to IHI population in 2023

By 31 December 2023, IHI had launched nine individual representative samples (one sample of representative audits was drawn in June 2023). Audits were finalised from the first seven samples. A total of 101 representative audits sampled by IHI were finalised. In addition, 20 risk-based audits were finalised by the end of 2023.

Audit coverage (cumulative)

The table below shows the coverage in completed audits (representative and risk based) compared to the accepted IHI contributions.

	Total population	Audited	Audit coverage
Contributions accepted by IHI (EUR, cumulative)	832 494 418[44]	93 173 740	11.19 %

The following table gives an overview of the status of individual audit assignments as of 31 December 2023.

	Total audits	Audits finalised	Audits ongoing
Representative	115	101	14
Risk-Based	33	20	13
Total	148	121	27

In 2023, 27 audits were finalised in total.

Representative and residual error rates specific to IHI's population as of 31 December 2023

At this point, the error rates on IHI population are as follows:

- **Cumulative Representative Error Rate** (RepER) resulting from the 101 finalised audits considered representative is 3.74 % in terms of IHI contribution.
- **Cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.99 % in terms of IHI contribution.

Implementation of audit results and extension of audit findings

[44] Figure as of 31/12/2023.

Following the finalisation of each audit by the CAS, IHI 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 on a cumulative basis, as of the cut-off reporting date of 31 December 2023.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
75	70	93 %	3 165 433

Extension of audit findings

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

Implementation of extension of systemic findings	Beneficiaries
Audits finalised	121
Pre-information letters / letters of conclusion sent	121
Of which affected by systemic errors[45]	15
Extrapolation feedback received from beneficiary	15
Of which implemented	15
Amount implemented (EUR)	368 631

Under H2020, extension of audit findings on IHI actions may also be triggered by audits performed by other EU services on IHI beneficiaries. For these cases, IHI provides its opinion to the coordinating unit, the Common Audit Service, and implements the correction. As of 31/12/2023, IHI has implemented 22 out of the 22 extensions of audit findings triggered by audits performed by other EU services on IHI beneficiaries.

Reporting on the implementation of all audit results and extensions (negative, positive and neutral results)

Following the adoption of a guidance note on the monitoring of the implementation of ex-post audit results by the CIC Executive Committee in December 2022, the following tables illustrate the common set of data that EU services must use to monitor the implementation of all audit results and extensions: negative, positive and neutral results. Results correspond to a financial audit opinion or a closed extension of systemic audit findings for one beneficiary in one grant.

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

For implementations done outside the grant management module, therefore outside the audit result implementation Compass workflow (called “AURI”), such as non-joint ECA audits and implementations processed before the entry into service of Compass tools in IMI2 on 24 May 2018, the results are manually added to the statistics produced by Compass.

Implementation of audit and extension results (cumulative from H2020 start to 31/12/2023

IMI2 JU	Audit results processed	Audit results pending	Total
Audits	154	15	169
Extensions	60	7	67
Total	214	22	236

Time to implement audit and extension results in a financial year 2023

IMI2 JU	0-6 months	above 6 months	Total number
Closed projects	13	-	13
Negative adjustments with recovery	4	-	4
Negative adjustments without recovery	2	-	2
Positive or zero adjustment	7	-	7
Ongoing projects	44	-	44
Negative adjustments	18	-	18
Positive or zero adjustment	26	-	26
Total	**57**	**-**	**57**

The above figures demonstrate that the JU implements in a timely manner all audit and extensions results enabling IHI to meet all targets set by the EC guidance note on monitoring of the implementation of ex-post audit results.

Horizon Europe Framework Programme

IHI JU signed the first 16 grant agreements under Horizon Europe Framework Programme. No representative error rate for Horizon Europe is available in 2023 as no interim or final payments were made. The common ex-post audit campaign for the programme is planned for launch in 2024/2025 by the Common Audit Service, once a meaningful number of payments is available for audit.

4.1.2 Efficiency of controls ('time to')

In 2023, IHI JU continued to ensure the efficiency and robustness of its granting process as reflected by the three performance indicators described in the following table.

- **Time to Inform (TTI)** represents the time needed by IHI JU to manage the evaluation and selection phase from the call deadline to informing the participants. In 2023, the average TTI was 68 days, against a legal target of 153 days.

- **Time to Grant (TTG)** represents the maximum eight months between the call deadline and grant signature. In 2023, the average TTG was 234 days, against a legal target of 245 days.

Indicators - in days	Target	2023
Total average Time to Inform (TTI)	153 days	68
Total average Time to Grant (TTG)	245 days	234

- **Time to Pay (TTP)** represents the outcome of the process for the payment of costs claimed by beneficiaries. As IHI JU implements the legacy portfolio of IMI1 and IMI2, the table below presents the TTP for those project payments done in 2023.

IMI1 + IMI2+ IHI Indicators - in days	Target	2023		
		IHI	IMI2	IMI1
Total average Time to Pay (TTP) - for cost-claims and final payments	90 days	N/A[46]	68	65
Total average Time to Pay (TTP) - for pre-financing	30 days	7	N/A[47]	N/A[48]

For the IMI2 and IMI1 projects, the actual TTP averages respectively reached 68 and 65 days against a target of 90 days. This demonstrates the efficiency of financial management within the IHU JU.

The graph below demonstrates the efficiency of the Programme Office by meeting all the targets for payments as defined in the Financial Rules[49]. The average TTP results (in days) are below the maximum threshold number of days for all types of operational transactions executed in 2023 and support the efficiency trend[50].

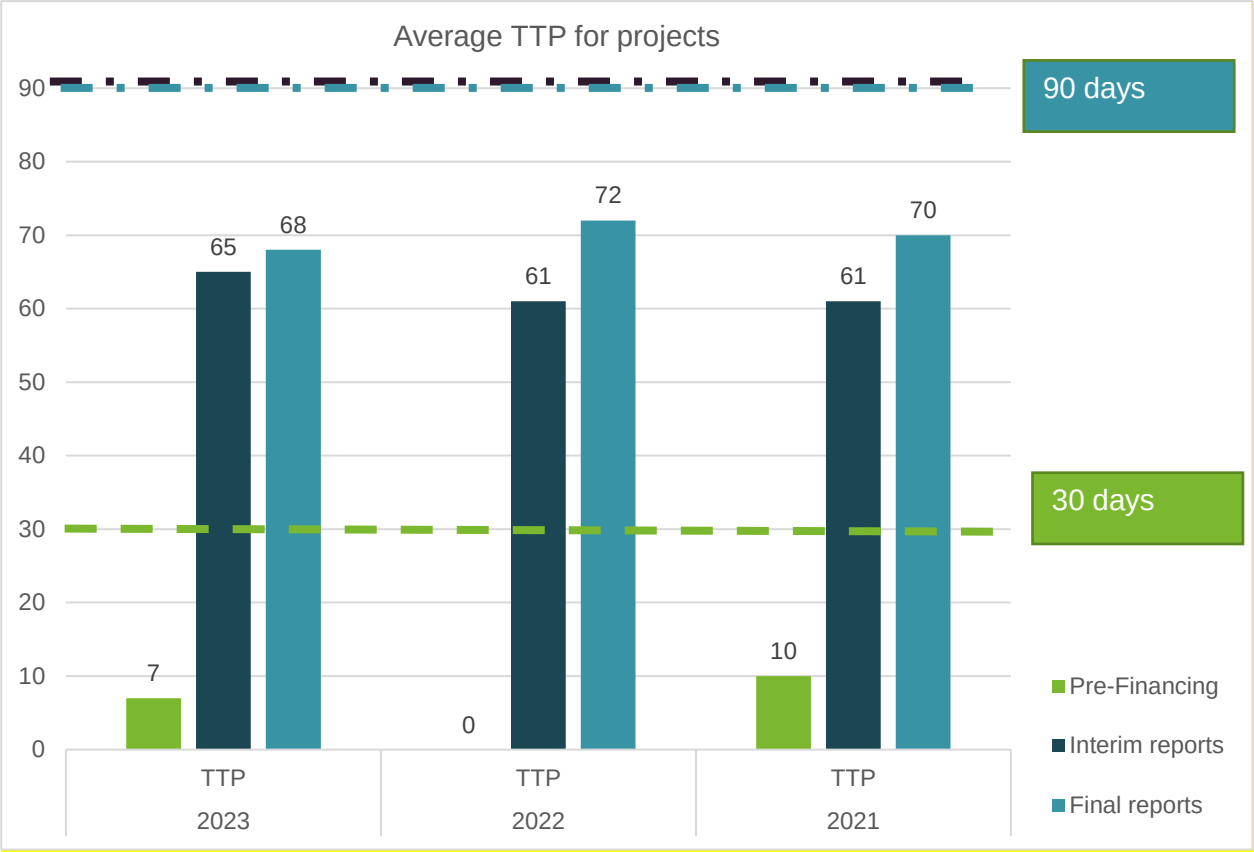
[46] There were only pre-financing payments for IHI projects in 2023.

[47] There was no pre-financing for IMI2 projects in 2023.

[48] There was no pre-financing for IMI1 projects in 2023.

[49] 30 days for pre-financing, 90 days for interim and final project payments.

[50] The table shows the average TTP per year and for all programmes (IMI1, IMI2 and IHI) for the given year.



In addition to good results for timely project payments, the JU has also demonstrated efficiency in payments to project monitoring experts (under Title 2) and call for proposals evaluation experts (under Title 3). There were no late payments to experts for project monitoring in 2023 and only one late payment for evaluation experts. This confirms that the measures taken to control the workflow were effective.

The average TTP was 7 days for the pre-financing in 2023. The average TTP was 15 days for the evaluation experts which is an improvement vs 2022 (18 days). The average TTP is substantially below the maximum allowed, i.e. 30 days.

Payments to project monitoring experts

Expert payments made in 2023 - Title II	#	%
# of payments	52	100%
# of late payments	0	0%
# of payments on time	52	100%
Average time to pay (days)	15	
Total amount paid (EUR)	96 075	

Payments to evaluation experts

Expert payments made in 2023 -Title III	#	%
# of payments	62	98%
# of late payments	1	2%
# of payments on time	61	100%
Average time to pay (days)	15	
Total amount paid (EUR)	113 670	

4.1.3 Economy of controls

The section below describes the cost-effectiveness of IHI controls related to the overall control cycle (ex-ante controls on call management and evaluation, grant award and project implementation and ex-post controls).

The cost for ex-ante controls represents 1.27 % of operational expenditure in 2023 and can be quantified as ca. EUR 45 thousand per Grant Agreement.

A complete assessment of the cost-effectiveness of the JU'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	2023	2022	2021
Cost of controls / Total expenditure (administrative and operational)	1.29%	1.69%	1.12%
Cost of controls / Operational expenditure	1.33%	1.75%	1.17%
Cost of controls / Total accepted costs (only beneficiaries' cost claims)	1.87%	1.80%	1.27%
Cost of controls / Total accepted costs (both beneficiaries' cost claims and validated industry contribution)	0.85%	0.77%	0.50%

The different indicators presented above provide an indication of the cost effectiveness of the control system put in place by the JU 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.

4.2 Audit observations and recommendations

4.2.1 Internal audit

The Internal Audit Service (IAS) of the European Commission performs the internal audit function for the JU 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 has confirmed the organisational independence of the internal audit activity to the Executive Director and the Governing Board[51].

In 2023, the IAS concluded the Strategic Internal Audit Plan 2023-2025 for IHI JU[52] and issued the 2023 audit plan[53]. On that basis, in June 2023 IAS announced an audit[54] on 'IHI JU Governance and relations with stakeholders' and started the preliminary survey. The audit team held interviews with IHI JU senior management, the Governing Board chairperson and vice-chairperson, the vice-chair of the Science and Innovation Panel, and key process owners. The IHI Office supported the audit team by providing exhaustive documentation and organising interviews. The audit continues and will be finalised in 2024 as foreseen in the 2024 audit plan.

The IAS also performed at the end of the year an update of the risk assessment in preparation for the 2024 audit plan.

The annual audit plans of the IAS are coordinated with the European Court of Auditors, the external auditor of all European Union institutions and bodies. The coordination activities aim to avoid duplication and to minimise any overlaps in thematic areas proposed for audits by internal and external auditors.

4.2.2 Audit of the European Court of Auditors

Audit on IHI JU annual accounts for the financial year 2022

On 14 November 2023, the European Court of Auditors (ECA) published its 'Annual report on the EU Joint Undertakings for the financial year 2022'[55].

The ECA gave a clean bill of health for IHI JU, issuing an unqualified ('clean') opinion on the reliability of the accounts as well as on the legality and regularity of the revenue and payments underlying the annual accounts.

Without calling into question its 'clean opinion', the ECA also provided some observations in the specific chapter on IHI JU on the following subjects:

- *Insufficient information on members' contributions at programme level:* The ECA observed that in the 2022 annual accounts, the amounts of contributions recognised per member category (EU and private members) differ significantly from each other. The ECA considered that the gap between the recognised amount of cash contributions and in-kind contributions was not clearly explained.

[51] IAS letter Ares(2024)1821382 of 08/03/2024

[52] Ares(2023)638585 of 27/01/2023 and Ares(2023)4372271 of 23/06/2023

[53] Ares(2023)1950758 of 17/03/2023

[54] Ares(2023)3818192 of 02/06/2023

[55] https://www.eca.europa.eu/en/publications/SAR-JUS-2022

Following the ECA's remarks, IHI JU made an effort to improve the presentation of member contributions in the final version of annual accounts 2022 and is working closely with the BOA Accounting services on a common template for a harmonised and complete presentation of the necessary information in the 2023 annual accounts.

- *Implementation of the FP7 programme:* The ECA noted that JU had not yet completed the implementation of the FP7 projects.

IHI JU took note of the observation and provided an up-to-date overview of the FP7 situation with one remaining project to be completed in 2024.

Audit on IHI JU annual accounts for the financial year 2023

In accordance with Article 54 of the JU Financial Rules, the 2023 annual accounts are audited by the external audit company. The specific contract was signed in 2022 with Baker Tilly Belgium to cover the audit of financial years 2022 and 2023. The audit work for the accounts for 2023 will be completed by issuing an opinion on the final accounts by 15 June 2024.

The Court of Auditors will draw the final audit opinion on the 2023 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's dedicated team. The final report is due in November 2024.

4.2.3 Follow-up of audit recommendations

IHI has implemented the audit recommendations from previous IAS and ECA audits.

In 2023, the IAS performed a follow-up audit of a remaining open recommendation to assess the progress made in implementing it[56]. Based on the results of the follow-up audit, the IAS concluded[57] that the recommendation had been adequately and effectively implemented and was therefore closed. All IAS recommendations from the audit on Horizon 2020 grant implementation addressed to the IHI JU have thus now been closed.

ECA closed its observations referring to the employer part of pension contributions from 2021 Special Annual Report IHI specific chapter. ECA has acknowledged that '*IHI paid the relevant employer's contributions to the EU pension scheme, for the year 2022, as invoiced by the Commission. The calculation of the annual contribution was based on the Commission's guidance. Further actions regarding the conflicting legal provisions are outside the remit of the JU.'*

56 Reference made to the only open action under recommendation No. 1 (rated 'important') related to fraud risk assessment and antifraud actions, stemming from the audit report on 'Horizon 2020 grant implementation in the Innovative Medicines Initiative 2 Joint Undertaking' issued on 27 January 2021. At the end of December 2022, the JU provided evidence on the implementation of the action and requested the IAS team to review and close the recommendation. As recommended by the IAS, IHI adopted a revised anti-fraud strategy reflecting the modalities of funding under the Horizon Europe framework programme and the new related action plan aligned with the horizontal research family approach.

57 Ares(2023)2314959 of 30/03/2023

4.3 Assessment of the effectiveness of internal control systems

IHI JU's internal control framework is designed to provide reasonable assurance regarding the achievement of the following five objectives:

- effectiveness, efficiency and economy of operations;
- reliability of reporting;
- safeguarding of assets and information;
- prevention, detection, correction and follow-up of fraud and irregularities;
- adequate management of the risks relating to the legality and regularity of the underlying transactions, taking into account the multi-annual character of programmes as well as the nature of the payments concerned.

The JU's internal control framework is based on 17 control principles[58] which are aligned with the European Commission control framework. All the principles of the control model are embedded across the JU'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, control of data quality, promotion of ethical behaviour and zero tolerance to fraud, prevention of conflict of interest and integrated risk management. The Programme Office at all levels ensures the implementation of the internal control framework.

The self-assessment of the effectiveness of the internal control framework in 2023 is based on the criteria set out in the internal guidance, namely:

- a set of indicators with targets and baselines;
- staff and management surveys and analysis of the results on the functioning of internal control;
- state of implementation of internal control action plan;
- state of implementation of recommendations and observations by internal (Internal Audit Service) and external auditors (independent financial auditors and the European Court of Auditors).

In order to assure that all aspects of the internal control system and business operations were covered by the self-assessment, the 17 control principles have been analysed both individually and as part of the corresponding control component.

4.3.1 Fraud prevention detection and correction

The JU has been implementing the anti-fraud strategy aligned with the Commission Anti-Fraud Strategy (CAFS 2019) and the Common Anti-Fraud Strategy for the Research family (RAFS 2019) which addressed the fraud risks of the entire sector of research in the European Commission. Actions implemented on grants and operational activities are coordinated with the Directorate-General for Research and Innovation (DG RTD) and other research agencies through a multiannual action plan coordinated by the Fraud and Irregularity in Research (FAIR) Committee.

In addition to the common approach for the research sector, IHI is implementing a specific JU-level anti-fraud strategy and action plan[59] adopted in 2022. The action plan is built to meet four core objectives, namely to:

[58] https://commission.europa.eu/document/download/f163e193-bf9b-4823-bd4b-dceb8739f46e_en?filename=revision-internal-control-framework-c-2017-2373_2017_en.pdf

[59] ED decision No 39 of 16 December 2022.

- maintain and enhance a culture of fraud prevention underpinned by high levels of awareness, integrity and transparency within the JU and its stakeholders;
- strengthen capacities and measures for fraud detection;
- develop and maintain effective coordination and synergies within the research family (FAIR, CIC / CAS, JUs);
- maintain good cooperation and responsiveness to OLAF/ EPPO.

In 2023, IHI JU anti-fraud activities were directed towards:

- cooperation with the FAIR Committee on the 2023 update of the Common Anti-Fraud Strategy in the Research and Innovation Family (2023 RAFS);
- maintaining staff awareness on anti-fraud measures. New staff members followed a mandatory training on fraud prevention.

Additionally, attention was given to cross-cutting issues such as risks linked with conflicts of interest, outside activities, gifts and hospitalities, and the code of good administrative behaviour. An extensive ethics campaign was organised including:

- a mandatory workshop on ethics and integrity for all staff (2 sessions in March);
- an 'ethics week' (in June) featuring a communication campaign. A custom-made IHI e-learning workshop was prepared and is available for staff members to follow.

We recorded good results (well over the target of 85%) on fraud prevention awareness and fraud perception by means of the staff survey on internal control in 2023.

In 2023 the Programme Office reported two instances of suspicion of fraud to OLAF. The Programme Office has been closely cooperating with OLAF and responded to all requests or enquiries. One case was dismissed by OLAF and one investigation was opened.

4.3.2 Assets and information, reliability of reporting

In view of the internal control objective to safeguard assets, the JU has established internal procedures and processes. The inventory check of fixed assets has been performed and documented, and relevant write-offs were done. The annual assessment (including declassification decision, calculations of net book value for IT and furniture to be disposed, and SAP bookings) was performed before the year-end operations as set out in the internal procedure.

In view of the objective of reliability of reporting, the JU ensures data quality and accuracy via managerial supervision, segregation of duties, and external reviews and audits. The 2023 annual evaluation (related to the period January 2022 to June 2023) of IHI JU local financial systems was performed by the accounting officer, part of the BOA, according to Article 25 (d) of the JU Financial Rules. The evaluation did not identify any internal control weakness which would have a material impact on the accuracy, completeness and timeliness of the information required to draft the annual accounts and produce reliable reporting.

On the basis of the available evidence, the accounting officer concluded that the internal control systems are working as intended.

4.3.3 Risk assessment and management

Risk management is a proactive process for identifying and assessing any event that could pose a threat to the achievement of the IHI JU objectives and determining how the corresponding risks should be managed.

Therefore, risk management is an integral element of the strategic planning and monitoring cycle.

Following the risk assessment exercise carried out by the Programme Office, two critical risks were identified: an operational risk linked to the IHI JU's reliance on an externally owned programme management platform, and a reputational risk connected to external stakeholders' diverging points of views and agendas.

Both risks were recorded in the corporate register and reported to the GB. In addition, several processes and actions were put in place to mitigate them. In case of the identified reputational risk, the mitigation measures were based on the strategic objectives of the IHI Communication Policy adopted by the IHI Governing Board in 2022.

In order to control the risks identified, the Programme Office ensures their monitoring and continuous reviewing, considering the corresponding mitigating measures identified and taking further actions where necessary to ensure controls remain effective. Relevant IHI JU financial needs and the budget for 2023 have also been appropriately estimated. The staff is regularly informed on the objectives, activities and new planning.

4.3.4 Prevention of conflicts of interest

In accordance with the IHI JU legal framework, the Executive Director and staff of the Programme Office ensure transparency and compliance with ethical rules including the absence of any conflict of interest with the operational and administrative activities of the JU. A conflict of interests exists where the impartial and objective exercise of the functions of a financial actor or other person is compromised for reasons involving family, emotional life, political or national affinity, economic interest, or any other direct or indirect personal interest.

The objective of controls on the conflicts of interest is to prevent, detect and address any situation that can undermine the reputation of the IHI JU partnership.

The JU has developed a comprehensive set of rules and procedures that are effectively implemented across its entire governance structure, as follows.

- When joining the Programme Office team, each staff member agrees to follow and comply with the Staff Regulations and signs a declaration of honour on the management of conflicts of interest, including the declaration of potential conflict of interest.

- IHI JU applies by analogy, mutatis mutandis, the 'Code of Good Administrative Behaviour[60]' for staff of the European Commission in their relations with the public.

[60] https://commission.europa.eu/about-european-commission/service-standards-and-principles/ethics-and-good-administration/good-administration/code-good-administrative-behaviour-and-complaints_en

- Conflict of interest procedures are in place for the members of the IHI JU Governing Board as adopted in December 2021 in the scope of the rules of procedure of the GB for the IHI JU[61]. The declarations are made available on IHI JU website[62]. The rules of procedure for IHI State's Representative Group[63] as well as the rules of procedure of the IHI Science and Innovation Panel[64] include explicit requirements for declaration of conflict of interest.

- The conflict-of-interest prevention policies for staff and for governing bodies were updated in 2023 and are in the process of adoption by the Governing Board.

- Specific measures have been implemented for the prevention and management of conflicts of interest of experts in charge of the evaluation of grant applications and of the review of projects and tenders.

- A holistic conflict of interest prevention and detection campaign was conducted within the Programme Office in 2023.

- All IHI JU staff members were required to submit their up-to-date declarations during the year. Declaring conflicts of interest is a continuous process as any conflict situation must be declared within a month and on a proactive basis.

- Mitigating measures are implemented and closely followed-up in case of a conflict of interest (real or perceived) declaration.

4.3.5 Conclusion on internal control systems

The JU uses the organisational structure and the internal control system 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.

IHI JU has systematically examined the available control results and indicators as well as the observations and recommendations issued by the internal auditor and the European Court of Auditors. These elements have been assessed to determine their impact on management's assurance about the achievement of the control objectives.

In line with its internal control framework, the JU has assessed its internal control system during the reporting year 2023 and has concluded that it is effective, and the components and principles are present and functioning well. Areas where some further improvements can be made have been identified and will be prioritised in 2024.

[61] HI-GB-DEC-2023-21_Decision of 17 August 2023 repealing IHI-GB-DEC-2021-01

[62] https://www.ihi.europa.eu/about-ihi/who-we-are

[63] www.ihi.europa.eu/about-ihi/who-we-are/states-representatives-group

[64] www.ihi.europa.eu/about-ihi/who-we-are/science-and-innovation-panel

4.4 Conclusion on the assurance

4.4.1 Review of the elements supporting assurance

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

IHI JU 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 JU management team[65];
- reporting by the internal control officer;
- reports and recommendations by the JU audit manager;
- results of ex-ante and ex-post controls
- Governing Board assessment and recommendations.

Findings and opinions from internal and external audits:

- reports and follow up notes by the Internal Audit Service;
- reports by independent financial auditors;
- reports and annual audit opinion by the European Court of Auditors.

External verifications and investigations (when available):

- reports by the JU Accounting Officer;
- reports by the Ombudsman;
- reports by the European Data Protection Supervisor;
- conclusions by the European Anti-fraud Office.

Independent external reviews (when available):

- interim and final evaluation reports;
- project interim review reports;
- bibliometric analysis.

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 12. The overall cumulative residual error rate is below 2% for the operational programmes implemented by IHI. The control strategy sets out the implementation of further controls during subsequent years designed to detect and correct these errors.

No significant weaknesses were identified or reported under Section 2 ('Support to operations') and Section 4 ('Financial management and internal control').

65 Head of Administration and Finance, Head of Scientific Operations, Head of Communications and Institutional Relations

The total results of grant management operational indicators (time to pay, time to grant, time to sign, time to inform) are below the legal targets. Four instances of deviations from the payment target and two instances of deviations from time to grant target were recorded. The root causes were thoroughly analysed, and additional monitoring measures put in place. Overall, the results demonstrate the maturity of financial management and the robustness of IHI's control systems.

Furthermore, the management considers that, given the scope of the statement of assurance and taking into account the controls and monitoring system in place, there are no significant weaknesses that could call into question reasonable assurance as to the use of resources for their intended purpose, in accordance with the principles of sound financial management. The implemented control procedures and results provide the necessary assurance on the legality and regularity of the underlying transactions.

4.4.2 Reservations

There are no reasons for introducing any reservations.

4.4.3 Overall conclusion

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

4.5 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 the Revision of the IMI2 JU internal control framework and IHI JU Governing Board Decision No 2021-3 as amended by Decision No 2023-14, I have reported my advice and recommendations on the overall state of internal control in the IHI JU to the Executive Director. I hereby certify that the information provided in the present Consolidated Annual Activity Report and in its annexes is, to the best of my knowledge, accurate and complete.

Brussels, 20.06.2024

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

Brussels, 20.06.2024

Signed

Hugh Laverty, Head of Scientific Operations

4.6 Declaration of assurance

I, the undersigned

Executive Director of the Innovative Health Initiative Joint Undertaking

In my capacity as authorising officer

Declare that the information contained in this report gives a true and fair view[66].

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, 20.06.2024

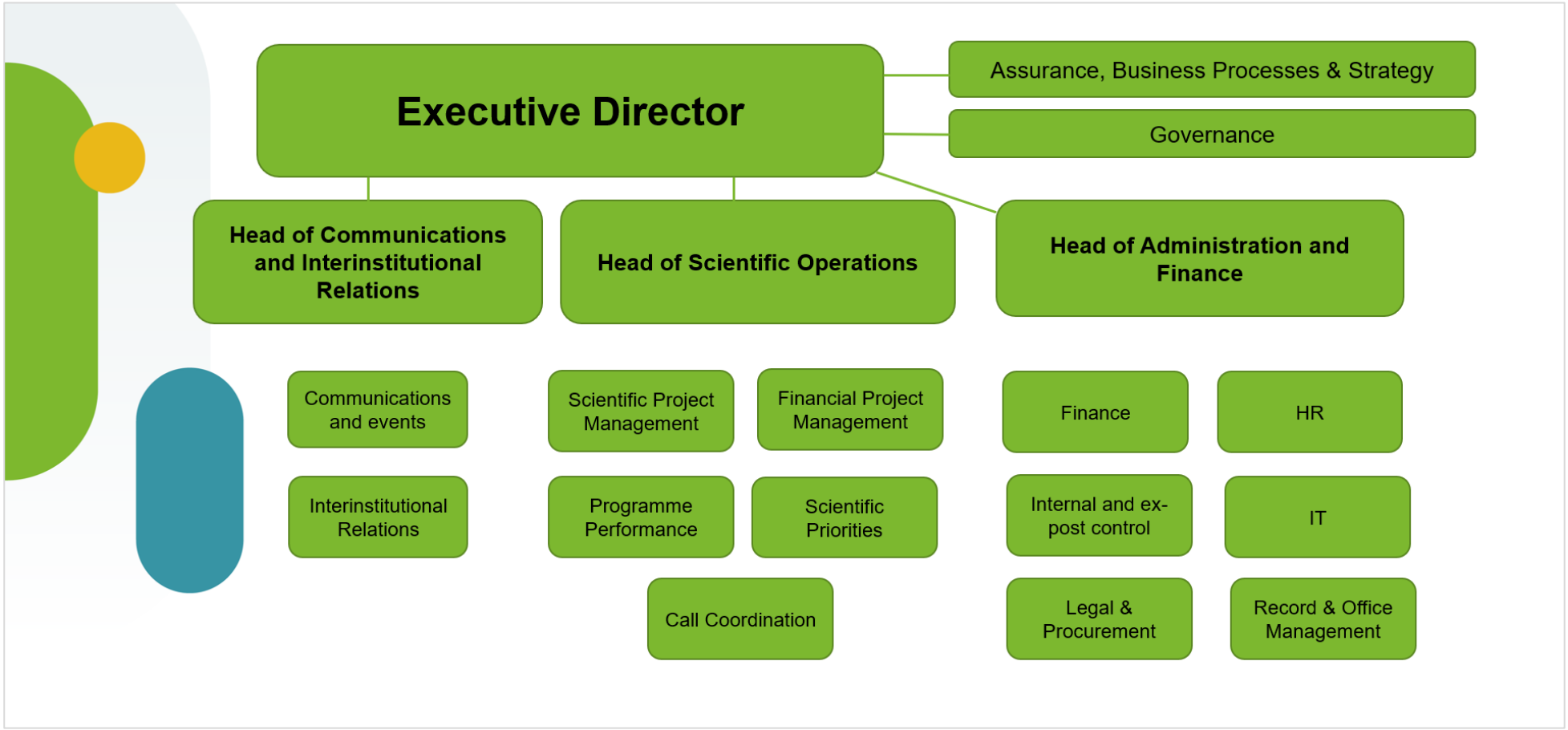
Signed

Niklas Blomberg
Executive Director

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

Annexes

Annex 1 – Organisational chart



Annex 2 - Establishment plan and additional information on HR management

Function group and grade	YEAR N-1				YEAR N			
	Authorised posts		Posts actually filled as of 31/12/2022		Authorised posts		Posts actually filled as of 31/12/2023	
	Perm.	Temp.	Perm.	Temp.	Perm.	Temp.	Perm.	Temp.
AD 16								
AD 15								
AD 14		1		0		1		0
AD 13								
AD 12		2		1		2		1
AD 11		2		2		2		2
AD 10		1		2		1		2
AD 9		7		4		7		4
AD 8		6		3		6		3
AD 7		3		3		4		3
AD 6		10		6		9		5
AD 5		2		11		3		11
TOTAL AD	**34**		**32**		**35**		**31**	

AST 11								
AST10								
AST 9								
AST 8		1		1		1		1
AST 7								
AST 6								
AST 5								
AST 4		4		2		3		2
AST 3				1				
AST 2								
AST 1								
TOTAL AST		**5**		**4**		**4**		**3**
AST/SC 6								
AST/SC 5								
AST/SC 4								
AST/SC 3								
AST/SC 2								
AST/SC 1								

TOTAL AST/SC							
TOTAL AD+AST+ AST/SC							
GRAND TOTAL	**39**		**36**		**39**		**34**

Contract Agents	Authorised	Actually filled as of 31/12/2023
Function Group IV	4	3
Function Group III	11	7
Function Group II		
Function Group I		
TOTAL	**15**	**10**

Annex 3 – Project outputs

In order to track progress against the ambitious goals of the IMI programmes, IMI project outputs are categorised 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 by 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 following tables set out IMI project outputs per category. Unless stated otherwise, all projects listed are from IMI2.

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result(s)
AIMS-2-TRIALS	The balance between excitation and inhibition signals (E/I balance) in the brain is considered a critical mechanism altered in autism and related comorbidities like epilepsy, and the unravelling of molecular pathways modulating such mechanisms could therefore be relevant for development of new treatments. The consortium demonstrated that genetic disruption of the BMP-SMAD1 (Bone morphogenetic protein - Suppressor of Mothers against Decapentaplegic1) pathway in interneurons (essential for maintaining E/I balance) results in seizures in rodent models – linking with autism/epilepsy that is also studied in the project's human cohort studies.
Beat-DKD	The single-cell transcriptomic landscape of early diabetic nephropathy revealed by Beat-DKD researchers, shows that mechanosensitive signalling pathways could play a driving role in the protective effect of the sodium–glucose cotransporter 2 (SGLT2) inhibition, opening the search for novel druggable downstream targets of SGLT2. The findings are published in Genome Medicine.
BIOMAP	In a paper published in Human Genomics, the project explains how they uncovered unknown genetic factors associated with the onset of the skin disease psoriasis. By integrating experimental driven results with curated functional information from public repositories, the

	consortium exploited an efficient approach to empower knowledge generation about psoriasis and may be applicable to other complex diseases.
CARE	Bioanalytical and inactivation procedures were developed and validated to analyse plasma and tissue concentrations of different new chemical entities (NCE) in a Biological Safety Level-2 environment in small animal models. These studies followed the efficacy experiments and help to draw pharmacokinetic-pharmacodynamic relationships of the NCEs.
CARE	To identify novel broad-spectrum coronavirus treatments, the project developed a high-content imaging platform compatible with high-throughput screening, which was used to screen ~900 000 compounds and further prioritise relevant hits. The platform is broadly applicable as it can be adapted to include other cell types, viruses, antibodies, and dyes. It is described in a paper in Antiviral Research.
CARE	A transgenic SARS-CoV-2 mouse model was established by the project. Different from the hamster model, these human angiotensin-converting enzyme 2 (hACE2)-expressing animals more closely resemble more severe infections. The optimal inoculum and viral replication kinetics were determined. Antiviral activity could be demonstrated both in a prophylactic and therapeutic setting using this model.
CARE	An air-liquid interface culture assay, which models the human respiratory system, was developed by the project, using human nasal epithelial cells and used to assess antiviral activity against SARS-CoV-2. The quantification of antiviral activity in this type of cultures has proven to be essential in the decision of whether or not to proceed with the further development of compounds. The assay can run in prophylactic and therapeutic formats. In addition to basal compound exposure, combined basal and apical compound exposure is included to not miss weaker hits. A serum-shift assay was also developed in this model to assess the impact of human serum proteins on the compounds. This gives an indication of the free compound fraction which is then used for human dose predictions.
CARE	The project developed another model for evaluating the mode of action against SARS-CoV-2 of compounds. The model uses (baby hamster kidney) BHK-21 cells which constitutes a single round infection system to study post-entry antiviral effects and a circular polymerase extension reaction infectious clone system to efficiently generate site-directed mutant viral genomes.
CARE	Lead optimisation efforts on a compound series, previously identified via phenotypic screening, led to the development of compounds with potent antiviral activity in various cell systems against SARS-CoV-2 and SARS-CoV-1. This compound series targets the viral membrane protein, which represents a novel mode-of-action, distinct from the currently approved antivirals. *In vivo* activity of this series was shown in a SARS-CoV-2 infection mouse model with significant viral load reduction in lungs. This series is further being progressed towards preclinical candidate selection.
CARE	A potent corona-antiviral compound series targeting NSP14 (a protein involved in viral RNA replication) is being developed. Hit-to-lead efforts led to compounds with potent activity in biochemical and cell-based assays and generated a good understanding of optimisation parameters, also helped by several co-crystals. This series is being progressed towards preclinical candidate selection.
CARE	A second phenotypic programme has finalised hit-to-lead optimisation and recently achieved a positive proof-of-concept in a SARS-CoV-2 infection animal model with a lead compound from the series. Additional lead compound profiling and optimisation activities are ongoing. Target deconvolution is underway to identify the precise mode of action, but it has already been shown that this compound series acts through a novel unknown mechanism.
COMBINE	COMBINE has launched a preclinical bacterial strain repository to support the harmonisation and comparability of preclinical efficacy studies for antimicrobial drug development. It contains bacterial pathogens which are currently evaluated in a COMBINE consensus infection protocol as putative reference strain for preclinical efficacy studies.
ConcePTION	Development of a generic lactation physiologically based pharmacokinetic (PBPK) model to predict medicine concentrations in human milk. The model, which is described in the journal

	Pharmaceutics, represents an important step towards an evidence-based safety assessment of maternal medication during lactation, applicable in an early drug development stage.
EBiSC2	To increase ready access to high quality, well-characterised and functional iPSC-neurons for research use, EBiSC has released a pre-differentiated iPSC cell product, EBiSC-NEUR1. By supplying iPS cells in a pre-differentiated state, Users are able to rapidly access qualified and consistent iPSC-neurons and the use of iPSC-neurons in research is made accessible for those users with minimal experience in the handling and differentiation of iPSCs. NEUR1 was developed with extensive feedback from private partners, generated using upscaling approaches developed during the project period and has been fully qualified according to EBiSC standards. NEUR1 is accompanied with open access user protocols, quality control data and direct user support.
EBiSC2	To further enable and extend the use of pre-differentiated iPSCs, a joint venture between EBiSC2 and the EIT Health project R2U-Tox has enabled the development and dissemination of two different and novel ready-to-use cell models which can be shipped as pre-plated cultures in 96 well plates. IPS cells are pre-differentiated to cardiomyocytes or brain cells (neurons and astrocytes), pre-plated into specific multi-well plates (selected for compatibility with various end use screening platforms) and after shipping, can be used immediately. This allows the user to avoid lengthy differentiation protocols, saving them time and increasing reproducibility by providing access to robust, consistent and qualified cells. Access to iPSC cardiomyocytes and iPSC neuronal-astrocyte co-cultures which are ready for use, will increase relevance of drug development by supplying human cell models for toxicity screening, opening the door to users with minimal experience in handling iPSC differentiations.
EPND	The project developed a Standard Operating Procedure (SOP) for Biomarker Validation, which outlines key parameters and protocols for the technical validation of fluid-based biomarkers. By detailing specific procedures linked to these parameters, the SOP provides valuable guidance for researchers who are validating fluid biomarker tests in their own laboratories.
EPND	EPND is developing an accessible, secure, scalable, and sustainable platform to facilitate access to sharing data and samples from across Europe. Biosamples and data must be harmonised and standardised to the highest possible quality for this effort to be successful. To this end, the EPND consortium has published Best Practices for Biobanking, a set of standard operating procedures for the harmonisation and standardisation of biospecimens.
ERA4TB	ERA4TB aims to create a world-class ‘platform’ that brings together the expertise, tools and resources needed to accelerate the development of anti-TB drug combinations. MBLA (Molecular Bacterial Load Assay) Molecular Biomarkers for preclinical samples. This biomarker enables the quantification of *Mycobacterium tuberculosis* (Mtb) bacillary load based using primers and dual-labelled probes for 16S ribosomal ribonucleic acid (rRNA). This technique can contribute to accelerate the process to determine bacterial load, eventually reducing the time of assays.
ERA4TB	The macrophage and lung-on-chip models of *M. tuberculosis* infection and drug treatment were both tested for the first time in the project and found to be suitable for studying treatment efficacy through long-term time-lapse imaging.
ERA4TB	Advanced analytical strategies based on washing and on-tissue chemical derivatisation led to a 20-fold improvement in sensitivity for isoniazid compared to previous limits of detection, allowing the method to be applied to isoniazid-treated animal model used in the consortium. 7 drugs can now be imaged by mass spectrometry imaging (MSI): Isoniazid, Rifampicin, Ethambutol, Bedaquiline, Pretomanid, Moxifloxacin and Rifapentin.
ERA4TB	Optimised Time Kill Assays (OPTIKA) technique has been consolidated. OPTIKA is a methodology that dramatically increases traditional Time Kill Assays (TKA) capacity, and allows for easy and dynamic interrogation of drug interactions with a colony-forming unit (CFU)-free methodology, allowing the analysis of up to 770 unique conditions at the time, obtaining results after 10 days. A total of 141 different combinations in two different media have been tested with OPTIKA.
ERA4TB	The Hollow Fibre System (HFS) has been consolidated. 4 standard drugs have been validated to be used in the HFS, as well as work with combinations has started. The use of the additional

	Mycobacterium tuberculosis (Mtb) strains in the HFS has been implemented. This is important because until now, there was no HFS capacity in the EU and strains had to be sent to the US for analysis.
ERA4TB	Launched an implementation of an imaging web platform (XNAT), a web platform designed for the central archival and processing of preclinical tuberculosis positron emission tomography / computed tomography (PET/CT) data. The platform is now open to all ERA4TB consortium members and currently hosts 181 image sessions, on 29 different subjects, from 3 different collecting institutions.
ERA4TB	Development of microPET/CT tool for respiratory motion reduction software tools for improved microPET/CT image quality via respiratory motion reduction. This will enable a more accurate quantification of lung lesion in drug efficacy preclinical trials.
ERA4TB	Development of Mtb time-lapse microscopy video processing tool. This is a novel technique to automatically detect the bacterial mass and infer the growth rate and growth speed over a time-lapse microscopy sequence with a method based on a weakly-supervised deep learning. A related manuscript is under preparation.
ESCulab	The European Lead Factory (ELF; funded through the ESCulab IMI2 project) is a screening service with a vast chemical library that can be used by researchers to boost their drug discovery programmes. So far, 100 programmes by the industry/Associated Partner were accepted and 62 programmes had their Qualified Hit List (QHL) delivered. Also, 37 public (crowdsourced) programmes were accepted, and 12 programmes had their QHL delivered. The accepted proposals show a coverage of different therapeutic areas and diseases (i.e., cardiovascular & haematology, CNS & neurology, infectious diseases, inflammatory & immunology, metabolic diseases and oncology). Most proposals came from academia (62%) while the submission of proposals coming from SMEs was significant (38%).
ESCulab	An article was published based on the exploitation of results coming out of the screening of the ELF Compound Library and the generation of the Public Compound Collection. More specifically, this work includes results which were based on the exploitation of scaffolds coming out of the ELF Public Compound Collection.
IM2PACT	IM2PACT investigates mechanisms and models predictive of accessibility of therapeutics into the brain. The project has developed a novel protocol for isolation of neurovascular cells from the human brain which allows to understand the molecular networks in both vascular and parenchymal cells for the first time (manuscript in preparation). IM2PACT has generated an important single nuclei RNA sequencing dataset from 10 Alzheimer's disease (AD) and 10 control donors. The comparison between AD and control is very useful for researchers as it indicates key disease-associated changes that may change the field's understanding of disease mechanism. The brain endothelial cell single nuclei RNA sequencing data of AD and healthy controls' donor brains has been made available as open access dataset and is accessible via this link.
IM2PACT	Neurotropic viruses have evolved to access the brain across the blood-brain-barrier. The project has identified the proteins in brain endothelial cells that these viruses interact with. This work has highlighted that these types of viruses may bind to multiple proteins rather than a single specific receptor for brain entry. This will help guide future research to develop different strategies for passage across the blood-brain-barrier (paper in preparation).
IM2PACT & RESOLUTE	Molecular analysis performed by the project has highlighted that the SLC7A1 (solute carrier family 7 member 1) transporter is a promising disease target candidate to enable brain therapeutic access. The project has performed a variety of experiments to validate this transporter as a promising target and subsequently initiated a multitude of efforts to generate novel tools against SLC7A1 to enable *in vivo* proof of concept for brain delivery. The collaboration with the IMI2 project RESOLUTE was crucial in developing the new tools. A manuscript describing the identification has been submitted for publication.
imSAVAR	The aim of the project is to develop a platform for integrated nonclinical assessments of immunomodulatory therapy safety and efficacy. An initial version of an immune related adverse

	outcome pathway (irAOP) for hepatotoxicity mediated by checkpoint inhibitors (CPIs) was developed, and is currently undergoing representation on the MINERVA tool. MINERVA is a free web-based knowledge management tool. It is integrated with standard representation of pathways to enable users to visualise and obtain detailed representations of biological mechanisms.
imSAVAR	The project established an *in vitro* leakage assay using primary human endothelial cells for the analysis of drug-induced vascular leakage as severe side effect.
INNODIA / INNODIA HARVEST	A novel mechanism for the development of T1D has been described. Investigating the beta cell response to stress, the consortium revealed that autoimmunity can be initiated via the release of mitochondrial DNA and activation of cytosolic sensors, introducing a possible participation of sterile inflammation in the development of T1D. These findings were published in Frontiers in Endocrinology.
INNODIA / INNODIA HARVEST	A platform of iPSC-derived beta-cells suitable for immune-based therapeutics screening has been established and is continuously improved with genetically engineered PSCs models of major T1D candidate genes.
ITCC-P4	The consortium continued working on the establishment, characterisation and preclinical testing of patient derived xenograft (PDX) models with single compound and innovative combination testing (drug-drug and radiotherapy-drug). At the end of 2023, 790 PDX models were registered in the project's IT resource R2 and 392 of these models were fully established spanning all major paediatric tumour types including rare solid and non-solid entities. Out of these 392 established models, 368 were fully characterised together with matching patient samples whenever available. The proof-of concept drug testing has been conducted for each entity with a panel of single compounds (standard of care n=3; novel targeted therapies, n=6) or combinations (with each other or with chemo- or radiotherapy). 48 genetically engineered mouse models (GEMMs) models were established; initial drug testing was initiated on organoids generated from paediatric neuroblastoma patients (from primary and relapse) with matched PDX/organoid drug testing as a direct comparison. In addition, an expansion of organoid development from other tumour types was initiated. These models are powerful tool to investigate the biology of paediatric cancer which ultimately will contribute to prioritise the development of innovative therapeutic options for childhood cancer patients.
MAD-CoV 2	The project published a review in Cell summarising the angiotensin converting enzyme 2 (ACE2) functions, highlighting its relationship with SARS-CoV-2, describing implications for long COVID, and providing a framework for developing universal therapeutic strategies against current and future SARS-CoV-2 variants by exploring the ACE2 pathway and interfering with the spike-ACE2 interaction.
MAD-CoV 2	The project's work led to the development of a standard operating procedure (SOP) for using 3D kidney organoids for SARS-CoV-2 infection. This protocol presents the use of SARS-CoV-2 isolates to infect human kidney organoids, enabling exploration of the impact of SARS-CoV-2 infection in a human multicellular in vitro system.
MELLODDY	The MELLODDY consortium has successfully trained multi-partner models in a distributed and privacy-preserving way, on proprietary data, at scale. By definition, multi-partner models draw on data from multiple partners, and more partners = more data = better data, but data sharing between partners is not always permissible, so new techniques were needed, and MELLODDY delivered these. The project's multi-partner, collaborative models out-perform single-partner models across all the pharmaceutical partners: - collaborative models were typically 4% better at categorising molecules as either pharmacologically or toxicologically active, or not active; - the collaborative model also showed a 10% increase in its applicability domain, i.e. its ability to yield confident predictions when applied to new types of molecules; - the collaborative models were typically 2% better at estimating values of toxicological and pharmacological activities. Performance gains proved more prominent for a subset of the assays relating to pharmacokinetics and toxicology, and for assays with ongoing data acquisition. Collectively,

	these results show improvements to predictive models that support the drug discovery process and should time savings in drug discovery.
MELLODDY	Software to prepare public data (ChEMBL) to test the federative learning pipelines is freely available. Python modules in the processing directory perform: - assay filtering to satisfy the selection criteria, - assay fusion (statistical for binding and functional assays, type-based for physicochemical assays), - binning of continues values into categories, - computation of descriptive statistics for the resulting dataset, - formatting of the final dataset, - building a reference for assay IDs in case the original (pre-fusion) IDs are needed.
MELLODDY	While the models developed within the project remain confidential, much of the platform and software developed in the project is publicly available. These are key technical enablers for privacy-preserving federated machine learning and should be of interest to the broader privacy-preserving ML community:
PREMIER	Predicting biodegradability of pharmaceuticals is challenging because of variability and uncertainty. An inference model was developed for estimating average half-lives, their variability and uncertainty, providing a reliable data source for building predictive models urgently needed to manage existing chemicals and to design benign chemicals. The model is described in Environmental Science and Technology Letters.
RealHOPE	RealHOPE aims to measure real-life events during drug handling to develop methods for simulating these events Through a failure mode and effect analysis, the project published a study that revealed critical vulnerabilities in managing protein drugs, especially monoclonal antibodies. Identified potential stress factors included temperature fluctuations, shock by impact, vibration and light exposure. There were also risks associated with porters' and healthcare professionals' lack of awareness and access to information. Failure to address these issues may compromise drug efficacy and quality, risking patient safety. Recommendations include validated and protocol-based compounding in cleanroom, training, and secure transportation measures to ensure drug integrity.
RESOLUTE	RESOLUTE's aim is to generate new tools and knowledge to boosts research on solute carriers (SLCs), and ultimately, facilitate their use as targets for drug development. RESOLUTE has developed a novel assay using an electrophysiology-based approach to determine the function of SLCs. Further information can be found here along with the published step-by-step protocol of this approach.
RESOLUTE	RESOLUTE has developed a computational screening pipeline to find new inhibitors against the high-affinity norepinephrine transporter (NET/SLC6A2). This study (published here) demonstrates a data-driven approach to diversify known chemical space to identify novel ligands and is first to select this set based on the sequence similarity of related targets.
REsolution	REsolution aims at maximising the chances that solute carriers (SLCs) will become successful drug targets and uses the growing amount of data becoming available on genetic variations and disease association to assign pathophysiological relevance to individual transporters. REsolution has expanded its SLC Knowledgebase, a public data base, with additional publicly available evidence on genetic variation in SLC genes and their association with diseases. The phenotypes linked to SLC variants were associated with specialised ontologies for human diseases or biological entities, highlighting the relevance of the data in a translational context.
REsolution	REsolution has used the Alphafold Protein Structure Database and other structural data to assess and update the current classification of SLCs at the family and fold levels. This analysis uncovers new ancestral relations between solute carrier genes, provide insights into the evolution of remote homologs and a platform to test hypotheses of functional deorphanisation. The results of this study are published here.
SOPHIA	The project identified gut proteins that cause insulin-resistance and metabolic response to bariatric/metabolic surgery. Understanding the intestinal regulation of metabolism could provide

	therapeutic options to reverse metabolic diseases. The findings are published in Nature Communications.
TransQST	To minimise unexpected toxicities in early phase clinical studies of new drugs, it is vital to understand fundamental similarities and differences between preclinical test species and humans. To this end, the project investigated species differences in hepatic stress response capacity. Their findings, published in Toxicological Sciences, are likely to inform the selection of appropriate species for the preclinical safety assessment of drug candidates, based on understanding of mechanism of toxicity and similarity of animal models to humans.
TRIC-TB	The aim of TRIC-TB is to advance the development of two molecules that could boost the infection-fighting ability of the anti-TB drug ethionamide. Development of bioanalytical techniques to quantify alpibectir and ethionamide levels in cerebrospinal fluid (CSF). CSF concentrations can be used as a surrogate measure of the central nervous system's (CNS) availability of drugs. CSF penetration in research model studies is used for assessment of a CNS drug delivery in early preclinical drug development.

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

Project title	Description of result(s)
3TR	Core Outcome Measures sets in paediatric and adult severe asthma (COMSA) to allow comparison of the results from available therapies clinical studies have been developed. These COMSAs can inform the methodology of future clinical trials, enhance comparability of efficacy and effectiveness of biological therapies, can help assessing the socioeconomic value of therapies, and finally, can inform definitions of non-response/response to severe asthma therapy. The COSMAs are described in the European Respiratory Journal.
AB-DIRECT	Developed models that enable to predict the tissue exposure in humans after various doses of gepotidacin. The tissue distribution can be related to the effect of the drug. These models will be a critical tool for future gepotidacin dose selection when considering infections where tissue distribution is likely to play an important role in efficacy, for example in infections of the throat or prostate.
AIMS-2-TRIALS	Shiftability clinical studies are studies where a chemical probe/compound is used to study if it causes a ‘shift’ in a specific mechanism/signal to provide proof of concept for whether a given compound can successfully modulate (i.e. ‘shift’) a biological mechanism(s) underpinning clinical features. It can be used as a mechanistic proof of concept of target engagement in the human brain (many drugs cannot pass the brain-blood barrier and thus never reach their target in the brain). It can be also used for validation studies for a biomarker/endpoint. The consortium published their model design/protocol for shiftability studies so that these can be utilised by the broader scientific community.
AIMS-2-TRIALS	The consortium showed that infants with a high likelihood of autism based on family history have elevated sleep problems apparent from 14 months of age. These correlate with later social attention differences during eye-tracking and increased autistic traits/decreased socialisation and cognitive abilities at age 3 years. Thus, interventions targeted towards supporting families with their infant's sleep problems may be useful in this population. The research is published in the Journal of Child Psychology and Psychiatry.
AIMS-2-TRIALS	The consortium published results detailing maturation of functional connectivity in the neonatal brain during the postnatal period (and how this is modulated by preterm birth). Furthermore, they showed that a repertoire of dynamic states of brain connectivity is present in the neonatal brain differing with age and prematurity and that these dynamics soon after birth are also associated with neurodevelopmental outcomes and autistic traits at 18 months of age.
AMYPAD	The primary results of the AMYPAD Diagnostic and Patient Management Study (840 patients enrolled in 8 European memory clinics) were published in JAMA Neurology providing real-world

	evidence on the utility of amyloid-PET during the diagnostic work-up of patients with suspected Alzheimer's disease.
BEAMER	The main objective of the project is to create BEAMER, a disease-agnostic behavioural and adherence model for improving quality, health outcomes and cost-effectiveness of healthcare, through improving the quality of life of individuals and enhancing healthcare accessibility and sustainability. An extensive literature review on adherence reviewed 41 393 articles and identified 140 for analysis. Based on this analysis, the consortium developed a two-tier BEAMER model. This model integrates significant behavioural factors within existing structural factors. This model will identify patients' support needs and predict relative adherence to treatment. Preliminary statistical analysis of data from patients supports theoretical and empirical results. This work has been accepted for publication in the Journal of Pharmacology Research & Perspectives. 50 stakeholders were also interviewed to collate user needs for the model development.
ConcePTION	Publication of expert consensus on 11 recommendations for investigation of neurodevelopmental outcomes in pregnancy pharmacovigilance studies. These recommendations will improve neurodevelopmental investigations which will reduce the risk to the foetus and increase maternal confidence in medication use during the childbearing years.
ConcePTION	Development of the LifeTIME system aiming at monitoring longer-term child health and neurodevelopmental outcomes in children exposed to medications in utero. The system, composed of a set of questionnaires which will be the primary source of standardised data collection and the development of infrastructure to collect the data, is being tested in a pilot study.
ConcePTION	Results published from an observational clinical lactation study showed that cetirizine and levocetirizine, antihistamines used for allergic disorders, may be considered safe for breastfeeding mothers, as their transfer into breast milk is minimal and compatible with breastfeeding. The study also showed the feasibility of the approach using the European breast milk infrastructure developed within the project.
eTRANSAFE	eTRANSAFE has published a text mining strategy to identify proteomic and genomic biomarkers used in clinical trials and classify them according to the methodologies by which they are measured. More than 3 000 biomarkers used in the context of 2 600 diseases were identified and analysed.
HARMONY	A model providing individualised outcome estimations in adults with acute myeloid leukaemia (AML) with intensive treatment approaches was developed. Predictions for relapse-free survival, cumulative incidence of relapse and overall survival were more accurate than those in the current ELN2022 risk stratification at all predefined time points. The model is accessible online via an interactive web calculator, and with further validation and refinement, it could be used in the future for clinical decision-making.
Hypo-RESOLVE	The impact of hypoglycaemia in people with diabetes can be assessed with the health-related quality of life (QoL) patient reported outcome measure (PROM) developed by the Hypo-RESOLVE consortium. This Hypo-RESOLVE QoL shows validity and reliability and discriminates between those who have and have not experienced a recent hypoglycaemic episode. It is available for use in clinical trials and, potentially, for decision making in clinical practice. The European Medicines Agency (EMA) has provided Qualification Advice with a request to validate the tool in clinical trials.
IDEA-FAST	IDEA-FAST has developed a Python package to facilitate the analysis of the data collected in the context of the feasibility study. This package allows users to efficiently read data from the files in which they are stored, format them and perform analyses. This package will be adapted to the ongoing clinical observational study data.
IDEA-FAST	During the IDEA-FAST Feasibility Study, participants had the option to donate biological samples (blood, urine and stool) to be stored in the IDEA-FAST Biobank housed at the University of Newcastle. Approximately 25% of the participants agreed to donate one or more types of biological sample as part of the study. These samples will continue to be collected during the clinical observational study and will be invaluable for further research into understanding the pathobiology of fatigue and sleep disturbances.

IMI-PainCare	Published an article on the results of a Delphi process involving the INTEGRATE-Pain Consortium (an initiative between IMI-PainCare consortium and the National Institutes of Health (NIH)) to reach consensus on core outcome sets (COS) of domains for acute, the transition from acute to chronic, recurrent/episodic, and chronic pain. This process was the first of its kind to generate four separate, overarching core outcome sets to facilitate international data harmonisation within and across different pain categories. As consensus on the COS was reached between a broad field of stakeholders from Europe and the United States, their adoption in research and clinical practice will facilitate comparisons and data integration globally and across pain studies to improve pain care.
IMI-PainCare	The primary results were published from a postoperative pain treatment non-interventional trial aiming to evaluate sensitivity-to-change of patient-reported outcome measures assessing the core outcome set of domains pain intensity (at rest/during activity), physical function, adverse events, and self-efficacy. The results indicate that a range of domains seems to be necessary for reliably estimating the efficacy or effectiveness of perioperative pain management.
IMI-PainCare	Published an article on results from the Translational Research in Pelvic Pain (TRiPP) sub-project of IMI-PainCare. The study included 769 female participants of reproductive age who completed an extensive set of questions derived from standardised questionnaires. Four pain groups were included, namely, endometriosis-associated pain, interstitial cystitis/bladder pain syndrome, comorbid endometriosis-associated pain and bladder pain syndrome, and pelvic pain only. This work demonstrates the negative impact that chronic pain has on a patient's quality of life and that novel approaches to classifying women with chronic pelvic pain are needed.
IMI-PainCare	The IMI-PainCare project has developed a new electrode to investigate pain perception in a clinical recreation of chronic pain, a condition which affects 1 in 5 Europeans. It is now on the market.
Immune-Image	Macrophages play an important role throughout the body. Anti-inflammatory macrophages expressing the macrophage mannose receptor (MMR, CD206) are involved in disease development, ranging from oncology to atherosclerosis and rheumatoid arthritis. [68Ga]Ga-NOTA-anti-CD206 single-domain antibody (sdAb) is a PET tracer targeting CD206. A first-in-human study of the project evaluated the safety, biodistribution, and dosimetry of this tracer. The tracer is safe and well tolerated. It shows rapid blood clearance and renal excretion, enabling high contrast-to-noise imaging at 90 min after injection. The radiation dose is comparable to that of routinely used PET tracers. These findings and the preliminary results in cancer patients warrant further investigation of this tracer in phase II clinical trials.
Immune-Image	Several research groups have collaboratively worked on designing, synthesising, and developing new tracers for positron emission tomography (PET) and optical imaging. All tracers are to be used to assess the effects of immunotherapy in patients with cancer or inflammatory diseases. Several tracers were successfully made, and from these, a special committee of independent Immune-Image researchers has selected a radio-labelled nanobody targeting CD163 as the most viable new tracer for a first-in-human study. CD163 is expressed on a subset of macrophages, which are activated due to inflammatory processes in the human body around tumours. When CD163 is highly expressed on the macrophages, the human immune system is less active, and the tumour can grow. Immunotherapy should lead to a decrease of macrophages expressing CD163, resulting in activation of the patient's immune system, which subsequently will attack the tumour and reduce the tumour activity and size. Thus, a successful immunotherapy treatment would reduce the uptake of the CD163 targeting PET tracer.
imSAVAR	The consortium developed an immune-related Adverse Outcome Pathway (irAOP) for chimeric antigen receptor (CAR)-T mediated cytokine release syndrome (CRS) and assigned cellular key events leading to this immune-related adverse event (irAE). To identify molecular biomarkers which can be integrated into improved nonclinical test systems, samples and data sets from 180 patients undergoing chimeric antigen receptor (CAR)-T cell therapy were collected so far.
imSAVAR	The consortium established a murine model of systemic lupus erythematosus (SLE) and identified six potential biomarkers to monitor disease severity. The chosen markers are plasma levels of 1) IL-6, 2) TNFalpha, 3) total IgG, 4) anti-double-stranded-DNA IgG, 5) anti-SmD1 IgG and 6) immune cell population (Ly6G+ neutrophils, PD-1+ cells) in the peripheral blood. These biomarkers are being used to assess the efficacy of a low-dose interleukin-2 treatment, which has been shown to be effective in a genetic SLE mouse model.

INNODIA HARVEST	A proof-of-concept study provided the first clinical evidence that radio-labelled exendin imaging can be used to quantify viable β-cell mass in intrahepatic islet grafts of T1D individuals, proving the feasibility of this new imaging method (Monitoring β-Cell Survival After Intrahepatic Islet Transplantation Using Dynamic Exendin PET Imaging: A Proof-of-Concept Study in Individuals With Type 1 Diabetes | Diabetes | American Diabetes Association (diabetesjournals.org)). This new method is now used to measure beta-cell viable mass before and after treatment with verapamil sustained release (SR) in newly diagnosed T1D patients in the Image-Ver-A-T1D study carried out in INNODIA HARVEST.
LITMUS	Proof-of-principle that nuclear magnetic resonance (NMR)-based metabolomics can be used to find non-invasive metabolic biomarkers to measure NASH onset and progression has been established. It includes a 31P nuclear magnetic resonance (NMR)-based method to study the liver 'phosphorome' through the simultaneous identification and quantification of multiple hydrophilic and hydrophobic phosphorylated metabolites.
NECESSITY	In collaboration with a third party deep-tech company ScientaLab specialised in artificial intelligence, the project developed predictive algorithms to identify Sjögren's populations, standardisation of measures and identification of histological biomarkers. The algorithm autonomously learns from clinical data and labial salivary gland biopsy slides. It effectively utilises lymphocyte aggregates to achieve an 87% accuracy in predicting focus score and an 84% accuracy in diagnosing Sjögren's syndrome. This technology is meant as a support tool in assisting non-expert pathologists in obtaining an accurate diagnosis and it has been presented at the 2023 EULAR and ACR meeting (eular_2023_abstract_book_may2023.pdf page 166).
NECESSITY	NECESSITY has identified serum protein biomarkers (Galectin-9, CXCL10, CXCL11) that can predict and monitor clinical response upon Leflunomide/hydroxychloroquine therapy. The research is published in RMD (Rheumatic and Musculoskeletal Diseases) Open.
T2EVOLVE	Prompt recognition of acute chimeric antigen receptor T (CAR T)-cell–mediated toxicities is crucial because adequate and timely management can prevent or reverse potential life-threatening complications. T2EVOLVE has produced a set of patient- and caregiver-reported signs to facilitate the early recognition of CAR-T therapy toxicities. This study provides a core set of patient- and caregiver-reported signs and symptoms and definitions of red flags warranting immediate action to include in a daily checklist for support at home, with the goal to make outpatient post–CAR T-cell care safer, optimise patient and caregiver support, and thereby facilitate an early discharge/hospital visit reduction strategy.
TRISTAN	The consortium reported a panel of two imaging biomarkers (hepatic uptake (khe), and biliary excretion (kbh)) with potential for detection and quantification of drug-induced liver injury (DILI).

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
AMYPAD	Published an article in EJNMMI Physics outlining the necessary steps for accurate amyloid-PET acquisition and quantification to ensure the proper use of this technique in research and clinical settings.
BigData@Heart	The consortium published a paper 'Sex Differences in the Generalizability of Randomized Clinical Trials in Heart Failure with Reduced Ejection Fraction', which highlights the need for more representative clinical trials in patients with heart failure and reduced ejection fraction (HFrEF), taking into account sex differences in order to improve the generalisability of the results to the broader population
c4c	Held two additional multistakeholder meetings (MSM) gathering young patients and advocates, clinicians, academics and researchers, pharmaceutical companies and regulators to discuss scientific and/or regulatory challenges encountered in a specific field and to agree on a new development path:

	MSM on medical devices in paediatric type I diabetes focusing on how to improve the timely development and access of medical devices for children with type I diabetes, properly address paediatric unmet needs, introduce innovative development pathways in the regulatory environment and increase accessibility for all patients. MSM on perinatal asphyxia looking at the steps toward a strategy to improve the timely development and access to additional therapies to therapeutic hypothermia, properly addressing neonate unmet needs, introducing innovative development pathways in the regulatory environment and increasing accessibility for all patients. These meetings demonstrate the importance of having open debate and exchange between all relevant stakeholders (mock up that can used for further meetings) to advance the paediatric fields.
c4c	Process of providing strategic feasibility advice to sponsors further improved. In total since this process became operational, over 50 advice requests have been received from industry and academic c4c partners (covering any clinical, methodology and patient and public involvement aspects of paediatric drug development), of which 37 advices have been completed. About 30% these experts' advices have been used by sponsors when discussing their paediatric investigation plan with the Paediatric Committee at the European Medicines Agency (EMA).
CARDIATEAM	Refinement of diagnostic algorithm for silent diabetic cardiomyopathy
COMBACTE-NET (IMI1)	Online tool RShiny app developed that can visualise the probability of observing an event of interest, like ventilator-associated pneumonia, over time, and how discharge and death influence the likelihood of observing it. This tool can be used to plan clinical trials on novel interventions against multi-drug resistant organisms, and optimise sample size. It can also be useful for regulatory authorities to understand hidden effects in published randomised trials. For example, there may be a lot of early deaths that are overlooked if only judging the effectiveness of an intervention by looking at the overall, reported effect estimates. Finally, it provides a deeper understanding of the interaction of different time-dependent processes in the studied population.
COVID-RED	The consortium ran a clinical trial (NL9320) testing a novel algorithm ingesting data from a wearable device to provide personalised, real-time alerts about a potential SARS-CoV-2 infection to the subjects for potential of personalised biofeedback during a global pandemic. This trial is the first of a kind and the many learnings from it will definitely benefit the research community. A checklist was developed to communicate lessons learned from the COVID-RED project, and to support the set-up of similar projects in the area of remote monitoring and technologies for infectious diseases. The checklist is publicly available as Deliverable 3.7.
EU-PEARL	EU-PEARL developed a suite of templates including a generic master protocol for users who are developing platform trials in any disease area and in the four specific disease areas of major depressive disorder (MDD), tuberculosis (TB), liver disease non-alcoholic steatohepatitis (NASH), and neurofibromatosis (NF). In addition, a best practices tool was developed to help in the operational planning and development of platform trials. The tool looks at the main tasks involved in planning a clinical trial and highlights the special considerations that arise when designing a platform trial on top of those that are typical for a conventional trial. All resources developed in the EU-PEARL project are publicly available and can be downloaded here. The Children's Tumor Foundation and the Global Coalition for Adaptive Research announced that they will set up a platform trial for neurofibromatosis 1 (NF-1) and schwannomatosis based on the framework created for planning and rolling out a platform trial in EU-PEARL.
EU-PEARL	EU-PEARL has developed a community engagement framework to ensure fair and efficient participation of the community in the design and implementation of TB clinical platform trials. This work showed that early engagement of the EU-PEARL community advisory board significantly contributed to the development of a community-acceptable master protocol for TB trials.
H2O	The feasibility study protocol to assess and compile recommendations for the sustainable growth of health outcomes observatories which are systematic and organised framework/institutions dedicated to monitoring, assessing, and analysing health outcomes over time, has been pre-published and is accessible to the public.

H2O	H20 has established and designed a digital system for the collection of patient data. This is composed by three primary blueprints, 1) on the development of a new data collection site, 2) on the addition of a new technology provider, and 3) on the inclusion of a new H2O-accredited disease outcome set. The purpose of the blueprint is to compile H2O approaches related to establishing and/or expanding the H2O model, developed within different work streams, and to provide guidance on how these can be applied. As new countries, data sources, diseases, and technology partners are brought into the H2O network, this blueprint can help steer future collaborators. As the H2O consortium is already starting to expand beyond the initial four countries, they needed a documented approach that can be used not only for any expansion during the remaining years of IHI funding but also for the management of the growth of the network once this becomes fully independent.
H2O	An internal project protocol was developed to the standardise the process of questionnaire translations across all four tier one countries. This document ensures that one consistent and scientifically sound process is used by each country when translating a needed questionnaire when a local language is not available.
H2O	The Health Outcomes Observatory developed user profiles for patients with chronic illnesses and considered the usability of the technology for populations with physical and mental burdens resulting from their disease. These profiles will be used by the technology design and implementation teams to ensure that all H2O technologies and systems are user-friendly for patients and healthcare providers. These profiles provide information on new sub-populations by level of capability needs. A paper on the results of these technical requirements and patient sub-groups has been pre-published.
HARMONY PLUS	The ability to compare clinical trials is limited due to differences in their measured outcomes. Aiming at improving clinical trial design and also allowing and facilitating comparison of different clinical trials outcomes in the future, the following disease specific outcomes were defined for the blood cancers comprised in HARMONY PLUS: In chronic myeloid leukaemia: overall survival (OS), complete remission (CR), major molecular response (MMR), progression-free survival (PFS), event-free survival (EFS), duration of response (DOR), and time to progression (TTP).
imSAVAR	The consortium has formulated a template for the compilation of subject and sample metadata utilised in experiments or experimental designs with the purpose to catalogue data using controlled vocabularies, based on Standard PREanalytical Code (SPREC). This Excel-based template is entirely compatible with the REDCap data capture system which is an instrument to compile information and capture essential metadata related to studies and cohorts. This compatibility will allow storing (meta)data collected via excel template taking into account the FAIRification process.
INNODIA / INNODIA HARVEST	A new master protocol for interventions in newly diagnosed T1D patients using combination therapies has been developed and has received positive advice by the European Medicines Agency (EMA). A new combination trial, ‘T1D Plus’, is planned by INNODIA iVZW non-profit organisation, which will use this master protocol.
MACUSTAR	Published an article on the properties of measurements from device-based testing of visual function in a study involving participants with intermediate age-related macular degeneration (iAMD). The study indicated that the measurements used had adequate test-retest variability and are all moderately good at separating people with iAMD from controls.
MACUSTAR	MACUSTAR aims to develop novel clinical endpoints in patients with intermediate age-related macular degeneration (iAMD). To that end the consortium is overseeing a clinical study (NCT03349801) with two parts, a cross-sectional and a longitudinal part in 7 European countries at 20 participating clinical sites with 719 participants. The longitudinal part of the study is ongoing with 440 patients enrolled by the end of 2023. Sufficient data collection in the longitudinal part will support the qualification of outcome measures as endpoints for future age-related macular degeneration (AMD) trials.
Mobilise-D	Published an article on the acceptability by study participants of using a wearable device to remotely measure mobility in the Mobilise-D technical validation study (TVS) and the acceptability of using digital tools to monitor health. This work suggests that waist-worn devices were

	supported by study participants and that patients may in general be willing to use new digital tools to help them manage their health.
PROMISE	Developed generic protocols for assessing the effectiveness of immunisation products against respiratory syncytial virus (RSV) using register-based cohort as well as test negative case control study designs. These protocols have been shared with WHO and ECDC (the European Centre for Disease Prevention and Control).
RADAR-AD	Published an article in PLOS ONE on the ethics review process of the RADAR-AD clinical study protocol by local research ethics committees. The article indicates that review processes in similar multi-site studies would benefit from harmonisation in research ethics governance processes.
Trials@Home	The Trials@Home RADIAL study (EUCT number: 2022-500449-26-00) focuses on people living with type 2 diabetes and aims to compare decentralised and hybrid clinical trial approaches with a conventional clinical trial arm. The study has been approved in Germany, Denmark, Spain, Italy, Poland, and the UK and patients are currently being recruited.
Trials@Home	Trials@Home have developed quality criteria and assessment procedures for the quality assessment of the technologies for their pan-European decentralised clinical trial pilot study.
Trials@Home	Draft recommendations based on in-depth research into remote decentralised clinical trial methods have been released. They apply to all aspects of DCTs from design, planning and set-up to close-out and reporting. There are three key recommendations: (1) answer an important research question; (2) keep the focus on participants; (3) simplify the participant experience whilst maintaining quality and scientific rigour.
Trials@Home	Since clinical trials (CTs) are authorised and supervised at the national level in the EU, relevant national legislation and guidance can impact CTs conducted differently throughout Europe. Trials@Home have mapped and analysed the pre-COVID-19 legal and ethical framework at the EU and Member State (MS) levels to identify opportunities and challenges and provide recommendations to others on conducting decentralised clinical trials (DCTs). The mapping includes EU and national legislations, including legal, regulatory, ethical and GCP (good clinical practice) aspects that may be relevant to DCTs.
VALUE-Dx	The aim of the PRUDENCE trial (20/NW/0385) is to find out whether having a diagnostic test result available for community-acquired acute respiratory tract infections, such as sore throat or cough, when health care professions make a decision about antibiotic prescribing, leads to more appropriate prescribing decisions without causing harm to patients. The PRUDENCE trial includes participants recruited by primary care clinicians and in Long Term Care Facilities (LTCF). Up until the end of 2023, PRUDENCE has reached its recruitment target of 2,500 enrolled participants. Patients have been recruited in 37 sites in 10 different countries (primary care), and in 6 sites in 6 different countries (LTCF).
VALUE-Dx	ADEQUATE (NCT04547556 and NCT04781530) is a randomised controlled trial of rapid syndromic diagnostic testing for enhancing the quality of antibiotic prescribing for community acquired acute respiratory tract infection (CA-ARTI) in Emergency Rooms in Europe. The ADEQUATE study consists of a paediatric protocol and recruits patients aged from 0 to 17 years at 6 sites in 5 different European countries. To date, 504 participants have been enrolled, out of an overall target of 520 patients.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s)
VITAL	A statistical model to predict 'vulnerability to infectious diseases' as a potential 'immunosenescence' phenotype is under validation. This model could be used to identify people with increased susceptibility to infectious pathogens and poor vaccine responses.
VITAL	VITAL has identified 3 immune profiles for people with a certain cellular immune profile associated with poor and good response to influenza vaccination. These immune signatures could be used to identify people with poor response to influenza vaccination. The study is described in Aging Cell.
VITAL	VITAL has developed and validated a novel metric of immune perturbation that is associated with vaccine immune response in a specific patient group known to respond less well to vaccination. (A manuscript is in preparation) These immune signatures and the immune perturbation metric could be used to identify individuals at risk of low vaccination response. The predictive value of the signatures may lead to future implementation of these signatures in vaccination practice.
VITAL	A high-quality gene expression dataset was generated for whole blood samples of 150 individuals in the clinical vaccination study at 3 time points after Influenza and Pneumococcal vaccination. A first analysis indicates a rich vaccine specific signature for both vaccines with relevant significant innate, adaptive blood transcriptional modules and differences between age groups. Additional analyses will be performed in the context of antibody responses and underlying (immune) phenotypes.

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

Project title	Description of result(s)
HIPPOCRATES	An initial multiomic study has been completed aiming to identify molecular biomarkers of progression from psoriasis to psoriatic arthritis. Serum samples were analysed from patients from the Biomarkers for COMorbidities (BioCOM) study, distributed equally across participants with established psoriatic arthritis and psoriasis with and without clinical features to suggest musculoskeletal disease. Samples were subjected to omics analyses (targeted and affinity-based proteomics, genomic, metabolomic and lipidomic).
NECESSITY	The project compiled a roster of top-performing antibody clones to phenotype various immune cell markers on paraffin-embedded formalin-fixed salivary gland tissue, encompassing both parotid and labial salivary glands. The objective was to validate tissue biomarkers with the utmost discriminatory potential to categorize patients and forecast their response or resistance to various synthetic disease modifying anti-rheumatic drugs (DMARDs) and/or biological therapies assessed across diverse randomized control trials.
NECESSITY	A first version of a causal disease model of Sjögren's disease in the blood has been produced by using network computing, in the form of an interactome of dysregulated genes. This approach will be applied to the four clusters of Sjögren's patients based on molecular profiling, in order to identify candidate biomarkers allowing to categorise patients in each of those clusters and to compare molecular profiling of patients with myeloma versus the others.
NECESSITY	Using a longitudinal salivary gland biopsy analysis and the candidate STAR and CRESS composite endpoints developed in the project, the NECESSITY project identified salivary gland biomarkers (B cell density, T cell constimulation, epithelial absorption etc.) associated with clinical response to Rituximab. Rituximab is a monoclonal antibody that targets CD20 proteins on the surface of B lymphocytes, thus decreasing their activity, as in autoimmune diseases like Sjogren's the B lymphocytes are overstimulated causing inflammation. Also, the project identified serum biomarkers (peripheral CXCL13, IL-22, IL-17A, IL -17F and TNFα) which are associated with clinical response to Rituximab and will be proposed as

	candidate stratifiers for the identification of patients with a higher chance of clinical response to B cell depletion. The work has been accepted for publication in Arthritis and Rheumatology.
SOPHIA	The work of the consortium has led to the elucidation of the genetic differences between people with obesity that develop diabetes and those that do not, and to a better understanding of the mechanism that leads to the development of T2D by obesity. The research was published in Nature Metabolism.
SOPHIA	A multi-stakeholder consensus on the language to be used to describe obesity as a chronic disease has been achieved by the SOPHIA consortium researchers. The work, described in eClinicalMedicine, forms the basis for a unified language of obesity.

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

Project title	Description of result(s)
AB-DIRECT	A phase 1 clinical study to investigate tissue distribution of the novel antibiotic gepotidacin was completed in May 2023 with 48 subjects receiving a single dose of gepotidacin enrolled. The distribution was determined by *ex-vivo* microdialysis procedure, using tissues removed during surgery. Gepotidacin is a new first-in-class antibiotic for treating uncomplicated urinary tract infections. These are the most common bacterial infections affecting humans worldwide and one of the most frequently treated with antibiotics. ClinicalTrials.gov Identifier: NCT04484740
AIMS-2-TRIALS	The total participant enrolment in the project human cohort studies on autism and co-morbidities has now well surpassed 2 500 individuals, and in most of the studies each individual is comprehensively characterised by their clinical, cognitive and behavioural profiles, brain structure and function and contributing molecular processes, genetics/ genomics and environmental factors. This represents a unique resource for the research community including the developers of health technologies.
AIMS-2-TRIALS	The genetics of autism are very complex. Some autistic people have a genetic syndrome associated with autism, like Angelman syndrome or dup15q syndrome, whilst others do not. The consortium started the new study called EAGER (European Autism GEnomics Registry) to recruit autistic people and those with associated rare genetic conditions (target is 1500 people in 8 European countries – UK, Spain, Italy, Germany, Sweden, Ireland, France, and Portugal). The aim is to better understand the differences and similarities between the two groups and foster the development of evidence-based care for autistic people and those with associated rare genetic conditions across a range of intellectual abilities. The data from EAGER will be used to investigate the relationship between genetics and outcomes like mental and physical health and quality of life.
AIMS-2-TRIALS	The consortium completed recruitment for the phase 2 randomised, double-blind, placebo-controlled study (NCT03682978) of the efficacy, safety, and tolerability of arbaclofen administered for the treatment of social function in children and adolescents with autism spectrum disorders, with 141 participants recruited and 123 randomised successfully. Only one serious adverse event was recorded throughout the entire trial. Data analysis has started. Preliminary results show that phenotypic matching was successful, with no significant differences between drug and placebo groups. Data will be combined with 90 participants from the parallel Canadian trial of 90 participants (ARBA Study, US NCT number: NCT03887676) to maximise statistical power of further analyses. This demonstrates the capability of the project clinical trial network and the added benefit of the project international dimension.
BEAMER	The consortium used statistical techniques to analyse data from the registries of the health system of Madrid, which includes 163 000 patients, and the health system of Catalonia, with 900 000 patients, to evaluate the different structural factors in adherence to treatment. The study is not related to any specific treatment because it encompasses patients with different types of

	diseases. In addition, several different adherence targets (morisky scale, polymedication, risk level) were also used.
c4c	To test the viability of the paediatric network, the non-industry proof of viability (PoV) studies are ongoing and progressing towards completion of recruitment: – TREOCAPA (paracetamol in premature babies; over 500 out of the 794 children recruited in phase III; – KD-CAAP (Kawasaki disease coronary artery aneurysm prevention trial; at the end of December 2023: 78 participants recruited out of 262). 2 industry PoV studies are also ongoing involving c4c network sites, open for recruitment: – Operetta 2 (for children and teenagers living with relapsing-remitting multiple sclerosis (RRMS); – Fiona (chronic kidney disease and proteinuria). And for 2 other industry studies, clinical sites from the c4c network are being selected (Janssen phase 3 study on ulcerative colitis and Novartis phase 3 study in asthma). These PoV trials covering all countries represented in the network involve a range of different designs, populations and outcomes, at distinct stages of trial delivery (i.e. some ongoing, others during trial setup or earlier at a product development level) and with different operational setups. This is essential to refine processes and optimise the way the c4c network works.
CARDIATEAM	Development of a prospective multicentric cohort of diabetic and non-diabetic patients with and without heart failure with preserved ejection fraction (NCT04303364). So far 831 have patients recruited from 5 countries (France, UK, Netherlands, Germany, Spain) out of 1 600 patients expected.
COMBACTE-CARE (IMI1)	Further results published from the international matched case-control-control study (EURECA) showing that the main risk factors for carbapenem-resistant Enterobacteriaceae (CRE) infections in hospitals with high incidence included previous colonisation, urinary catheter and exposure to broad spectrum antibiotics. These results of EURECA carried out in 50 hospitals with high CRE incidence from March 2016 to November 2018 and investigating different aspects of infections caused by CRE could help with decisions about using empirical drugs active against CRE in patients, and for better selecting the most patients to be recruited for randomised trials testing drugs against these pathogens. (NCT02709408). Furthermore, in this study genomic data of 687 carbapenem-resistant strains were recovered among clinical samples from 41 hospitals in 9 Southern European countries and these were compared with the previous EuSCAPE collection (2013-2014). Results showed the evolution of *K. pneumoniae* high-risk clones circulating in Europe, providing important insights useful for implementing local control strategies.
COMBACTE-CARE (IMI1)	Completion of Phase 3 REVISIT study that evaluated the efficacy, safety and tolerability of the novel antibiotic combination aztreonam-avibactam (ATM-AVI) in treating serious bacterial infections caused by Gram-negative bacteria, including metallo-β-lactamase (MBL)-producing multidrug-resistant pathogens for which there are limited or no treatment. Results support that ATM-AVI is effective and well-tolerated, with no new safety findings and a similar safety profile to aztreonam alone. Approximately 50% of all subjects randomised were from the COMBACTE clinical network Clin-net (out of 165 global sites activated for enrolment, 75 were from the COMBACTE Clin-net network; and 201 out of the 422 patients randomised globally were from the Clin-net network).
COMBACTE-MAGNET (IMI1)	Consolidation of the EPI-Net Excellence Centers Network - a network of healthcare centres sharing surveillance data for epidemiological research. Information on active members of the EPI-Net Excellence Centers whose clinical research portfolio are available for download has been released.
COMBACTE-MAGNET (IMI1)	Publication of the results of the One Health consensus initiative, conducted between March 2021-January 2022 in The Lancet Regional Health - Europe. This paper outlines recommendations from a panel of 56 experts from 20 countries to guide strategic reporting of antimicrobial resistance (AMR) and antimicrobial consumption surveillance data from the human, animal, and environmental sectors.

COMBACTE-MAGNET (IMI1)	The consortium worked extensively on looking at impact of host- and pathogen-related factors on the incidence of *P. aeruginosa* ICU pneumonia, on the improvement of diagnostics, patient prognosis and *P. aeruginosa* ICU pneumonia control. Two manuscripts were published, one showing that pulmonary populations of *P. aeruginosa* are often polyclonal, and resistance emergence is through selection for pre-existing resistant strains. However, strong trade-offs between resistance and fitness occur in polyclonal populations that can drive the loss of resistant strains when antibiotic pressure is weak. These data show that the within-host diversity of pathogens plays a key role in shaping the emergence of resistance in response to treatment (Nature Communications). The other published study explores predictive biomarkers of *P. aeruginosa* ventilator-associated pneumonia in blood/plasma due to dysregulation of proinflammatory and endothelial factors at time of admission (Critical Care). All of the work done by the consortium during the project has created very novel and useful insights into earlier detection and prevention of *P. aeruginosa* ICU pneumonia as well as adding considerations to treatment options and even potential vaccines or new treatment targets.
EPND	EPND aims to accelerate research in neurodegenerative diseases and is starting this effort by providing a catalogue of international studies across the neurodegenerative spectrum in one place. The catalogue, available here, already has over 60 studies with metadata on participants, bio sample collections, imaging and cognitive data.
ERA4TB	A clinical trial network comprised of clinical trial units (CTU) from academic and industry had been established at the beginning of the project to develop the FTIH (first time in human) trials on the consortium's molecules. ERA4TB now counts 6 CTUs, 5 in academic institutions and 1 in industry. In terms of geographical distribution: one in the Netherlands, one in Germany and 4 in Spain. This network will stimulate a new era of research and new funding incentives with significant impacts on academic research in terms of new knowledge creation, better understanding of the disease, implementation of assays and techniques already validated and sourced from the consortium members or collaborating partners, potential for new techniques and assay validation, access to a wealth of data generated in diverse studies and better integration.
H2O	The observatory in Germany was established in 2023. Thus, all four tier one countries (Austria, the Netherlands, Spain, and Germany) now have formally established data observatories with the start of the data entering. H2O-NL formed a collaboration with PRO-Lung study in the PROFILES Registry in the Netherlands, combining their registries and expanding the outcomes collected, which creates a larger and more rich data set. H2O support of and alignment with the diabetes registry at the Medical University Vienna: the addition of this registry will enrich the H2O-Áustria observatory and will include novel data beyond the scope of the core outcomes sets developed by H2O.
H2O	H2O has developed the diabetes outcome sets to allow for, to foster, and to promote research using diabetes PROs (Network). This will promote the use of the H2O set around the world and especially with the association with ICHOM (International Consortium of Health Outcomes Measurement), which is a large-scale, well-established, and trusted global PROM institution, which accredited the set. The association with ICHOM should improve the odds that an organisation collects an H2O outcome set, making it more likely that they pursue a formal collaboration with the H2O project as a new observatory or as an extension of an existing one.
HIPPOCRATES	A large, pan-European and multi-centre clinical network was established as part of the HIPPOCRATES Prospective Observational Study (HPOS). HPOS has been designed to enable web-based online recruitment of 25 000 people with skin psoriasis to be followed prospectively for the development of psoriatic arthritis. The study was initially launched in the UK and Ireland before being rolled out to other European countries. By the end of 2023, 1 211 psoriasis patients had already been recruited.
iABC (IMI1)	By painting a detailed picture of the lung disease bronchiectasis in different European countries, the iABC project is helping to drive new research on the disease. In a paper published in The Lancet Respiratory Medicine, researchers used an international clinical research network to describe the clinical characteristics of bronchiectasis and compare the disease between different European countries. The network established by EMBARC is being used by pharmaceutical companies to support clinical trials, and the first clinical trials delivered directly by the EMBARC consortium have been initiated (ISRCTN70034823).

iABC (IMI1)	Completion of the phase 2 study, a randomised, subject and investigator-blinded, placebo-controlled, parallel group to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of QBW251, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, in subjects with bronchiectasis. 20 patients were randomised. (clinicalTrials.gov NCT04396366). Following the database lock in September 2023, data collected are being analysed together with data from a separate study carried out under the same protocol in parallel in China.
iABC (IMI1)	Completion of healthy volunteer Spexis sponsored study with inhaled murepavadin in a total of 39 subjects. Results showed favourable tolerability, safety and pharmacokinetic profile of murepavadin inhalation solution and could support further clinical trials in people with cystic fibrosis (CF) or non-CF bronchiectasis.
IDEA-FAST	IDEA-FAST aims to identify digital endpoints that provide reliable, objective and sensitive evaluation of activities of daily life (ADL), disability and health related-quality of life (HRQoL) for the following neurodegenerative diseases (NDD): Parkinson's disease (PD), Huntington's disease (HD) and the following immune-mediated inflammatory diseases (IMID): rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), primary Sjögren's syndrome (PSS), and inflammatory bowel disease (IBD). By the end of 2023, regulatory approvals had been obtained and nearly 1 000 patients recruited in 18 sites.
IMMUcan	IMMUcan is a group of university and industry partners that collects tumour material and clinical data from several thousand cancer patients. The group generates biological data for research that is being made available for the scientific community. IMMUcan aims to study the tumour microenvironment in a bid to gain a deeper understanding of how the immune system and cancer cells interact at the molecular level. IMMUcan is accessing patient biological material and linked clinical data via the EORTC (European Organisation for Research and Treatment of Cancer) SPECTA platform. 175 principal investigators from 126 clinical sites from 20 countries have been authorised to recruit patients in SPECTA as of December 2023. In addition, the project accessed 7 clinical studies, cohorts or archival material collection outside EORTC SPECTA.
Immune-Image	Within Immune-Image, seven small clinical studies are planned to demonstrate the efficacy of PET tracers as well as fluorescently labelled tracers to be used with optical imaging as markers for the effectiveness of immunotherapies. Five of these studies currently recruit patients, and the first results have been obtained. Although these results are still preliminary, they are very promising. For instance, the PET tracer [18F]fluoro-PEG-folate has been used in rheumatoid arthritis patients during treatment. A reduction of the PET tracer uptake is observed upon treatment, indicating successful therapy. Currently, eight patients that were included have passed the complete clinical studies.
ImmUniverse	ImmUniverse aims to understand the crosstalk of tissue and immune cells in progression/remission of ulcerative colitis (UC) and atopic dermatitis (AD), and to correlate tissue-derived signatures with circulating signatures detectable in liquid biopsies using omics technologies. The parallel study of two different immune-mediated diseases will enable the identification of both disease-specific as well as cross-disease signatures and underlying pathological pathways. The consortium has established a network of clinical partners to create an open-label cohort of patients receiving first time targeted therapies during standard clinical care. A total so far of 144 AD and 205 UC patients have been prospectively recruited by the active centres.
imSAVAR	The consortium has devised a REDCap instrument to compile information and capture essential metadata related to studies and cohorts. This represents a fundamental aspect of the FAIRification process.
PRISM 2	The PRISM 2 clinical study that seeks to determine the reproducibility and generalisability of the identified quantitative biological parameters for social dysfunction and default mode network (DMN) integrity that accounted for patient stratification in PRISM, has now successfully recruited 107 participants out of the 160 planned.
PROMISE	PROMISE is conducting a case-control validation study to validate biomarkers. The study population consists of previously healthy infants with respiratory syncytial virus (RSV) of different

	severity (ventilated infants, hospitalised non-ventilated infants, medically attended non-hospitalised infants and healthy controls without RSV). Recruitment and data and sample collection took place between November 2021 and June 2023. In total, 102 infants have been recruited.
PROMISE	Building on the RESCEU project, PROMISE aims to fill knowledge gaps in respiratory syncytial virus (RSV) to design public health strategies and promote the development and use of RSV vaccines and therapeutics. PROMISE published a study investigating the age profile of RSV burden in preschool children of low- and middle-income countries. This work suggests that the ideal prophylactic strategy may require multiple products to avert the risk among preschool children.
PROMISE	Conducted a study with 14 studies from a systematic review and 47 studies from international collaborators to investigate the changes in RSV hospitalisation burden in young children during the COVID-19 period. The study results indicate that the hospitalisation burden of RSV-associated acute lower respiratory infection (ALRI) in children younger than 5 years was significantly reduced during the first year of the COVID-19 pandemic. The findings are now published in Lancet Infectious Diseases.
PROTECT-trial	PROTECT-trial has prepared the protocol of their 'photon vs proton' clinical trial. The study will test the hypothesis that proton therapy will result in lower pulmonary complication rates in oesophageal cancer compared to standard photon therapy. 396 patients are expected to be recruited. A summary of the protocol is available on the project website. ClinicalTrials.gov identifier: NCT05055648.
RADAR-AD	Successfully completed the RADAR-AD clinical study (EudraCT number: 2020-004925-22) to assess the utility and feasibility of using remote monitoring technologies such as smartphones or wearable devices to assess function and cognition in a real-world setting. Participants were selected from memory clinics and ongoing observational studies. In total, data was collected for 272 participants.
RESCEU	RESCEU studied the cost-effectiveness of employing monoclonal antibodies (mAb) and material immunisation interventions against respiratory syncytial virus (RSV) in infants in six European countries. The results were published in the journal Vaccine and may be used to inform decision making on the implementation of RSV intervention programs in infants.
RESCEU	RESCEU published several articles looking at the burden of respiratory syncytial virus (RSV)-associated hospitalisations in the European Union. One study estimated RSV-associated hospitalisations in adults by gathering data from several European countries over the period 2006 to 2017. This work suggests that the average annual hospitalisation estimate in adults was of a similar magnitude to the estimate in young children. Another study estimated RSV-associated hospitalisations in children under 5 years in the European Union by gathering data from several European countries over the period 2006 to 2018. The estimates provided can be used to optimise public health responses to RSV and support planning for future RSV immunisation programmes.
RESCEU	The results from a multicentre, prospective, observational birth cohort study in healthy term-born infants investigating the healthcare burden of respiratory syncytial virus (RSV) were published in The Lancet Respiratory Medicine. The results show that RSV causes substantial morbidity in healthy term-born infants in high-income settings, indicating that immunisation of pregnant women or healthy term-born infants during their first winter season could reduce the healthcare burden caused by RSV.
RTCure	Several clinical trials aimed at the prevention of rheumatoid arthritis (RA) were performed within the RTCure umbrella, in collaboration with other initiatives. These include the use of methotrexate and corticosteroids to delay RA and reduce its symptoms, or the use of abatacept showing a major delay of onset of RA during an active treatment period, with statistically significant preventive effects also after 1 year of non-treatment follow-up. These studies demonstrate how interference with adaptive immunity can delay or prevent RA, thereby setting the scene for additional and in the end more specific immunotherapies for prevention of RA.

STOPFOP	The STOPFOP clinical trial (EudraCT: 2019-003324-20; ClinicalTrials.gov: NCT04307953) investigates the repositioning of saracatinib, originally developed for ovarian cancer treatment, to treat patients with fibrodysplasia ossificans progressiva (FOP). FOP is a rare condition which causes bone to form in muscles, tendons and ligaments. All patients required for this study have enrolled. The majority have completed the first phase and moved to the second (final) phase of the trial with promising results obtained so far. This study will provide data to support the treatment of a serious condition for which no treatment currently exists. A peer reviewed article has been published on the design of the study.
UNITE4TB	The final study protocols for the phase 2B trial (DECISION) and phase 2B/C trial (PARADIGM4TB) were finalised including trial design, selected compounds and combinations to be tested. For PARADIGM4TB, a dedicated EMA scientific advice was sought on an initial version of the protocol and the feedback was incorporated into the final version. DECISION (BTZ-043 Dose Evaluation in CombInation and SelectION, NCT05926466) is a phase 2B, dose finding study, comparing the safety and efficacy of different doses of BTZ-043 administered with a backbone of bedaquiline and delamanid, in participants with drug-sensitive tuberculosis. Participants will be assigned to receive either one of three BTZ-043-containing regimens or a comparator regimen of bedaquiline, delamanid and moxifloxacin. The objective is to find the optimal dose of BTZ-043 to be used in subsequent studies. PARADIGM4TB is an innovative seamless phase 2B/C platform trial that will be active in approximately 30 trial sites on four continents (Europe, Asia, Africa and South America), with the goal of delivering novel phase 2B/C clinical trials that will accelerate the development of new TB drugs and regimens with a higher probability of success in subsequent phase 3 clinical trials. The Phase 2B/C clinical trial programme has had its first participant enrolled at its trial site in Cape Town, South Africa. This is a major milestone for the project and the TB community as a whole, helping to advance TB science and enhance the efficiency with which new treatments are delivered.
VHFMODRAD	A cohort at 2 centres (Sweden and Turkey) established within the VHFMODRAD consortium has been used for validation of assays for diagnostics developed by the consortium during 2023.
VITAL	VITAL has produced age- and gender-stratified frailty prevalence estimates in all European countries. 311 915 individuals were analysed from 29 countries. Observed and predicted data on frailty rates by country are provided in the interactive Frailty Atlas for Europe and published in the journal Geroscience. This information helps predict and evaluate prevention from infectious diseases in older adults.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
BEAMER	Statistical assessment of factor strength and correlation of clinical factors influencing adherence to treatment. Based on the analysis of the regional healthcare data from 163 000 patients in the Madrid region and almost 900 000 in Catalonia, the project showed good alignment between analytical results and theoretical and empirical approaches indicating that the BEAMER model is appropriate and accurate in identifying factor strength and correlation of clinical factors influencing adherence to treatment.
BIGPICTURE	BIGPICTURE is constructing a huge repository of pathology images for use in artificial intelligence (AI). Efficient conversion of original 'Whole Slide Image' files to the global DICOM (Digital Imaging and Communications in Medicine) standard is crucial for rapid upload of multiple images. The consortium has developed a superfast converter (from 4 minutes per slide to 10 seconds) while maintaining quality. The following source image formats are supported: Aperio svs, Hamamatsu ndpi, Philips tiff, OME-tiff, Zeiss czi, Mirax mirax, Leica scn, Sakura svslide, Trestle tif, Ventana bif, Olympus vsi.
BIOMAP	A glossary enabling harmonisation and improving the compatibility converting similar variables to a common format was published (PMID: 34137018). It allows to improve comparability of existing

	studies with different methodologies, research objectives and outcomes and to facilitate large-scale cross-cohort analyses, it was also made publicly available.
BIOMAP	With the help of harmonised datasets, large-scale genome-wide association studies could be conducted, which identified novel disease mechanisms (PMID: 37794016, 37873414) for psoriasis and atopic dermatitis.
COMBINE	The COMBINE machine learning model will help identify new hit compounds or prioritise existing antibacterial compounds for future antibiotic drug discovery. This algorithm uses highly curated harmonised public data as a training set to predict whether a compound will be active for broad spectrum (Gram positive, Gram negative, and acid-fast) bacterial strains. The workflows implemented demonstrate the advantages of FAIR data working to generate the necessary model predictions.
COVID-RED	The consortium has made all relevant, anonymised data (plus metadata) available for future research addressing the public health emergency using DataverseNL, a publicly accessible data repository platform developed with FAIR principles, suitable for making the collected data available and reusable to other researchers, and ensuring that the long-term impact and visibility of the research project can be maximised. As the platform is supported by several large academic institutes and Dutch science organisations, its longevity, and thus the data, can be ensured to remain available for researchers to access it.
EHDEN	The EHDEN portal contains very granular metadata on the databases in the EHDEN data network. By the end of 2023, the portal contained 258 million patient records from 145 data sources covering 28 European countries. These numbers will continue to grow as more data sources enter the portal.
ERA4TB	ERA4TB Drug Development Information Management (DDIM) supports the standardisation and integration of tabulated project pipeline data. The number of experiments included in the platform increased to a total of 38 project pipeline jobs/activities. During 2023, 14 sources of data (9 x *in vitro*, 2 x *in vivo* and 3 x GLP Tox) were standardised and integrated into the platform. All standardised data sources are available to ERA4TB partners.
FACILITATE	The consortium published a draft ethical framework on the secondary use of clinical trial data and the ethical framework on the return of clinical trial data to patients. This draft sets out the key ethical principles that will guide both ethical frameworks and identify the key concepts and processes that will facilitate the implementation of both ethical frameworks in practice.
Gravitate Health	Gravitate-Health have collaborated with the wider Health Level Seven International (HL7) community through the FHIR (Fast Healthcare Interoperability Resources) Vulcan Connectathon track for ePI / e-labelling to develop the prototype FHIR electronic Product Information (ePI) Implementation Guide. This will be further developed in the future.
Gravitate Health	In collaboration with the UNICOM H2020 project, Gravitate Health are working on implementing the Identification of Medicinal Products (IDMP) FAIRplus standard. A position paper with the UNICOM H2020 project elaborating common engagement was finalised during this reporting period. In future periods, Gravitate Health will explore a use case leveraging the project's G-lens focusing mechanisms to further the benefits of IDMP implementation.
Gravitate Health	Gravitate Health has developed an early prototype version of their patient information app. The final version will be split into 7 main categories: medication management; adherence and medication recommendation; health literacy; metadata, transnational or transregional; verification, regulation, and certification; and others. Questionnaires have also been developed to get feedback on the prototype from end-users.
H2O	The project developed a new way to formalise patients' control over their health data through the H2O Patient Agreement. Patients who sign on to this agreement join the H2O patient network, allowing them to measure both their own health outcomes and control how their data is used for research.
HARMONY	A public version of the acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL) dashboards are accessible in the HARMONY website to facilitate the visualisation of baseline

	data and to foster the generation of new research ideas, where researchers can select the characteristics of the cohort and see the number of cases currently available in the platform.
HARMONY	HARMONY project has included 44 129 new cases for analysis in their big data platform in 2023, coming from 140 data sources from 39 countries, resulting in a total of 106 899 records transferred and over 163 000 cases identified in total. Of those new cases, 33 590 patients' records came from national registries or international studies.
IDEA-FAST	IDEA-FAST's Data Management Platform which facilitates the assessment of fatigue, sleep and activities of daily living in neurodegenerative disorders and immune-mediated inflammatory diseases, was released as open source. Its source code and documentation are accessible via the project's GitHub repository.
imSAVAR	The consortium has devised a REDCap instrument to compile information and capture essential metadata related to studies and cohorts. This represents a fundamental aspect of the FAIRification process which has been applied to two datasets. A comprehensive data catalogue, accompanied by an end-to-end system, has been implemented under the auspices of ELIXIR Luxembourg, a special data storage and database which aims to facilitate long-term access to those research data and to tools for scientists in both academia and industry, to disseminate the information related to cohorts, studies and datasets in a FAIRification manner.
LITMUS	Clinical outcomes data has been added to the liver stiffness measurements dataset making it the largest dataset of its kind ever to be reported on. It contains demographic, clinical, histology and laboratory data and simple serum-based biomarkers (FIB-4, NAFLD fibrosis score) and vibration-controlled transient elastography (VCTE.) This dataset may be used in the future as a validation set for other biomarker studies and to derive new composite biomarkers.
Mobilise-D	Published an article in Nature Scientific Data providing guidelines for accessing, understanding, and re-using the data that will be made available from the Mobilise-D study. These guidelines highlight the challenges encountered and the solutions adopted to facilitate the standardisation and integration of data in other studies and, in turn, to increase and facilitate comparison of data recorded in the scientific community.
PIONEER	PIONEER expanded its Big Data Platform, welcoming 8 new data providers from 7 countries in 2023.
PIONEER, OPTIMA, EHDEN	Three IMI projects contributed to UroEvidenceHub, a platform that will provide physicians with personalised healthcare recommendations for patients with urological conditions.
PrIMAVeRa	PrIMAVeRa collects, gathers and analyses data from existing databases with individual patients' data on infections caused by resistant bacteria (and susceptible bacteria or no infection as reference group) to inform modelling. Historical anonymised data from observational studies, interventional studies, epidemiological studies and clinical and administrative databases was gathered and harmonised (study registered at Clinicaltrial.gov NCT05880069). Data sets: six pathogens with resistance to multiple antibiotics (methicillin resistant *S. aureus*, vancomycin resistant *E. faecium*, third generation cephalosporin or carbapenem resistant *E. coli* or *K. pneumoniae*, carbapenem resistant *P. aeruginosa* or *A. baumannii*), and six specific infection types (bloodstream infections, urinary tract infections, respiratory tract infections, surgical site infections, and skin- and soft-tissue infections). Data was collected from studies reporting pathogen-infection specific measures that were carried out in Europe and published from 1990-2022. If no data was available, studies from other high-income countries were also included.
RADAR-CNS	RADAR-CNS published their findings on how speech recordings could be used to monitor depression. Speech data from 585 participants was collected for 18 months in 3 countries (UK, NL, ES). Participants with more severe depressive symptoms spoke more slowly and quietly, regardless of the language used. There was strong evidence to support the use of speech-rate measures as digital phenotypes of depression.
RADAR-CNS	RADAR-CNS published their results on how remote monitoring of thinking difficulties could help manage depression. Problems in concentration, attention and memory have a clear relationship with severity of depression, but it is rarely monitored as it's challenging for clinicians and patients.

	RADAR-CNS monitored 500 participants for 2 years via smartphone apps. The study showed that remote monitoring is feasible and could help patients and clinicians manage symptoms of depression.
RADAR-CNS	A study on patient preferences for mHealth technologies to manage depression was published. Gathering data through mobile technologies should allow the onset of depression to be predicted earlier. However, barriers to adoption exist. Understanding these barriers is vital to ensure maximum adoption. Using a discrete choice experiment of 171 people with a history of depression, RADAR-CNS found that adoption of technology is primarily driven by the desire for accurate detection of symptoms. However, in some cases, people are willing to compromise on accuracy for more privacy and clinical support.
VALUE-Dx	The clinical algorithm within the VALUE-Dx project has three main components and utilises machine learning methodology. It involves screening over 30 000 publications, extracting data from more than 400 sources, and incorporating specific datasets. The algorithm employs a decision tree based on clinical symptoms and point-of-care test results to determine the probability of viral versus bacterial aetiology in respiratory infections.
VITAL	5 723 people were included with 31 375 contacts in a social contact matrix study. The results highlighted the impact of heterogeneity within the population by age and health conditions. This is also influenced by factors that vary between countries (social development, family structure, and social demographics). This information could help to predict and evaluate prevention for infectious diseases in older adults.

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

Project title	Description of result(s)
AMYPAD	The PET Pearls online learning module for assessing amyloid-PET images was created using PET scans from the AMYPAD study. Access to this learning module is free and was set up in collaboration with Springer Healthcare. The module is targeted at clinicians and researchers active in the field of Alzheimer's disease who want to familiarise themselves with or improve their knowledge of visual assessment of amyloid-PET imaging.
BIOMAP	The project generated a series of lay language summaries, addressing relevant topics such as the links between lifestyle and skin bacteria, or measurable predictors linked with negative health complications in psoriasis.
c4c	The c4c Academy platform has continued to be populated with new or new editions of short training courses, such as competence development Good Clinical Practice courses deepening aspects of the Good Clinical Practice Basic course, and accredited advanced courses. The platform has over 2 000 enrolled users and 40 courses available thus far. All these courses are still currently internal to the c4c consortium and staff involved in the national hubs sites to build capacity of the network.
ConcePTION	Publication of a Toolkit on how to plan and initiate a communication campaign for the general population, pregnant women/women of reproductive age and health care professionals (HCPs) to stimulate reporting of medicine use during pregnancy and breastfeeding. This toolkit provides hands-on guidance for teratology information services (TIS)-centres, health authorities and other stakeholders to support them in setting up their local, tailored campaigns.
EHDEN	The freely accessible EHDEN academy contains 23 courses for anyone working in the domain of real-world data and real-world evidence. The academy is now used in 100 countries with 4 400 enrolees worldwide since launch.
FAIRplus	FAIRplus organised a fellowship programme to educate the next generation of experts for further FAIRification of data sets within IMI projects, EFPIA partners and beyond. The 15 fellows improved the FAIR levels of their own data sets, used and contributed to the FAIR Cookbook and learned how to apply the Dataset Maturity (DSM) model. After completing the programme, the

	fellows had the confidence to lead, advise and initiate FAIR data processes in their respective companies and organisations. The FAIR Fellowship e-learning materials are open and can be accessed for reuse through the ELIXIR training materials platform.
H2O	The consortium developed the PRO / outcome set implementation advice which is a 10-step guide that can be used by other implementation teams from around the world to more efficiently create similar structures for the digital collection of patient data by reviewing H2O lessons learned and paths to success.
H2O	H2O has created a new video and infographic to explain patient-reported outcomes, the role of data in treating disease, and the possibilities enabled by H2O in terms of patient empowerment and better conversations with healthcare providers in lay language. These materials help patients and anyone unfamiliar with PROs to easily and quickly understand the concepts and what H2O is doing.
H2O	H2O collaborated with EHDEN and the European Patients' Forum to produce an introductory course on PROs for the EHDEN Academy. This course for non-experts provides a more detailed introduction to health outcomes, in particular patient-reported, and health data overall. It includes the benefits of sharing data and what safeguards are in place, important information to support wider understanding of and participation in collecting health data at the European level. Access is free, but requires registration.
H2O	Together with Data Saves Lives, H2O co-hosted a webinar on PROs and their potential to revolutionise European health systems (in German).
NECESSITY	A NECESSITY partner in charge of the development of the salivary gland ultrasound sub-study filmed a very technical and detailed video as a training tool for all 30 centres participating in the NECESSITY clinical trial. The video aims to show and guide on the use of regular ultrasound imagining and Doppler effect in order to gain particular clarity of the salivary glands; thus evaluating the level of their pathogenicity according to OMERACT guidelines (organisation committed to the improvement out outcome measures in rheumatology) for use prior to and post NECESSITY clinical protocol. The training video can be found in the scientific information section of the NECESSITY website.
OPTIMA	OPTIMA has provided trainings in OMOP mapping (the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM)). A series of four trainings were given by partner GMV to various members in the consortium.
SISAQOL-IMI	SISAQOL-IMI ran an educational workshop highlighting the need for patient involvement in the design process of clinical trials to have true input on the analysis and reporting of patient reported outcomes (PRO) data for the WECAN Academy 2023 Training Event for Educating Cancer Patient Advocates from Around the World in July 2023. The training event featured an impressive line-up of 24 sessions by 22 expert patient advocates.
T2EVOLVE	The patient hub on the T2EVOLVE website is an online dynamic repository for information on CAR T-cell therapy and the results of the T2EVOLVE consortium for patients and caregivers. Available educational materials on CAR T-cell therapy for patients and caregivers in 5 different European languages were identified, categorised and references to these materials were incorporated in the T2EVOLVE patient hub. The T2EVOLVE website also includes a section with resources for healthcare professionals.
UNITE4TB	UNITE4TB organised a 3-Day Tuberculosis Academy with TBnet especially for students, residents, fellows, doctoral students and post-docs (up to 3 years post exam). This is a forum for young clinicians and researchers in the field of tuberculosis to exchange ideas and to learn from each other under expert guidance and mentorship.
VHFMODRAD	A Belgian SME (CORIS) has provided protocols to Institut Pasteur in Dakar for putting in place the manufacturing of CORIS's lateral flow tests in Dakar. Protocols included manufacturing and quality control; these were paper protocols and a movie for training purpose, so that the Institut Pasteur can produce the lateral flow test in Dakar.

Impact on regulatory framework

Project title	Description of result(s)
COMBACTE-CARE (IMI1)	Start of the EMA accelerated procedure to review the marketing authorisation application of aztreonam-avibactam (ATM-AVI) in September 2023. If approved, ATM-AVI could be an important treatment option for patients with life-threatening Gram-negative bacterial infections resistant to almost all currently available antibiotics.
EBOVAC3	A type II variation to update the paediatric label information of the Janssen Ebola vaccine regimen was submitted to the EMA in January 2023 and approved in July 2023. Data from different studies funded by IMI: EBL2005 (EBOVAC3), EBL2011 (EBOVAC1) and PREVAC (partly funded by EBOVAC1) were included.
IDEA-FAST	The project team published its perspectives on the regulatory qualification of a cross-disease digital measure. IDEA-FAST is developing novel digital measures of fatigue, sleep quality, and impact of sleep disturbances. The consortium met with the EMA to receive advice on its plans for regulatory qualification of these measures. The EMA highlighted the challenges of developing a cross-disease measure, though benefits potentially include: reduced resources for the technology developer & health authority; faster access to innovation across different therapeutic fields; feasibility of cross-disease comparisons. The insights included in the publication can be used to guide the development of cross-disease digital measures intended for regulatory qualification.
LITMUS	The project submitted a NASH Biomarker Qualification Package to FDA for the context of use 'Diagnostic Enrichment.' This submission includes: - PRO-C3, the pro-peptide of type lll collagen, an abundant protein in NASH liver tissue; - ADAPT combines Age, presence of DiAbetes, PRO-C3 & platelet count; - FibroScan-AST (FAST) score is a combination of imaging techniques.
LITMUS	LITMUS has published a manuscript summarising the lessons they learned during their regulatory interactions with the FDA and EMA. This document, published in the Journal of Hepatology, has been made available to support the wider biomarker development community in their regulatory interactions.
PIONEER	Published a policy paper on 'Lessons learned from implementing PIONEER to inform current and future policy making'. The aim of this deliverable was to inform regulators at EU, national and regional level of the PIONEER prostate cancer policy strategy and clearly outline how the PIONEER recommendations and research outputs can be translated into policy.
T2EVOLVE	In a paper published in Frontiers in Immunology, the T2EVOLVE project has made regulatory recommendations for workshops, multi-disciplinary teams for advice and specific guidelines allowing for a more adaptive approach to testing multiple variations of a new therapy in clinical trials. In the article, the T2EVOLVE consortium explores opportunities to expedite the development of CAR and TCR engineered T cell therapies in the EU by leveraging tools within the existing EU regulatory framework to facilitate an iterative and adaptive learning approach across different product versions with similar design elements or based on the same platform technology.
TRIC-TB	TRIC-TB receives Orphan Drug Designation (ODD): The U.S. Food and Drug Administration (FDA) has granted ODD to alpibectir (BVL-GSK098) and ethionamide fixed-dose combination for treatment of tuberculosis (TB). The ODD reflects the urgent need for more research to overcome resistance to TB medicines, and the potential for alpibectir and ethionamide to improve treatment options for TB patients. Alpibectir, a small molecule acting through a novel mode of action, represents a totally new concept of overcoming resistance by significantly potentiating the activity of an existing antibiotic, ethionamide. It is being developed for pulmonary and meningeal TB.
VALUE-Dx	The project mapped potential barriers and facilitators in health technology assessment (HTA), pricing, and funding policies related to the use of rapid diagnostics in patients with community-acquired acute respiratory tract infections. The work is published in Diagnostics.

Implementation of project results inside industry

Project title	Description of result(s)
ERA4TB	The first time in human trials site feasibility tool developed by ERA4TB could help the academia and industry to validate academic clinical trial units where the industry can develop their FTIH trials.
VHFMODRAD	6 assays: 3 assays for Crimean Congo haemorrhagic fever antibodies (IgM and IgG) and Crimean Congo haemorrhagic fever antigen Sero-K-SeT test, similar to numerous easy-to use lateral-flow tests already used in primary care centres, have been developed. Validation data are very promising when combining all 3 assays. The test is intended to be used as a first screening assay to have a tool for detecting an emerging outbreak and to screen patients in case of an outbreak or suspicion of active infection (a manuscript is planned). 3 assays: Lassa fever virus Abs (IgM and IgG) and Lassa Ag Sero-K-SeT test are easy to use, similar to numerous lateral-flow tests already used in primary care centres. Laboratory data are very promising. These assays will be further validated before potential exploitation.
VHFMODRAD	5 Lassa fever virus monoclonal antibodies have been generated and characterised to allow their use in a lateral-flow assay. All monoclonal antibodies generated during the project, either directed against Crimean Congo haemorrhagic fever virus or Lassa fever virus have been sequenced to secure their long-term production.

Accessibility of resources/outputs beyond consortium

Project title	Description of result(s)
AMYPAD	AMYPAD has developed the NiftyPAD software package for the versatile analysis of static, full or dual-time window dynamic brain PET (positron emission tomography) data. NiftyPAD is freely available on GitHub.
AMYPAD	The dataset of the AMYPAD prognostic and natural history study (PNHS) was made publicly available via the Alzheimer's Disease Data Initiative (ADDI) Workbench. This dataset represents the largest European PET dataset phenotyping longitudinally individuals at risk of Alzheimer's disease-related progression.
BIGPICTURE	A suite of open-source Python tools to facilitate use of BIGPICTURE's pathology image repository is freely available. paquo: A tool designed to facilitate the use of bioimage analysis software, QuPath tiffslide: An alternative to the commonly used openslide python library, with a focus on performance and cloud native whole slide image access pado: A dataset library for managing whole slide image datasets pavo: A visualisation tool to allow the inspection of digital pathology datasets and the easy prototyping of new visualisations
BIGPICTURE	Aligning consecutive tissue images enables pathologists to easily evaluate multiple markers in a single area. However, it is extremely challenging, not least because of the huge file size of these high resolution 'Whole Slide Images'. BIGPICTURE has developed an open-source Python library, DeeperHistReg, to automatically, accurately, and efficiently align these images. This software won the ACROBAT breast cancer tissue competition at the Medical Image Computing conference 2023.
c4c	Set-up of the conect4children-Stichting as a Dutch non-profit legal entity to sustain achievements of c4c. It will offer services to all academic and industry sponsors, including contract research organisations (CROs) related to:

	Strategic expert advice on all aspects of paediatric clinical trial design, feasibility (input from children, young people and > than 400 experts in innovative methodology and clinical trials). Support and coordination of clinical trial conduct through National Hubs in 21 countries (incl. site identification & feasibility, site set-up, recruitment, engagement). Education and training about paediatric drug development, and data standards for paediatric research.
COMBINE	The machine learning model algorithm for predicting whether a compound will be active for broad spectrum bacterial strains is available on GitHub and will be made publicly available for reuse on Biomodels. A related publication is in preparation.
COMBINE	The preclinical bacterial strain repository is available on the PEI website and deposited in the German Collection of Microorganisms and Cell Cultures (DSMZ) for distribution. Strains are accessible to the whole scientific community without restrictions.
ConcePTION	Core data elements (CDE) to be collected in primary source pregnancy medication safety studies publicly released on IMI ConcePTION website. The CDEs comprise 98 individual data elements, arranged into 14 tables of related fields and the process for development of these CDE recommendations was published in Drug Safety. These CDEs will allow standardisation of data collection (the way researchers, pharma companies collect data about medication exposure and pregnancy outcome and) data generation, thereby improving data harmonisation, and will allow for a faster accumulation of useful evidence that can be used to inform healthcare professionals and women about medication safety in pregnancy.
DRAGON	DRAGON partner CDISC released version 2.0 of the COVID-19 Therapeutic Area User Guide (TAUG v2.0) which is publicly accessible. TAUG v2.0 will support public health researchers to utilise the WHO Novel Coronavirus (nCoV) Acute Respiratory Infection Clinical Characterisation Data Tool which is being used as the foundation for many COVID-19 research studies globally across numerous countries.
EBiSC2	A new pre-differentiated cell product, EBiSC-NEUR1 is openly available for a transfer fee via the EBiSC catalogue for research use by non-profit and commercial organisations worldwide. Terms of use are openly accessible and equal across both organisational types. EBiSC-NEUR1 can be used across a broad range of research and development activities including cell modelling, assay development and basic biology research. Open access to well characterised, pre-differentiated cells simplifies the inclusion of human neuronal cell models within research applications, especially in high scale applications or by users who otherwise would not have the expertise to handle and use iPSCs.
EBiSC2	Two different ready-to-use iPS cell models developed and disseminated as a joint venture between EBiSC2 and EIT Health project R2U-Tox are openly accessible as service provision activities via the EBiSC catalogue, for a non-profit fee. Ready access to pre-differentiated, pre-plated cells will enable researchers to avoid having to perform lengthy and inconsistent differentiation protocols themselves. Provision of 'ready-to-use' cells will speed up research outcomes. Pre-differentiated and pre-plated cells can be used for a broad range of research and development activities including disease modelling and assay development.
EBOVAC3	The results of the EBL2005 clinical study studying the safety and immunogenicity of the Janssen vaccine regimen against Ebola virus in infants aged 4–11 months in Guinea and Sierra Leone were published open access in Lancet Global Health. The main finding was that the Janssen vaccine regimen against Ebola was well tolerated and induced strong humoral responses in infants younger than 1 year. There were no safety concerns related to vaccination.
ERA4TB	The clinical data generated by ERA4TB is uploaded to the TB Platform for Aggregation of Clinical TB Studies (TB-PACTS) and the access for researchers is contingent on the following; (1) applicant is a scientific researcher, (2) is affiliated with a legitimate organisation, (3) access request is based upon sound research goals or educational reasons, (4) terms and conditions have been accepted, and (5) majority approval by the access review committee.

	During 2023 the project processed the following clinical sources, standardised them into CDISC SDTM and integrated them into the TB-PACTS: LIN-CL001 (NCT02279875), NC-006 STAND (NCT02342886) and STREAM Stage 2 (ISRCTN18148631). As a result, the number of data sources within the platform, which is accessible to authorised researchers, further increased to 29 clinical studies.
eTRANSAFE	A dataset of protein and genetic biomarkers evaluated in clinical trials has been created as part of the eTRANSAFE project. This dataset, complemented with information from the scientific literature, has been made available online.
EUbOPEN	The first version of EUbOPEN's gateway has been made publicly available to facilitate access to the results and outputs of EUbOPEN to the scientific community. The gateway is an interactive tool and will be continuously optimised to allow searching of data for different user communities, including chemists, biologists and informaticians. It will provide direct links to EUbOPEN datasets in public repositories. This will allow direct downloads of data in formats amenable for integration with other data and to enable other analyses such as machine learning approaches. To date, it includes an open access chemogenomic library comprising about 5 000 well annotated compounds covering roughly 1 000 different proteins; data on 1 540 targets / cell lines; and descriptions of 22 875 assays.
EUbOPEN	Images associated with the biological quality control of the chemogenomic compounds generated by the EUbOPEN project have been deposited in the BioImage Archive. As part of the EUbOPEN project, the Diamond Light Source XChem facility offered the opportunity to partner suitable external XChem projects of human targets with the EUbOPEN consortium. Successful projects worked in collaboration to progress XChem hits into successful chemistry campaigns and deliver high quality chemical probes. 6 000 compounds synthesised by EUbOPEN consortium members have been distributed to the scientific community with labs in Europe, North America and Asia. These compounds will facilitate drug-discovery research programmes throughout the world. 64 chemical probes were generated that can be used to generate new knowledge on biological processes and guide drug discovery processes. Data and material have been made available to the research community without any restrictions on use. 1 338 chemogenomic compound candidates covering 569 targets (228 kinases, 151 GPCRs, 10 ion channels, 28 nuclear receptors, 81 epigenetic targets, 6 proteases, 23 targets from the arachidonic acid cascade and 42 other targets) have been acquired and annotated regarding their *in vitro* and cellular activity, selectivity and their physiochemical properties. The compounds were acquired from commercial vendors or sourced from academic EUbOPEN members and EUbOPEN collaboration partners. 160 in vitro assays and 109 cellular screening assays were established which cover a variety of target families, including E3 ligases and solute carriers which will facilitate the development of chemical probes and thus drug discovery.
FAIRplus	Data 'FAIRification' framework: FAIRplus has developed a free resource to help organisations, projects and teams establish FAIRer data management habits through reusable templates, processes and guidance. The framework includes a step-by-step guide to help improve the FAIR level of datasets produced. The FAIR Cookbook: The FAIR Cookbook is a practical guide to data management that contains 82 public recipes (as of 2023) enabling the FAIRification of datasets. Almost 100 professionals from academia and pharma have contributed to recipes that include documenting the dataset selection process, ethics, components of FAIR and applied examples. Its creation and content, its value, use and adoptions, as well as the participatory process, collaborative plans for sustainability, and its adoption are detailed in a pre-print. The FAIR Cookbook has become a recommended service of ELIXIR-UK and ELIXIR-Luxembourg Nodes, and it is embedded in the new tasks of the ELIXIR Interoperability Platform. The FAIR Dataset Maturity (DSM) Model: The DSM is a model that can be used to guide FAIR maturity decision making by targeting data management investment towards the capabilities needed to most effectively improve data discovery, accessibility, interoperability and reusability; and establishing success metrics for evaluating how FAIR data assets are before and after investment. FAIRplus Interactive Flowchart: A digital, interactive flowchart was created to guide researchers through their first FAIRification journey. Step-by-step, they are presented with the possibilities, questions and challenges that come with a FAIRification process. The flowchart links to outside

	resources – i.e. the FAIR Cookbook, the DSM model, the Fellowship Programme, use cases – for solutions and help with technical issues. The flowchart is designed as a single landing page and hosted on a dedicated domain name, which should improve sustainability, and make it easier to find and to disseminate. FAIRified datasets: The main output of the project has always been to make FAIRification tools publicly available. To develop these tools, datasets from 20 IMI projects & EFPIA partners were worked on. Each dataset has increased its overall FAIRness level – some of them with a score of over 90%. The actual data that is FAIRified in IMI projects and internally at EFPIA partners will, in most cases, keep their original access rights, however, in some cases, datasets have also been made available. FAIR Use Cases: FAIRplus published six use cases to demonstrate the value of data FAIRification: - eTOX case study: Unlocking toxicology data for drug discovery - EBiSC2 case study: Improving FAIRness of stem cell data - APPROACH case study: Some data are more equal than others - COMBINE case study: The importance of data standards - EUbOPEN case study: Open by design saves time - IMI CARE case study: Quick-response COVID-19 effort opens FAIR data on ~5,500 compounds
iABC (IMI1)	The LungAnalysis website tool has been developed to serve as an image analysis laboratory for clinical research and for the development of innovative image analysis techniques for clinical care. Through the iABC project, the team have developed and validated a new CT (computed tomography) scoring method that can be used for clinical studies in which CT data is used as an outcome measure, and for the monitoring of disease in clinical follow up. They have also developed an automated analysis method for the airway:artery ratio, which could serve as an additional outcome measure for clinicians. A training package and over reading service for the use of lung clearance index (LCI) in clinical settings have been developed. Furthermore, LCI is a lung function parameter derived from the multiple-breath washout (MBW) test. An online tool was developed to provide training on MBW.
iABC (IMI1)	A biobank linked to the EMBARC registry has been established with external funding from the European Respiratory Society (NCT03791086) and is ongoing supporting translational research into bronchiectasis in multiple countries by providing access to bio-samples linked to high quality clinical data. The biobank is located at the University of Dundee. Furthermore, a bio-registry of patient samples resulting from the clinical studies conducted under the iABC, has been established at Queen's University Belfast and is available to all for research purposes.
IDEA-FAST	The IDEA-FAST consortium developed a new mobile application to capture socialisation and neurocognitive data respectively with extensive patient and public engagement. This 'WildKey: Social' application will be useful for other digital health projects.
Inno4Vac	For biomanufacturing platforms using mathematical modelling, one of the goals is to build digital twins for the downstream side of the vaccine manufacturing process (filtration, centrifugation, and chromatography). The consortium built a digital twin model for the chromatography step, which was published, implemented, and validated. An implementation of this model in CADET software (Chromatography Analysis and Design Toolkit) was made open access for the scientific community to test and use.
ITCC-P4	ITCC-P4 gGmbH was set up as a first non-profit company in the world to offer researchers at academic institutions and pharmaceutical companies access to a comprehensive array of cutting-edge laboratory models of children's cancers that have been generated in the project. This will help accelerate the development of new treatments by making it easier for researchers/companies to test their compounds for potential benefits in childhood cancers. Fee-for-service testing through ITCC-P4 gGmbH has been initiated.
PIONEER	The project ran the third PIONEER studyathon in June 2023. The research question focused on an observational health data analysis on the adverse events of systemic treatment in patients with metastatic hormone-sensitive prostate cancer. During the 4-day event a group of more than 50 participants contributed towards progression of work on the research question. With the

	analysis now finalised, four manuscripts are in the making, soon to be ready to be published. All developed resources from the studyathon are open source in GitHub.
PREMIER	Predicting biodegradation pathways of active pharmaceutical ingredients (APIs) in sludge is highly relevant but challenging. The project expanded the pre-existing EAWAG enviPath database and prediction system for APIs generated by PREMIER for better prediction. The updated tool generates suspect lists for further screening.
PrIMAVeRa	PrIMAVeRa is contributing to the existing epidemiological repository (Epi-Net) by providing data sets. In 2023 PrIMAVeRa developed three systematic reviews (2 were published and one is under review), and the data was transferred to Epi-Net. PrIMAVeRa collects, gathers and analyses data from existing databases with individual patients' data on infections caused by resistant bacteria (and susceptible bacteria or no infection as a reference group) to inform modelling. Historical anonymised data from observational studies, interventional studies, epidemiological studies and clinical and administrative databases was gathered and harmonised (study registered at Clinicaltrial.gov NCT05880069). Anonymised individual patient data is available to 3rd parties via an application form found on EPI-Net.
PROMISE	Established the PROMISE European RSV surveillance network with national public health institutes from 10 countries in the EU/EEA. With this network, the needs for and availability of RSV-specific surveillance systems and data were identified. Surveillance data that could be of value for the newly developed integrated respiratory virus surveillance platform of ECDC and WHO-EURO were evaluated. During the autumn and winter of 2023/24, 7 countries provided weekly RSV surveillance data that was published in the PROMISE RSV surveillance bulletin on a bi-weekly basis e.g. see for example the report for week 52 of 2023.
PROMISE	The project has developed an RSV awareness tool to track global public awareness of RSV by drawing on internet search data from Google Trends and Wikipedia Pageviews. By monitoring RSV searches online, the RSV awareness tool can help identify potential outbreaks or spikes in RSV cases and track the effectiveness of RSV awareness campaigns.
VHFMoDRAD	Crimean Congo haemorrhagic fever reference tests and selected reagents are accessible through the EVA-GLOBAL catalogue. The AMU developed lyophilised ready-to-use primers and probe (Lyoph-P&P) concept has proven efficiently transferable to CEPHEID technology and shows promising results for adaptation to other industrial point of care platforms for preparedness and response for emerging viruses. Also developed within the project and made available for academics and industrial researchers on the European Virus Archive web catalogue are: Lyoph-P&Ps for Dabie bandavirus, Marburg virus, Rift Valley fever virus, Lassa fever virus and yellow fever virus.

Miscellaneous

Project title	Description of result(s)
AIMS-2-TRIALS	The prevalence of epilepsy amongst autistic children is around 7%, rising to 26% in adolescents, in comparison to 1% prevalence in the general population. Epilepsy is a leading cause of premature mortality in autistic people. The recommended treatments for epilepsy are similar for autistic and not autistic people. The consortium examined the cost effectiveness of antiepileptic drugs in treating autistic children in four countries with different healthcare systems and practices providing data of relevance for healthcare providers. The team also flagged the substantial economic impact on families with an autistic child who has epilepsy, which is considerably higher than healthcare expenditure and it is currently not captured by available models. The research is published in the Journal of Autism and Developmental Disorders.
BEAMER	The consortium developed a two-tier BEAMER model to segment chronic patients according to their needs concerning treatment adherence.

	The BEAMER model, based on the theoretical framework of subjective experienced health, will enable the elicitation of the patient's needs to improve adherence to treatment. The elicitation of needs is primarily based on the segmentation of the patient population resulting in 4 patient groups based on the patient's level of acceptance and control over their disease.
DECISION	DECISION has developed an LED-activated micro-pumping system as part of the multi-step microfluidic workflow in their lab-on-a-chip diagnostic device. Development of the device, which is not specific to a disease, is still ongoing.
iConsensus	The aim of iConsensus is to develop new technologies in mammalian-cell based production of biopharmaceuticals which allow better manufacturing control and are tools to potentially reduce the time and costs of the process. Regarding spectrometry and chemometry innovations, the project has developed a generic chemometric partial least square (PLS) prediction model to predict glucose, glutamate and lactate concentration using Raman spectra from different Chinese hamster ovary cultures and different Raman spectrometers, and 2D fluorescence for metabolite monitoring in microtiter plates as described in papers in Bioengineering and the Journal of Biological Engineering.
iConsensus	iConsensus has made progress in the modelling of cell cultures in biomanufacturing by developing a mechanistic kinetic model of a fed-batch process by column generation and statistical approach for the kinetics and data-driven models able to predict the process behaviour. This work has been published in Computers & Chemical Engineering.
Mobilise-D	Published an article outlining the work undertaken in Mobilise-D to set up patient and public involvement and engagement (PPIE) structures to promote and support meaningful and efficient patient and public involvement in project activities. The approach followed by Mobilise-D may be used as a template for future consortia.
PREFER	Setting up of the PREFER Expert Network of pharmaceutical companies, academic institutions, consultants, and patient representatives to capitalise on the experience and expertise gained through the PREFER project, and support its sustainability: The PREFER Expert Network objectives are to: - exchange understanding, experience, and implementation practices of patient preference studies that that build on the PREFER Recommendations and their outcomes; - discuss policy and methodological questions related to patient preference research; - identify knowledge gaps and develop best practice of patient preference studies which may lead to new research topics.

IHI project results

As the first IHI projects only started in 2023, they have yet to hit any significant milestones and so their results are not divided into any categories.

Project title	Description of result(s)
CLAIMS	The consortium announced the release of a first version of their clinical decision support platform (the icompanion ms HCP platform) which offers the healthcare practitioner (HCP) a holistic view on the patient with multiple sclerosis by integrating new and existing biomarker data as well as the outcomes of the prognostic models for disease progression and treatment responses.
PROMINENT	Published an article in Frontiers in Neurology presenting the approach used in PROMINENT to build upon knowledge and already existing digital tools from several initiatives that address new models for early detection, diagnosis, and monitoring of Alzheimer's disease and other neurodegenerative disorders.

Annex 4 – Publications from projects

IMI projects regularly publish their findings in peer-reviewed journals. Lists of these and links to the papers can be found on the project pages of the CORDIS website and, often, on the projects' own websites.

Direct links to the projects' pages on CORDIS can be found on the project factsheets on the IHI website.

Hot publications in 2023

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

- Rinella, Mary E. et al. (2023) A multisociety Delphi consensus statement on new fatty liver disease nomenclature, HEPATOLOGY 78: 1966-1986
- Del Bufalo, Francesca et al. (2023) GD2-CART01 for Relapsed or Refractory High-Risk Neuroblastoma, NEW ENGLAND JOURNAL OF MEDICINE 388: 1284-1295
- Astin, Ronan et al. (2023) Long COVID: mechanisms, risk factors and recovery, EXPERIMENTAL PHYSIOLOGY 108: 45653
- Huang, Erich P. et al. (2023) Criteria for the translation of radiomics into clinically useful tests, NATURE REVIEWS CLINICAL ONCOLOGY 20: 69-82
- Wildenbeest, Joanne G. et al. (2023) The burden of respiratory syncytial virus in healthy term-born infants in Europe: a prospective birth cohort study, LANCET RESPIRATORY MEDICINE 11: 341-353

2023 publications featured in the top 10 Journals by JIF

- Rolland, Thomas et al. (2023) Phenotypic effects of genetic variants associated with autism, NATURE MEDICINE 29: 1671-+
- Cherubini, Alessandro et al. (2023) Interaction between estrogen receptor-α and PNPLA3 p.I148M variant drives fatty liver disease susceptibility in women, NATURE MEDICINE 29: 2643-+
- Krogvold, Lars et al. (2023) Pleconaril and ribavirin in new-onset type 1 diabetes: a phase 2 randomized trial, NATURE MEDICINE 29:
- Shekari, Saleh et al. (2023) Penetrance of pathogenic genetic variants associated with premature ovarian insufficiency, NATURE MEDICINE 29: 1692-+
- Heymans, Stephane et al. (2023) Dilated cardiomyopathy: causes, mechanisms, and current and future treatment approaches, LANCET 402: 998-1011
- Del Bufalo, Francesca et al. (2023) GD2-CART01 for Relapsed or Refractory High-Risk Neuroblastoma, NEW ENGLAND JOURNAL OF MEDICINE 388: 1284-1295
- Wilde, Harrison et al. (2023) Hospital admissions linked to SARS-CoV-2 infection in children and adolescents: cohort study of 3.2 million first ascertained infections in England, BMJ-BRITISH MEDICAL JOURNAL 382:

Highly cited publications in 2023

Highly cited publications have received enough citations to place in the top 1% of papers in their research field.

- Rinella, Mary E. et al. (2023) A multisociety Delphi consensus statement on new fatty liver disease nomenclature, HEPATOLOGY 78: 1966-1986
- Macchia, Stefania et al. (2023) GD2-CART01 for Relapsed or Refractory High-Risk Neuroblastoma, NEW ENGLAND JOURNAL OF MEDICINE 388: 1284-1295
- Baker, Mark R. et al. (2023) Long COVID: mechanisms, risk factors and recovery, EXPERIMENTAL PHYSIOLOGY 108: 45653
- Kinahan, Paul E. et al. (2023) Criteria for the translation of radiomics into clinically useful tests, NATURE REVIEWS CLINICAL ONCOLOGY 20: 69-82
- Viveiros, Anissa et al. (2023) Angiotensin-converting enzyme 2-at the heart of the COVID-19 pandemic, CELL 186: 906-922
- Robles-Diaz, Mercedes et al. (2023) A new framework for advancing in drug-induced liver injury research. The Prospective European DILI Registry, LIVER INTERNATIONAL 43: 115-126
- Korf, Hannelie et al. (2023) An adipocentric perspective on the development and progression of non-alcoholic fatty liver disease, JOURNAL OF HEPATOLOGY 78: 1048-1062
- Dacosta-Urbieta, Ana et al. (2023) The burden of respiratory syncytial virus in healthy term-born infants in Europe: a prospective birth cohort study, LANCET RESPIRATORY MEDICINE 11: 341-353
- Verrastro, Ornella et al. (2023) Accurate liquid biopsy for the diagnosis of non- alcoholic steatohepatitis and liver fibrosis, GUT 72: 392-403
- Pirmohamed, Munir et al. (2023) Pharmacogenomics: current status and future perspectives, NATURE REVIEWS GENETICS 24: 350-362
- Meggendorfer, Manja et al. (2023) Real-World Validation of Molecular International Prognostic Scoring System for Myelodysplastic Syndromes, JOURNAL OF CLINICAL ONCOLOGY 41: 2827-+
- Ekstedt, Mattias et al. (2023) A proteo-transcriptomic map of non-alcoholic fatty liver disease signatures, NATURE METABOLISM: n/a-
- Cunoosamy, Danen et al. (2023) Development of Core Outcome Measures sets for paediatric and adult Severe Asthma (COMSA), EUROPEAN RESPIRATORY JOURNAL 61: n/a-
- Carpenter, Linda L. et al. (2023) In Search of Biomarkers to Guide Interventions in Autism Spectrum Disorder: A Systematic Review, AMERICAN JOURNAL OF PSYCHIATRY 180: 23-40
- Saleh, Rasha N. M. et al. (2023) Hormone replacement therapy is associated with improved cognition and larger brain volumes in at-risk APOE4 women: results from the European Prevention of Alzheimer's Disease (EPAD) cohort, ALZHEIMERS RESEARCH & THERAPY 15: n/a-
- van der Water, B. et al. (2023) Papyrus: a large-scale curated dataset aimed at bioactivity predictions, JOURNAL OF CHEMINFORMATICS 15: n/a-
- Henry, Linda et al. (2023) The Global Burden of Liver Disease, CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 21: 1978-1991
- Stefan, Norbert et al. (2023) Metabolic health and cardiometabolic risk clusters: implications for prediction, prevention, and treatment, LANCET DIABETES & ENDOCRINOLOGY 11: 426-440
- Griffiths, Anne M. et al. (2023) Paediatric Inflammatory Bowel Disease: A Multi-Stakeholder Perspective to Improve Development of Drugs for Children and Adolescents, JOURNAL OF CROHNS & COLITIS 17: 249-258
- Juergensmeyer, Sabine et al. (2023) A Randomized Controlled Trial Comparing Apixaban With the Vitamin K Antagonist Phenprocoumon in Patients on Chronic Hemodialysis: The AXADIA-AFNET 8 Study, CIRCULATION 147: 296-309
- Glez-Vaz, Javier et al. (2023) mRNAs encoding IL-12 and a decoy-resistant variant of IL-18 synergize to engineer T cells for efficacious intratumoral adoptive immunotherapy, CELL REPORTS MEDICINE 4: n/a-

- Pedrotti, Patrizia et al. (2023) Consensus Statement on the definition and classification of metabolic hyperferritinaemia, NATURE REVIEWS ENDOCRINOLOGY 19: 299-310
- Vaysburd, Marina et al. (2023) Cytosolic antibody receptor TRIM21 is required for effective tau immunotherapy in mouse models, SCIENCE 379: 1336-+
- Platt, Jonathan et al. (2023) Liver, visceral and subcutaneous fat in men and women of South Asian and white European descent: a systematic review and meta-analysis of new and published data, DIABETOLOGIA 66: 44-56
- Dawed, Adem Y. et al. (2023) Pharmacogenomics of GLP-1 receptor agonists: a genome-wide analysis of observational data and large randomised controlled trials, LANCET DIABETES & ENDOCRINOLOGY 11: 33-41
- Szewczyk, Magdalena M. et al. (2023) Discovery of Nanomolar DCAF1 Small Molecule Ligands, JOURNAL OF MEDICINAL CHEMISTRY 66: 5041-5060
- Canard, Bruno et al. (2023) Kill or corrupt: Mechanisms of action and drug-resistance of nucleotide analogues against SARS-CoV-2, ANTIVIRAL RESEARCH 210: n/a-
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Annex 5 – Patents from projects

Since the start of the IMI2 programme, projects have been patenting developed technologies. The statistics below encompass 10 patent/trademark/registered design applications and 14 patents/trademarks awarded from the beginning of IMI2 until 31 December 2023.

- 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 enhancing immune responses’ and 2 patents awarded on ‘methods and compositions for inducing protective immunity against filovirus infection’.
- PHAGO – 1 patent awarded on ‘TREM2 cleavage modulators and uses thereof’ and 1 patent awarded on ‘up-scaled production of microglia-like/-precursor cells and macrophage cells using mesh macro carriers’.
- 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 – trademark applications for the EBiSC trademark.
- TRIC-TB – 6 patents awarded for ‘novel compounds’.
- GRAVITATE-HEALTH – 3 trademarks awarded and 1 trademark application on ‘G-Iens’, a digital health information tool.
- KRONO – 1 patent application on ‘an apparatus and associated methods for thermal cycling’.
- PRISM 2 - 1 application on ‘systems and methods for identifying transdiagnostic neurological disorder subtypes using DNA methylation marker analysis’.

There are no patent applications or patents awarded under IHI due to the recent launch of the programme.

Annex 6 – Scoreboard of Horizon 2020 H2020 legacy KPIs

This annex contains the scoreboards relating to the IMI2 programme which was part of Horizon 2020. Note that in the interests of space we have deleted the rows of the tables that are no longer relevant such as those relating to the launch and evaluation of Horizon 2020 calls for proposals.

KPIs specific to the Innovative Medicines Initiative 2 (IMI2) programme[67]

Reporting methodology: cumulatively reporting from the beginning of IMI2 until 31/12/2023. 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: 80 Budget committed: EUR 2 244 643 663	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…'	50	439	590

[67] 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
			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'			
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)	29 completed procedures: CE mark: 4 Inclusion in regulatory guidelines: 10 Regulatory letter of support: 2 Regulatory qualified opinion: 10 Submission for qualification opinion: 3 Number of projects: 20 Projects' budget: EUR 442 995 325.34	51 completed procedures: CE mark: 4 Inclusion in regulatory guidelines: 21 Regulatory letter of support: 8 Regulatory qualified opinion: 13 Submission for qualification opinion: 5 Number of projects: 36 Projects' budget: EUR 1 145 202 461

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	61 Number of projects: 23 Projects' budget: EUR 537 682 590	77 Number of projects: 30 Projects' budget: EUR 918 547 664
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 272.8 million (AP: EUR 203.5 million Partners in Research: EUR 69.3 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%	66.67 % Number of projects: 80 Budget committed: EUR 2 405 212 987	70.62 % Number of projects: 125 Budget committed: EUR 4 112 075 759.75
7	Co-authorships and cross-sector publications between	- Expressed as net figure	IMI2 Regulation objective a:	1 500	2 871	6 908

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
	European researchers on IMI2 projects (sectors include academia, small and mid-sized companies, pharma, regulators, patient organisations, etc.).	- Complemented by the number and budget of grant agreements that delivered them.	a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…'			
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	642 Number of projects: 60 Budget committed: EUR 1 335 930 229	956 Number of projects: 100 Budget committed: EUR 2 852 954 001
9	Share of projects involving patient organisations and healthcare professionals' associations (as consortium partners, members of advisory boards, members of stakeholder groups etc.).	- Complemented by the number and budget of grant agreements that delivered them.	IMI2 Regulation objectives a, and b1: a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…' b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'	80 %	63.33% Number of projects: 76 Budget committed: EUR 2 272 926 806	59.32% Number of projects: 105 Budget committed: EUR 3 168 810 335
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	20 %	SME participations: 16.5 % (382 out of 2 317) (IMI2 cumulative figures until 31/12/2023, beneficiaries receiving EU funding only)	SME participations: 16.5 % (580 out of 3 558) (IMI1 and IMI2 cumulative figures until 31/12/2023, beneficiaries receiving EU funding only)

KPI	Definition	Comment	Relates to	IMI2 target	IMI2 results	IMI1 + IMI2 results
			to promote the involvement of SMEs in its activities, in line with its objectives'			

Horizon 2020 Key Performance Indicators common to all JTI JUs[68]

	Correspondence to general Annex 1	Key Performance Indicator	Definition / responding to question	Type of data required	Target at the end of H2020	Results in 2023
INDUSTRIAL LEADERSHIP	12	SME - Share of participating SMEs introducing innovations new to the company or the market (covering the period of the project plus three years)	Based on Community Innovation Survey. Number and % of participating SMEs that have introduced innovations to the company or to the market	Number of SMEs that have introduced innovations	50 %	n/a
	13	SME - Growth and job creation in participating SMEs	Turnover of company, number of employees	Turnover of company, number of employees	To be developed based on FP7 ex-post evaluation and /or first H2020 project results	n/a
SOCIETAL CHALLENGES	14	Publications in peer-reviewed high impact journals	The percentage of papers published in the top 10 % impact ranked journals by subject category	Publications from relevant funded projects (DOI: Digital Object Identifiers); Journal impact benchmark (ranking) data to be collected by commercially available bibliometric databases.	[On average 20 publications per EUR 10 million funding (for all societal challenges)]	27.46%

[68] 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 2023
	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	10 patent applications 14 patents awarded
	16	Number of prototypes testing, activities and clinical trials[69]	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: Clinical trials: 147 Prototypes: 239 Testing activities: 323[70]
	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]	920 25.39%
	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: 51 New processes: 37 New methods: 45

69 Clinical trials are IMI specific.

[70] In the CAAR 2022 there was a clerical error. The data reported was 252 clinical trials, 136 prototypes, 164 testing activities. Instead, the data should have been 136, clinical trials, 164 prototypes, 252 testing activities.

Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs[71]

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
2	Widening the participation	2.1 Total number of participations by EU-28 Member State	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: Applications: 7495 Applicants: 2628 Beneficiaries: **2765**

Country	Participations (Participants)
Austria	61 (27)
Belgium	261 (80)
Bulgaria	2 (2)
Croatia	4 (4)
Czechia	12 (7)
Denmark	96 (32)
Estonia	6 (3)
Finland	44 (13)
France	321 (125)
Germany	443 (158)
Greece	11 (7)

[71] This table presents all indicators for monitoring of cross-cutting issues which apply to JTI JUs (Annex III - Council Decision 2013/743/EU). In this and the preceding table, 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 2023
					Hungary 8 (5) Ireland 36 (19) Italy 187 (96) Latvia 1 (1) Lithuania 1 (1) Luxembourg 35 (6) Netherlands 327 (105) Poland 9 (7) Portugal 28 (27) Romania 3 (3) Slovenia 8 (6) Spain 185 (81) Sweden 129 (34) United Kingdom[72] 547 (150) Total EU-28 **2765** (999) (Cumulative figures as of 31/12/2023)
		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 — IHI contrib., M EUR (%) Austria 38.4 (2.9%) Belgium 75.9 (5.6%) Bulgaria 0.2 (0%)

[72] To ensure easy comparisons with reports of previous years, the UK is kept with the EU-27 in the H2020 / IMI2 KPIs.

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023	
					Croatia	0.2 (0%)
					Czechia	3.1 (0.2%)
					Denmark	22.3 (1.7%)
					Estonia	2.8 (0.2%)
					Finland	19.6 (1.5%)
					France	134.1 (10%)
					Germany	165.6 (12.3%)
					Greece	3.7 (0.3%)
					Hungary	3.4 (0.3%)
					Ireland	25.2 (1.9%)
					Italy	69.3 (5.2%)
					Latvia	0.4 (0%)
					Lithuania	0.1 (0%)
					Luxembourg	12.5 (0.9%)
					Netherlands	270.0 (20.1%)
					Poland	1.7 (0.1%)
					Portugal	10,3.8 (0.8%)
					Romania	1.6 (0.1%)
					Slovenia	1.3 (0.1%)
					Spain	113.7 (8.5%)
					Sweden	54.6 (4.1%)
					United Kingdom	315.1 (23.4%)
					Total EU-28	**1345.4**
					(Cumulative figures as of 31/12/2023)	

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: Applications: 590 Applicants: 246 Beneficiaries: **256** Country — Participations (Participants) Iceland — 1 (1) Israel — 22 (12) North Macedonia — 1 (1) Norway — 30 (13) Serbia — 4 (4) Switzerland — 202 (53) Turkiye — 2 (2) Total Assoc. countries: — 262 (86) (Cumulative figures as of 31/12/2023)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
NA		Total amount of EU financial contribution by Associated Country (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country / IHI contrib., M EUR (%) Iceland 0.1 (0.1%) Israel 3.6 (4.6%) Norway 11 (14.2%) North Macedonia 0.1 (0.2%) Serbia 1.1 (1.4%) Switzerland 62.4 (79.5%) Turkiye 0 (0%) Total Assoc. countries: **77.9** (Cumulative figures as of 31/12/2023)
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: 382 out of 2317 (16,5 %) Participants: 261 out of 1003 (26.2 %) EU funding: EUR 177,8 million (12.1 %) (Cumulative figures as of 31/12/2023, beneficiaries receiving EU funding only)
6	Gender	6.1 Percentage of women participants in H2020 projects	Gender of participants in H2020 projects	YES	53 % of the total workforce working in IMI2 projects is female.
		6.2 Percentage of women project coordinators in H2020	Gender of MSC fellows, ERC principal investigators and scientific coordinators in other H2020 activities	YES	Data pending %

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
7	International cooperation	7.1 Share of third-country participants in Horizon 2020	Nationality of H2020 beneficiaries	YES	Eligible proposals: Applications: 242 Applicants: 162 Beneficiaries: 140 Country — Participations (Participants) Australia 2 (2) Benin 1 (1) Brazil 1 (1) Burkina Faso 1 (1) Canada 7 (7) China (People's Republic of) 1 (1) Congo (Democratic Republic of) 1 (1) Gabon 2 (1) Japan 2 (2) Kuwait 1 (1) Senegal 2 (1) Sierra Leone 3 (2) Singapore 1 (1) South Africa 3 (3) Tanzania (United Republic of) 1 (1) United States 110 (53) Total for third countries 140 (80) (Cumulative figures as of 31/12/2023)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
		7.2 Percentage of EU financial contribution attributed to third country participants	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country / IHI contrib. M EUR (%) Australia 0.3 (0.7%) Benin 0.6 (1.4%) Brazil 0.3 (0.7%) Burkina Faso 3.8 (9.1%) Canada 0.4 (1.1%) China (People's Republic of) 0 (0%) Congo (Democratic Republic of) 3.3 (7.9%) Gabon 0.9 (2.1%) Japan 0 (0%) Senegal 0.4 (1.0%) Sierra Leone 20.2 (48.8%) Singapore 0 (0%) South Africa 1.5 (3.6%) Tanzania (United Republic of) 0.5 (1.2%) United States 9.5 (23.1%) Total for third countries 41.4 (Cumulative figures as of 31/12/2022)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2023
NA		Scale of impact of projects (High Technology Readiness Level)	Number of projects addressing TRL[73] between (4-6, 5-7)		-3 projects TRL 4 -3 projects TRL 5 -1 project TRL 6 -3 projects TRL 7 -1 projects TRL 8 -6 projects TRL 9
11	Private sector participation	11.1 Percentage of H2020 beneficiaries from the private for-profit sector	Number of and % of the total H2020 beneficiaries classified by type of activity and legal status		Participations: 1 216 out of 3 167 (38.4%) Participants: 437 out of 1 165 (37.5 %)
		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		€197,8 million out of €1,465,0 million (13.5%)
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 1 452.1 million EU contribution
		12.2 PPPs leverage: total amount of funds leveraged through Art. 187 initiatives, including additional activities, divided by the EU contribution	Total funding made by private actors involved in PPPs - in-kind contribution already committed by private members in project selected for funding - additional activities (i.e. research expenditures/investment of industry in the sector, compared to previous year)		EFPIA & Associated Partners contribution (EUR 1 506 million) divided by EU contribution (EUR 1 452.1 million) = leverage of 103.7%

73 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 2023
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, websites, 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: 222 824 Total funding amounts: EUR 13 524 535
NA	Participation of RTOs and Universities	Participation of RTO[74]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: 566 (18.2 %) HES: 991 (31.9 %) % budget allocated: Res. org: EUR 349.2 million (23.8 %) HES: EUR 771.0 million (52.6 %) (Cumulative figures as of 31/12/2023)
NA	Audit	Error rates	% of common representative error; % residual error		For IMI2 H2020) population) Representative error rate: 3.74% (Residual error rate: **0.99%**
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		Cases implemented 70 (93%) Amount: EUR 3 165 433

74 RTO: Research and Technology Organisation.

Annex 7 – Scoreboard of Horizon Europe common key impact pathway indicators (KIP)

IHI projects have started in 2023 therefore it is too early to see any impacts to scientific, societal, and technological/economic pathways. The European Commission IT central service is developing a centrally managed dashboard to collect the micro-data behind the Key Impact Pathway indicators (KIP) for all parts of the Programme. So far, the dashboard could capture data concerning Key Impact Pathway number 2. IHI will report on the full set of KIP indicators as soon as more data will be available for IHI in the central dashboard. The calculations performed by the dashboard follow the methodology presented in the Indicator methodology and metadata handbook.

Key Impact Pathway[75]	Short-term	Medium-term	Longer-term	Detail per action or globally for Year 2023
Towards scientific impact				
1-Creating high-quality new knowledge	Publications -Number of peer-reviewed scientific publications resulting from the Programme	Citations -Field-Weighted Citation Index of peer-reviewed Publications resulting from the Programme	World-class science -Number and share of peer-reviewed publications resulting from the projects funded by the Programme that are core contribution to scientific fields	Data not available
2-Strengthening human capital in R&I	Skills -Number of researchers involved in upskilling (training mentoring/coaching mobility and access to R&I infrastructures) activities in projects funded by the Programme	Careers -Number and share of upskilled researchers involved in the Programme with increased individual impact in their R&I field	Working conditions -Number and share of upskilled researchers involved in the Programme with improved working conditions including researchers' salaries	Short term: 400
3-Fostering diffusion of knowledge and open science	Shared knowledge Share of research outputs (open data/publication/software etc.) resulting from the Programme shared through open knowledge infrastructures	Knowledge diffusion -Share of open access research outputs resulting from the Programme actively used/cited	New collaborations -Share of Programme beneficiaries which have developed new transdisciplinary/trans sectoral collaborations with users of their open access research outputs resulting from the Programme	Data not available
Towards societal impact				
4-Addressing Union policy priorities and global challenges through R&I	Results -Number and share of results aimed at addressing identified Union policy priorities and global challenges (including SDGs) (multidimensional: for each identified priority) Including: Number and share of climate-relevant results aimed at delivering on the	Solutions -Number and share of innovations and research outcomes addressing identified Union policy priorities and global challenges (including SDGs) (multidimensional: for each	Benefits -Aggregated estimated effects from use/exploitation of results funded by the Programme on tackling identified Union policy priorities and global challenges (including SDGs) including contribution to the policy and law-making cycle (such as norms and standards) (multidimensional: for each identified priority)	Data not available

[75] NB: For some KIPs, the data will not be available in the short or even medium term.

	Union's commitment under the Paris Agreement	identified priority) Including: Number and share of climate-relevant innovations and research outcomes delivering on Union's commitment under the Paris Agreement	Including: Aggregated estimated effects from use/exploitation of climate-relevant results funded by the Programme on delivering on the Union's commitment under the Paris Agreement including contribution to the policy and law-making cycle (such as norms and standards)	
5-Delivering benefits and impact through R&I missions	R&I mission results -Results in specific R&I missions (multidimensional: for each identified mission)	R&I mission outcomes Outcomes in specific R&I missions (multidimensional: for each identified mission)	R&I mission targets met - Targets achieved in specific R&I missions (multidimensional: for each identified mission)	Data not available
6-Strengthening the uptake of R&I in society	Co-creation -Number and share of projects funded by the Programme where Union citizens and end-users contribute to the co-creation of R&I content	Engagement - Number and share of participating legal entities which have citizen and end-users engagement mechanisms in place after the end of projects funded by the Programme	Societal R&I uptake -Uptake and outreach of co-created scientific results and innovative solutions generated under the Programme	Data not available
Towards technological / economic impact				
7-Generating innovation-based growth	Innovative results -Number of innovative products, processes or methods resulting from the Programme (by type of innovation) & Intellectual Property Rights (IPR) applications	Innovations -Number of innovations resulting from the projects funded by the Programme (by type of innovation) including from awarded IPRs	Economic growth -Creation, growth & market shares of companies having developed innovations in the Programme	Data not available
8-Creating more and better jobs	Supported employment -Number of full time equivalent (FTE) jobs created, and jobs maintained in participating legal entities for the project funded by the Programme (by type of job)	Sustained employment - Increase of FTE jobs in participating legal entities following the project funded by the Programme (by type of job)	Total employment -Number of direct & indirect jobs created or maintained due to diffusion of results from the Programme (by type of job)	Data not available
9- Leveraging investments in R&I	Co-investment -Amount of public & private investment mobilised with the initial investment from the Programme	Scaling-up -Amount of public & private investment mobilised to exploit or scale-up results from the Programme (including foreign direct investments)	Contribution to '3 % target' - Union progress towards 3 % GDP target due to the Programme	Data not available

Annex 8 – Scoreboard of common indicators for Horizon Europe partnerships

N°	Criterion addressed	Proposed common indicators	Baseline	Results for 2023	Target 2027
1	Additionality	Progress towards (financial and in-kind) contributions from partners other than the Union – i.e. committed vs. actual[76]	€ 1.506 billion	€ 189.8 million	€ 1.200 billion
2	Additionality/ Synergies	Additional investments triggered by the EU contribution including qualitative impacts related to additional activities[77]	N/A	N/A	N/A
3	Directionality	Overall (public and private in-kind and cash) investments mobilised towards EU priorities[78]	1.8% Green Deal 17% Digital 100% Resilience	0% Green Deal 95% Digital 95% Resilience	2% Green Deal 50% Digital 100% Resilience
4	International visibility and positioning	International actors involved[79]	15	10	N/A
5	Transparency and openness	Share & type of stakeholders and countries invited/engaged[80]	N° of applicants: 2 978 Types of applicants: Academia, secondary and higher education establishment 577, Associated	N° of applicants: 820 Types of applicants: Academia, secondary and higher education establishment 178, Contributing	N/A

[76] The baseline is the total budget committed by the partners other than the Union for IMI2 projects, in terms of IKOP+FC. The Results are the sum of IKOP+IKAA devoted to projects + FC, coming from Private Members, based on committed values, up to 31/12/2023. The IHI target is EUR 1.200 million for the partners other than the Union for the whole duration of the new partnership (1.000 million from funding industrial partners and 200 million from contributing partners).

[77] The information on further investments mobilized to exploit or scale-up project results is asked to project coordinators via SyGMa only for final reporting. Therefore, there is no data to report at the moment. It is not possible to provide a baseline as this element was not monitored in the past.

[78] This data set is extracted from SyGMa. In the "policy monitoring" section the EU priorities addressed by the projects are captured. IHI reported on the projects' budgets on 3 key priorities: Green deal (including biodiversity, clean air, climate action), Digital (including artificial intelligence for Europe and Europe fit for the digital age), Resilience (all IHI projects are resilient, with resilience defined as *the ability not only to withstand and cope with challenges but also to undergo transitions, in a sustainable, fair, and democratic manner* by the 2020 Strategic Foresight Report).

[79] "International actors" are intended as those entities other than members or beneficiaries based in Third Countries. So IHI will report on Contributing Partners outside the EU and associated Countries.

[80] The "stakeholders invited/engaged" are intended as the (unique) applicants to Calls. The baseline reports on IMI2 applicants and the results for 2023 reports on IHI applicants to the Calls that were launched up to December 2023.

			Partner 20, EFPIA 64, Non-profit research organisation 500, Others 759, Patient organisation 145, Regulatory/community bodies 60, SME 853 N° of countries of applicants: 66	partner 78, IHI industry partners 84, Non-profit research organisation 124, Others 185, Patient organisation 38, Regulatory/community bodies, 2 SME 131 N° of countries of applicants: 42	
6	Transparency and openness	No and types of newcomer members in partnerships and their countries of origin (geographical coverage)[81]	2	5	5
7	Transparency and openness	No and types of newcomer beneficiaries in funded projects (in terms of types and countries of origin)[82]	N° of newcomer beneficiaries: 802 Types of newcomers: Academia, secondary and higher education establishment 123; Associated Partner 32; EFPIA 77; Non-profit research organisation 152; Patient organisation 24; Regulatory/community bodies 11; SME 213; Others 170. N° of countries of newcomers: 48	N° of newcomer beneficiaries: 160 Types of newcomers: Academia, secondary and higher education establishment 16; Contributing partner 16; IHI industry partners 65, Non-profit research organisation 17; Patient organisation 6; SME 22; Others 18. N° of countries of newcomers: 24	N/A
8	Coherence and synergies	Number and type of coordinated and joint activities with other European Partnerships[83]	Strategic support & exchanges: 1	Strategic support & exchanges: 2 Operational support & exchanges: 4 Joint communication: 2 Memorandum of Understanding: 1	N/A

[81] IHI JU is an institutionalised public-private partnership (Art.187) between the European Union and industry associations representing the sectors involved in healthcare, namely COCIR (European Trade Association representing the medical imaging, radiotherapy, health ICT and electromedical industries); EFPIA, including Vaccines Europe (European Federation of Pharmaceutical Industries Associations); EuropaBio (the European Association for biotechnology industries); and MedTech Europe (European Association for the medical technology industry). Member States are not members of this joint undertaking. Likewise, IMI2 JU was an institutionalised public-private partnership (Art.187) between the European Union and EFPIA (European Federation of Pharmaceutical Industries Associations). Member States were not members of this joint undertaking.

[82] The 'newcomer' beneficiaries mean the (unique) beneficiaries involved for the first time in the activities of the partnership (so that did not participate in the previous partnership). The baseline reports on IMI2 newcomer beneficiaries that were not part of IMI1 and the results for 2023 reports on IHI newcomer beneficiaries that were not part of IMI2.

[83] In IMI2 there were no synergy objectives, nevertheless one synergetic activity was generated during IMI2.

9	Coherence and synergies	Number and type of coordinated and joint activities with other R&I Initiatives at EU /national/regional/sectorial level[84]	N/A	Strategic support & exchanges: 3 Operational support & exchanges: 3 Joint communication: 3	N/A
10	Coherence and synergies	Complementary and cumulative funding from other Union funds (Horizon Europe National funding, ERDF, RRF, Other cohesion policy funds, CEF, DEP, LIFE other)[85]	N/A	N/A	N/A
11	International visibility and positioning	Visibility of the partnership in national, European, international policy/industry cycles[86]	National info days: 25 Events: 42 News articles: 440 Newsletters: 88 Webinars: 130 Platforms: 2	National info days: 22 Events: 13 News articles: 44 Newsletters: 24 Webinars: 32 Platforms: 2	N/A

[84] The coordinated and joint activities with other R&I Initiatives reported here are those established at IHI partnership level (not at project level). In IMI2 there were no synergy objectives.

[85] This indicator is not applicable to IHI.

[86] Dissemination activities as well as passive and active communication activities that the partnerships put in place to increase its visibility and attract stakeholders.

Annex 9 – Scoreboard of KPIs specific to IHI

KPI Name	Unit of measurement	Baseline[87]	Target[88] 2023	Target 2025	Target 2027	Ambition >2027	Status
Resources (input), processes and activities							
1.1. Involvement of multiple health care stakeholders	Share of projects involving more than two types of healthcare stakeholders [research higher or secondary education organisations (private or public) small & medium enterprise (SME) large company (for-profit legal entity) non-governmental organisations (NGOs) healthcare professional organisation/healthcare provider patient / citizen organisation regulators or regulatory body notified body health technology assessment body (HTA) health care payer charity and foundation public authority] as project participants or advisors	50%	55%	60%	65%	70%	100%
1.2. Cross-sectoriality of the partnership	Share of projects bringing together private members and/or contributing partners (or their affiliated or constituent entities) from two or more technology sectors89	25%	70%	80%	85%	90%	94%
1.3 Engagement of regulators	Number of projects interacting with regulators90 to contribute to new or improved guidelines or methodologies	13	0	5	10	20	0

[87] Baselines are derived (where possible) from the Innovative Medicines Initiative (IMI2) as predecessor to IHI.

[88] Reporting methodology: cumulatively reporting from the beginning of IHI until 31/12/2030.

[89] The IHI private members COCIR, EFPIA, EuropaBio and MedTech Europe have members from several technology sectors. Contributing partners might also cover further technology sectors.

[90] In this document, the term 'regulators' refers to the different bodies involved in the processes regulating medical products (e.g. scientific assessment, production of scientific guidelines, scientific advice to manufacturers, granting/refusal/suspension of marketing authorisations, post-market surveillance, withdrawing/recalling of devices put on the market, authorisation and oversight of clinical trials). It includes the European Commission, National Competent Authorities (NCA), the Medical Device Coordination Group (MDCG), and the European Medicines Agency (EMA). Notified Bodies (NB), while designated to perform a regulatory function (verification of medical device/in-vitro diagnostics conformity), cannot be considered as regulators in the strict sense of this definition. However, the potential input and expertise of Notified Bodies may still be relevant for the design and implementation of the activities of the proposed initiative.

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
Outcomes							
2.1 Cross-stakeholders' collaboration	Share of multi-stakeholders' publications identified through bibliometric data analysis [research / higher or secondary education organisations (private or public), small & medium enterprise (SME), large company (for-profit legal entity), non-governmental organisations (NGOs), healthcare professional organisation / healthcare provider, patient / citizen organisation, regulators or regulatory body, notified body, health technology assessment body (HTA), health care payer, charity and foundation, public authority]	65%	65%	66%	67%	70%	Too early
2.2 Public-private collaboration	Share of publications across public and private stakeholders identified through bibliometric data analysis (academic, pharmaceutical, biopharmaceutical, medical technologies, biotechnologies)	65%	65%	66%	67%	70%	Too early
2.3 Project outputs for use in clinical practice and health research development and innovation (R&D&I)	Number of: new tools for studying new potential drug targets such as new pharmacological tools, therapeutic modalities, and patient-derived assays available to the scientific community; new tools to test diagnostically and/or therapeutically relevant hypotheses in pre-clinical models and/or clinically in uncharted areas of disease biology; new tools for prediction, prevention, interception, surveillance, diagnosis, treatment, and management options to prepare for major epidemic outbreaks; new biomarkers of disease (relevant for diagnosis, efficacy, safety, or prevention) identified and experimentally validated; new taxonomies of disease or new stratifications to define patient sub-populations.	100	0	50	120	150	0
2.4 Integrated health care solutions considering end-users' needs	Number of project outputs that combine people-centred integrated solutions (pre-competitive tools, methods, solutions as well as products/services or combined products)	No baseline available	0	3	7	10	0

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
Outcomes							
2.5 Methodologies for value assessment of integrated solutions	Number of Methodologies for the assessment of the added value of combinations of products/services or combined products (including development of patient reported outcomes / experience measures and statistical methods/tools) submitted to health care authorities and organisations91	No baseline available	0	2	3	5	0
2.6 New or improved clinical guidelines	Number of projects contributing to the development of new or improved clinical guidelines	13	0	5	10	20	0
2.7 Management of health data	Number of common standards, protocols and frameworks developed by the projects to enable better access to data, sharing and analysis of health-related data	No baseline available	0	3	7	10	0
2.8 Demonstration of data integration	Number of pilots developed by the projects demonstrating integration of data provided by the private and public sectors	No baseline available	0	5	10	20	0
2.9 Demonstration of AI in health care	Number of pilots developed by the projects demonstrating feasibility of use of artificial intelligence in health care	No baseline available	0	1	2	3	0

[91] Health care authorities and organisations to which it is referred here are HTA bodies and regulatory authorities, payers and public authorities.

- HTA agencies/bodies: http://www.adhophta.eu/toolkit/assets/tools/AdHopHTA_toolkit_tool24_document.pdf; https://www.eunethta.eu/about-eunethta/eunethtanetwork/)
- National and regional public procurement organisations
- National payer and reimbursement organisations (incl. health insurance companies)
- National healthcare authorities: examples are: Dutch NZA; http://www.euregha.net/ (membership list of regional and local health authorities); https://eurohealthnet.eu/list-of-members/ (first part of the membership not the research members)

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
Impacts							
3.1 Creation of sustainable resources and infrastructures that facilitate translation of the knowledge to innovations	Number of established new research networks, new clinical networks, further public-private collaborations on health R&D&I, research infrastructures, biobanks, collaborative platforms etc. (that outlive the project and are accessible to broader scientific community)	10	0	4	7	15	Too early
3.2 Development of preventive or therapeutic strategies in different therapeutic areas to address unmet public health needs	Share of projects that aim to develop new or improved existing methodologies also across disciplines addressing public health needs[92] included in the list of the WHO Europe Health 2020 priority areas[93]	No baseline available	90%	90%	90%	90%	100%

[92] SBA definition (article 125.1) “For the purpose of this Regulation, an unmet public health need shall be defined as a need currently not addressed by the health care systems for availability or accessibility reasons, for example where there is no satisfactory method of diagnosis, prevention or treatment for a given health condition or if people access to health care is limited because of cost, distance to health facilities or waiting times”.

[93] https://www.euro.who.int/en/about-us/regional-director/regional-directors-emeritus/dr-zsuzsanna-jakab -2010-2019/health-2020-the-european-policy-for-health-and-well-being/about-health-2020/priority-areas

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
Impacts							
3.3 Cross-sector activities established by the partnership that will help contribute to a globally competitive EU health care industry	Number of activities in which cross-sector collaboration drives health innovation, such as: Spin-off companies, entities or activities created based on outputs of the project (e.g. new commercial or non-profit entities) Collaboration agreements between large companies[94] & SMEs[95] established for purposes that go beyond the scope of the project during and/or after project lifetime. Other activities where the joint contribution of different al partners has generated cross-sectoral health innovation. Examples of collaboration activities across health industry sectors that contributed to the transition to a green and digital economy (as outlined in the new Industrial Strategy for Europe[96])	No baseline available	0	5	10	20	Too early

94 For-profit legal entities with an annual turnover of EUR 500 million or more (Single Basic Act, Art. 123.5).

95 Small and medium-sized enterprises (SMEs) are defined in the "EU recommendation 2003/361" (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361&from=EN) as of page 4 and in the European Commission "User guide to SME definition" (https://ec.europa.eu/regional_policy/sources/conferences/state-aid/sme/smedefinitionguide_en.pdf) especially in page 13.

96 "European industrial strategy 2019-2024" (https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy_en) and "Updating the 2020 New Industrial Strategy: Building a stronger Single Market for Europe's recovery" (https://ec.europa.eu/info/sites/default/files/communication-industrial-strategy-update-2020_en.pdf).

Annex 10 – IKAA report

In 2023, IHI private members reported EUR 3.5 million of costs for additional activities to the IHI Programme Office, of which EUR 129 615 were certified by an external auditor and validated by the JU GB.

The overview of the reported and validated IKAA in 2023 is available here, including descriptions of additional activities undertaken and their type (either programme IKAA or project IKAA).

These additional activities were carried out by one IHI private member established in Belgium.

TOTAL IKAA 2023: BREAKDOWN PER COUNTRY	
Country *(code)*	**value (€)**
BE	129,615

At the end of 2023, from the total reported IKAA amounting to EUR 3.5 million, the amount of EUR 3.4 million remains to be certified by an external auditor and validated by the JU GB.

TOTAL IKAA 2021- 2023 (Evolution - Value in €)		
Planned IKAA[97]	**Reported IKAA with pending certification**	**Certified IKAA**
41,484,144	3,419,717	129,615

[97] See the adopted IKAA Plan in WP 2024 on 14 December 2023. Note that additional activities planned for projects of IHI call 2 and 3 are not included in the last adopted IKAA Plan of 2023 as these projects were not yet signed at the time of the preparation of the IHI WP 2024. These planned additional activities will be included in the first amendment of the WP 2024.

Annex 11 – Annual accounts

The annual accounts are provided in a separate document, which is officially handed over to the budgetary authorities, the European Court of Auditors, and the external auditors.

They are also published on the IHI website.

Annex 12 – 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 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. 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:

JU 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, 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 JU contributions on completion of the audits but does not take into account the corrections and follow-up undertaken by the JU.

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[98]:

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

- n = total sample size;
- err_i = error rate (in %) in accepted JU 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 JU 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 the 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[99]:

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

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 JU contributions, expressed in euros;

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

99 Idem.

- **A** = total value of audited accepted JU contributions, expressed in euros;
- **E** = total non-audited amounts of accepted JU 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.

Annex 13 – Additional communications indicators

Website traffic

IHI's website is the programme's main information hub, and all communication channels link back to its content. As an example, the number of referrals from LinkedIn to the website amounted to 18%.

In 2023, the website received 161k visits, with a peak of over 18k unique visitors in June due to the launch of calls 4 and 5. Consequently, by far the most visited webpage, with over 9k page views, was the news item on the updated draft topic texts for IHI calls 4 and 5.

Around 49% of visitors arrive on the website via direct entry, which is a very high percentage when compared with similar websites but is consistent with the previous IMI website figures. Only around 40% of visitors reached the site via search engines and around 11% arrive via referrals, mainly through links on the europa.eu website, but also through the founding members' websites.

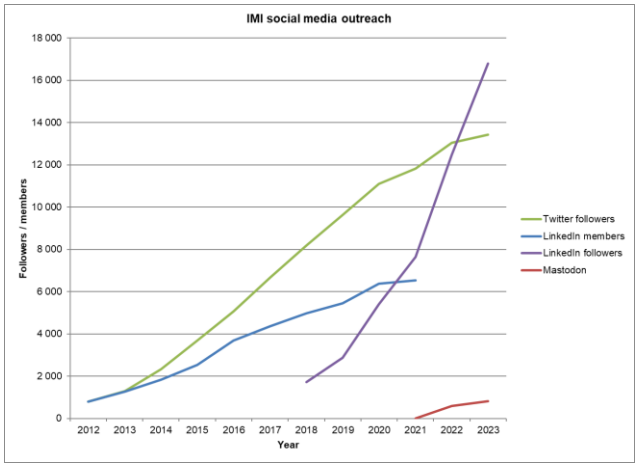
Further indicators are:

- Number of sessions: 244 862
- Number of page views: 649 371
- Average session time: 2m 21s
- Bounce rate: 66.19%
- Returning visitors: 18.13%
- Events per session: 3.05

With regards to the geographic location of website visitors, a vast majority came from Europe (over 62% of total visitors and 69% of the total sessions) followed by North America (20% visitors,16% sessions) and Asia (11% visitors, 9% sessions). Within the EU, most visitors came from Germany (7%), Belgium (6%), and Spain (5%). The UK and Switzerland's percentage of visitors was 8% and 4%, respectively.

Social media

We continued to primarily promote our editorial activities through IHI's social media channels. As the graph below shows, both the LinkedIn and Mastodon accounts experienced growth in the number of followers, while IHI's X account is holding ground despite the difficult situation faced by the platform since 2022.



By the end of 2023, IHI had 16 799 followers on **LinkedIn**, up from 12 487 at the end of 2022. Looking at the type of organisations that started to follow IHI's LinkedIn account, we can observe a balanced increase across all followers. IHI followers still come primarily from academia, including research centres and higher

education (19%), large industry (mainly composed of 15.6% from the pharmaceutical manufacturing sector and 3% from the medical equipment manufacturing sector) and the biotechnology research field (10.8%).

The account featured 426 posts of which 218 were drafted by IHI, while the rest were re-posts from our projects. Those 218 original posts received 289 817 impressions, 7 894 clicks, 5 928 likes, 87 comments and were shared 1 401 times. The engagement rate was 4.3%. The three posts with the highest engagement rate were on the launch of the first IHI projects, World Immunization Week and Brain Awareness Week, while the three top posts in terms of number of impressions were on the signing of the MoU with the EIT Health, the launch of the first IHI projects and on the Newborn Screening Awareness Month.

IHI has been active on **Mastodon**, the open-source EU based social media platform, since 2022. By the end of 2023, IHI's account had reached 827 followers.

In 2023, @IHIEurope tweeted 407 original messages in addition to regular retweets, generating over 320k impressions, 1 238 link clicks, 1 385 retweets and 2 538 likes, reaching overall 5 288 engagements. By the end of 2023, the **IHI X account** had 13 418 followers, experiencing a very modest increase compared to 2022.

Newsletter

Type of organisations	% subscribers
University	28.39%
SMEs	17.97%
Other research organisation	17.40%
Large pharmaceutical industry	8.52%
Other	6.12%
Consultancy	5.34%
Hospital	4.15%
Other large industry	3.74%
Government	3.22%
Patient Organisation	2.49%
European Institution	1.54%
Public Relations Agency	0.57%
Regulatory authority	0.54%
Total	100.00%

In addition to our social media channels, the IHI newsletter – published 12 times throughout the year – played a pivotal role in promoting our editorial content.

The most successful issues were in general those announcing news relating to IHI calls for proposals (such as the publication of draft topics, call launches, and registration for the IHI Call Days).

By the end of 2023, there were 8 035 subscribers (compared to 6 787 in 2022). The breakdown of subscribers' organisations is shown in the table on the left.

Press coverage

Throughout the year, the communications team tracked the number of press articles that mentioned IMI/IHI and its projects. There were 7 038 articles published worldwide, 2 300 of which were published in the EU. The headline / header presence of IMI/ IHI was around 2%.

Annex 14 – List of IHI projects

(Grant agreements signed as of 31 December 2023)

Project acronym	Full project title
AD-RIDDLE	Real-world implementation, deployment and validation of early detection tools and lifestyle enhancement
CLAIMS	Clinical impact through AI-assisted MS care
COMBINE-CT	Combining diagnostic data and interventional approaches for futureproof cardiology care
EDENT1FI	European action for the diagnosis of early non-symptomatic type 1 diabetes for intervention
GRIPonMASH	GRIP on MASH: global research initiative for patient screening on MASH
GUIDE.MRD	Guiding multi-modal therapies against MRD by liquid biopsies
HEU-EFS	Harmonised approach to early feasibility studies for medical devices in the European Union
iCARE4CVD	Individualised care from early risk of cardiovascular disease to established heart failure
IDERHA	Integration of heterogeneous data and evidence towards regulatory and HTA acceptance
IMAGIO	Imaging and advanced guidance for workflow optimization in interventional oncology
IMPROVE	Framework to IMPROVE the integration of patient generated health data to facilitate value based healthcare
LIVERAIM	A biomarker-based platform for early diagnosis of chronic liver disease to enable personalized therapy
PaLaDIn	Patient lifestyle and disease data interactium
PREDICTOM	Prediction of Alzheimer's disease using an AI driven screening platform
PROMINENT	Precision medicine platform in neurodegenerative disease
SASICU	Improving patient outcomes and reducing cognitive load of clinical staff in intensive care through medical-device interoperability and an open and secure IT ecosystem

Information on Innovative Medicines Initiative (IMI) projects

Details of all IMI1 and IMI2 projects can be found on the IHI website.

Annex 15 – List of acronyms

Acronym	Meaning
AA	Additional activities
AAR	Annual Activity Report
ABAC	Accrual Based Accounting System
ACE	Angiotensin converting enzyme
ACT EU	Accelerating Clinical Trials in the EU
AD	Alzheimer's disease
AD	Atopic dermatitis
ADA	Anti-drug antibody
ADHD	Attention-deficit/hyperactivity disorder
ADL	Activities of daily life
AI	Artificial intelligence
ALL	Acute lymphoblastic leukaemia
ALRI	Acute lower respiratory infection
AMD	Age-related macular degeneration
AML	Acute myeloid leukaemia
AMR	Antimicrobial resistance
AP	IMI2 Associated Partner
API	Active pharmaceutical ingredient
ARES	Advanced Records System
ASD	Autism spectrum disorder
ATM-AVI	Aztreonam-avibactam
ATMP	Advanced therapy medicinal product
BMGF	Bill and Melinda Gates Foundation
BMJ	British Medical Journal
BMR	Biannual Monitoring Report
BOA	Back office arrangements
BP	Biopharmaceutical
CA	Commitment appropriations
CA	Contract agent
CAAR	Consolidated Annual Activity Report
CAD	Coronary artery disease
CA-ARTI	Community-acquired acute respiratory tract infection
CADET	Chromatography analysis and design toolkit
CAFS	Commission Anti-Fraud Strategy
CAJU	Clean Aviation JU
CAR	Chimeric antigen receptor
CAS	Common Audit Service
CBE JU	Circular Bio-based Europe JU
CC	Confidential Counsellor

Acronym	Meaning
CCTA	Coronary computed tomography angiography
CDE	Core data element
CDM	Common data model
CE	Conformité Européenne
CERT-EU	Computer Emergency Response Team
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
CFU	Colony-forming unit
CH JU	Clean Hydrogen JU
CIC	Common Implementation Centre
CMS	Content management system
CNS	Central nervous system
COCIR	European Coordination Committee of the Radiological, Electromedical and Healthcare Information Technology (IT) Industry
COMPASS	H2020 workflow tool providing harmonisation between business processes & validation workflows
COMSA	Core outcome measures sets for paediatric and adult severe asthma
CORDA	Common Research Data Warehouse
COS	Core outcome set
COVID-19	Coronavirus disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
CPI	Checkpoint inhibitors
CR	Complete remission
CRE	Carbapenem-resistant Enterobacteriaceae
CRO	Contract research organisation
CRS	Common representative sample
CRS	Cytokine release syndrome
CSF	Cerebrospinal fluid
CT	Computed tomography
CT	Clinical trial
CTF	Children’s Tumor Foundation
CTU	Clinical trial unit
CV	Curriculum vitae
CVD	Cardiovascular disease
DCT	Decentralised clinical trial
DDIM	Drug development information management
DG	Directorate-General
DG RTD	European Commission Directorate-General for Research and Innovation
DICOM	Digital imaging and communications in medicine
DILI	Drug-induced liver injury
DMARD	Disease modifying anti-rheumatic drugs
DMN	Default mode network

Acronym	Meaning
DOI	Digital object identifiers
DOR	Duration of response
DSM	Dataset maturity
EAGER	European Autism Genomics Registry
EC	European Commission
ECA	European Court of Auditors
ECDC	European Centre for Disease Prevention and Control
eCDR	electronic Career Development Report
ED	Executive Director
EDPS	European Data Protection Supervisor
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFS	Early feasibility studies
EFS	Event-free survival
EFSA	European Food Safety Authority
EFTA	European Free Trade Association
EHDS	European Health Data Space
EIT	European Institute of Innovation and Technology
ELF	European Lead Factory
EMA	European Medicines Agency
EMBARC	European Bronchiectasis Registry
ENTIS	European Network of Teratology Information Services
EPPO	European Public Prosecutor's Office
EORTC	European Organisation for Research and Treatment of Cancer
EU	European Union
EU-Rail	Europe’s Rail JU
EuroHPC JU	European High Performance Computing JU
EuropaBio	European Association for Bioindustries
FAIR	Fraud and irregularity in research
FAIR	Findable, accessible, interoperable, reusable
FC	Financial contribution
FDA	US Food and Drug Administration
FG	Function group
FHIR	Fast Healthcare Interoperability Resources
FNIH	Foundation for the National Institutes of Health
FOP	Fibrodysplasia ossificans progressiva
FP	Full proposal
FP7	Seventh Framework Programme
FR	Financial rules
FTE	Full time equivalent
FTIH	First time in human
FWC	Framework contract

Acronym	Meaning
GB	Governing Board
GA	Grant Agreement
GAP	Grant Agreement preparation
GB	Governing Board
GCP	Good clinical practice
GDP	Gross Domestic Product
GEMM	Genetically engineered mouse model
GH EDCTP3	European & Developing Countries Clinical Trials Partnership 3
H2020	Horizon 2020
hACE2	Human angiotensin-converting enzyme 2
HCP	Healthcare provider / healthcare practitioner
HD	Huntington's disease
HE	Horizon Europe
HERA	Health Emergency Preparedness and Response Authority
HES	Higher or secondary education establishment
HFrEF	Heart failure and reduced ejection fraction
HFS	Hollow fibre system
HL7	Health Level Seven International
HR	Human resources
HRB	Horizon Results Booster
HRP	Horizon Results Platform
HRQOL	Health-related quality of life
HTA	Health technology assessment
IaaS	Internet as a service
iAMD	Intermediate age-related macular degeneration
IAS	Internal Audit Service of the European Commission
IBD	Inflammatory bowel disease
IC	Internal control
ICHOM	International Consortium of Health Outcomes Measurement
ICF	Internal control framework
ICT	Information and communication technology
ICU	Intensive care unit
IDMP	Identification of Medicinal Products
IHI JU	Innovative Health Initiative Joint Undertakings
IKAA	In-kind contributions to additional activities
IKC	In-kind contribution
IKOP	In-kind contributions to operational activities
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
IMID	Immune-mediated inflammatory disease
IO	Interventional oncology

Acronym	Meaning
IPCEI	Important Project of Common European
IPR	Intellectual property rights
iPSC	Induced pluripotent stem cell
IR	Implementing rule
irAOP	Immune related adverse outcome pathway
IT	Information technology
JIF	Journal impact factor
JUs	Joint Undertakings
KIP	Key impact pathway
KPI	Key performance indicator
LCI	Lung clearance index
LT	Long-term contract
LTCF	Long-term care facility
mAb	Monoclonal antibody
MASLD	Metabolic dysfunction-associated steatotic liver disease
MASH	Metabolic associated steatohepatitis
MBL	Metallo-β-lactamase
MBW	Multiple-breath washout
MDCG	Medical Device Coordination Group
MDD	Major depressive disorder
MDR	Multi-drug resistant
MMR	Major molecular response
MoU	Memorandum of Understanding
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MS	(EU) Member State
MSI	Mass spectrometry imaging
MSM	Multistakeholder meeting
Mtb	*Mycobacterium tuberculosis*
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCE	New chemical entity
NCP	National Contact Point
NDD	Neurodegenerative disease
NF	Neurofibromatosis
NGO	Non-governmental organisation
NHMRC	National Health and Medical Research Council
NIH	National Institutes of Health
NMR	Nuclear magnetic resonance
ODD	Orphan drug designation

Acronym	Meaning
OLAF	European Anti-Fraud Office
OMOP	Observational Medical Outcomes Partnership
OPTIKA	Optimised time kill assays
OS	Overall survival
PA	Payment appropriations
PET	Positron emission tomography
PBPK	Physiologically-based pharmacokinetic
PD	Parkinson's disease
PDX	Patient derived xenografts
PET	Positron emission tomography
PFS	Progression-free survival
PoV	Proof of viability
PPP	Public-private partnership
PRO	Patient reported outcome
PROM	Patient reported outcome measure
pSS	primary Sjögren's Syndrome
QHL	Qualified hit list
3Rs	Replace, reduce and refine (the use of animals in research)
R&D	Research and development
R&I	Research and innovation
RA	Rheumatoid arthritis
RAFS	Common Research Family Anti-Fraud Strategy
RCT	Randomised clinical trial
REC	Research organisation
RepER	Representative error rate
ResER	Residual error rate
RIA	Research and Innovation Action
RRMS	Relapsing-remitting multiple sclerosis
RSV	Respiratory syncytial virus
RTO	Research and Technology Organisation
SBA	Single Basic Act
SDG	Sustainable Development Goal
SEP	Staff establishment plan
SEP	Selection and evaluation phase
SEP	H2020 IT tool for submission and evaluation of proposals
SESAR 3 JU	Single European Sky ATM [air traffic management] Research 3 JU
SGG	Strategic Governing Group
SIP	Science and Innovation Panel
SIR	Staff implementing rules
SLA	Service level agreement
SLC	Solute carrier

Acronym	Meaning
SLE	Systemic lupus erythematosus
SME	Small and medium-sized enterprise
SNS JU	Smart Networks and Services JU
SNE	Seconded national expert
SNP	Single nucleotide polymorphism
SO	Specific objective
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SPREC	Standard PREanalytical Code
SRA	Strategic Research Agenda
SRG	States' Representatives Group
SRIA	Strategic Research and Innovation Agenda
SS	Single stage
SSbD	Safe and sustainable by design
ST	Short-term contract
STAR	Sjögren's Tool for Assessing Response
SyGMa	H2020 IT tool for grant management
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TA	Temporary agent
TB	Tuberculosis
TCR	T-cell receptor
TIS	Teratology information services
TRL	Technology readiness level
TTG	Time to grant
TTI	Time to inform
TTP	Time to pay
TTP	Time to progression
TTS	Time to sign
TVS	Technical validation study
UC	Ulcerative colitis
VCTE	Vibration-controlled transient elastography
VE	Vaccines Europe
WHO	World Health Organisation

Annex 16 – Governing Board assessment of the CAAR

Analysis and Assessment of the Consolidated Annual Activity Report 2023 (CAAR 2023) by the IHI JU Governing Board

Key objectives for 2023 were set out in the Work Programme (WP 2023) and its amendments and included: 1) execution of the **Strategic Research and Innovation Agenda** (SRIA) priorities; 2) ensuring continuity with and management of the **legacy from IMI2 JU**; 3) ensuring **sound budget implementation**; 4) promoting the cross sectorial partnership in health through **proactive outreach strategies** to attract high quality applications and engage with **new players and newcomers**; 5) demonstrating the EU added value of IHI JU through **assertive communication**; 6) exploring **synergies** with relevant programmes at Union, national, and regional level; and, 7) improving and broadening access to project outcomes by embedding **dissemination** and **exploitation** activities in all stages of the project lifecycle.

The Governing Board recognises **the progress made by the JU** towards achieving these objectives and notes that during the course of 2023, **IHI completed its second full year of operations**, dedicating efforts to implement and improve the governance structures, processes, tools and documentation to allow IHI to launch its first projects and new calls for proposals.

In 2023, IHI achieved the following:

- **Launch of the first IHI projects** – 16 grant agreements signed for a total value of EUR 184 million EU contribution plus EUR 190 million in contributions from IHI industry members and contributing partners.
- **Launch of two calls for proposals** (IHI calls 4 and 5) with a total of **10 topics**.
- Establishment of the **IHI Patient Pool** comprising around 120 patients and caregivers who are well placed to contribute their knowledge, expertise and experience to IHI's work.
- Gathered 16 ideas for IHI call topics via the **Ideas Incubator**, 6 of which passed the basic checks and were reviewed by the Science and Innovation Panel.
- Creation of **synergies** with related initiatives, including a Memorandum of Understanding with **EIT Health**.
- Implementation of the portfolio of **legacy projects** launched under **IMI and IMI2 programmes** and promotion of their successes.

Communication activities and achievements:

- Early publication and continuous **promotion of call topics** through various communication channels, from draft topic stage until the call deadline.
- Speakers and materials (e.g., brochures, factsheets, etc.) contributed in **external events** to promote IHI, e.g. MedTech Forum, BIO-Europe, Horizon4Poland 23
- Organisation of **IHI Call Days for calls 4 and 5**, featuring info sessions, pitching sessions, and an online brokerage platform.
- Targeting **IHI partners** and the **SRG** to raise awareness on IHI through the **#IHITransformingHealth campaign**
- Launch of a multi-lingual campaign - **#IdeasIncubator campaign** - to promote the "ideas incubator" platform for the collection of ideas from the wider stakeholder community.
- Publication of 41 articles on IMI project results on the IHI **website** and promotion on IHI's **social media** and featured in the monthly **newsletter**.

- 7 038 **press articles** published worldwide mentioning IMI/IHI and its projects, 2 300 of which were published in the EU.
- IHI **website** received 161k visits in 2023, with a peak of over 18k unique visitors in June due to the launch of calls 4 and 5.

IMI and IMI2 project achievements:

In 2023, **IMI projects** continued to deliver **impactful results,** including improving and accelerating the drug development process, developing diagnostic and treatment biomarkers for disease, and developing new therapies for diseases where there is high unmet need, including **tuberculosis** and **diabetes**. The projects also continued to deliver **knowledge** and **resources** used by the **wider research community** and several consortia still collaborating and publishing new papers creating **long-lasting, productive networks**.

The projects deliver outstanding outputs, leading to uptake of results in research processes, regulatory and clinical practice. **Success stories** of IMI projects[100] range from finding an earlier and more effective way to diagnose **Alzheimer's disease** using Amyloid imaging ("AMYPAD") to helping monitor effects of **depression** using smartphone apps ("RADAR-CNS"). Also, to secure the legacy of IMI projects through the up-take and use of their results, IMI2 project "**EU-PEARL**" delivered a range of resources, freely available online, including toolkits and plans to help in the operational planning and development of platform trials.

Other **key achievements** include putting in place the infrastructure needed to speed up and facilitate high-quality clinical testing of new treatments for the entire paediatric population via an extensive pan-European network of **paediatric clinical trial sites** ("C4C") and the identification of a range of **biological markers** offering important clues as to the state of a person's **liver** ("LITMUS") instead of undergoing a biopsy.

Since the start of the IMI2 programme, projects have been **patenting developed technologies**. From the beginning of IMI2 until 31 December 2023, 10 patent/trademark/registered design applications were submitted and 14 patents/trademarks awarded.

IHI achievements:

The first IHI projects were launched and grant agreements signed in spring 2023. The **five projects** funded under IHI call 1 address key challenges in health research including the use of **big data**, imaging and diagnostics to advance **cancer** diagnosis and treatment, and the creation of **digital platforms** to improve the care of people with **neurodegenerative** diseases (namely Alzheimer's disease and multiple sclerosis).

Later in 2023, IHI signed a further **11 grant agreements for projects** funded under IHI calls 2 and 3. These projects address topics on cardiovascular disease, early feasibility Studies, diseases of unmet public health need, rare diseases, mental health, hospital efficiencies, and patient-generated evidence.

New IHI calls were launched in July 2023 including topics on novel methods for combining diagnostics and treatment and patient-centric are, as well as topics on sustainable-by-design solutions for healthcare products and new manufacturing methods in the circular economy. These two latter topics show how IHI contributes to key European policies such as the **European Green Deal**.

[100] IHI website: https://www.ihi.europa.eu/projects-results

Furthermore, the following were carried out in 2023:

- As per Council Regulation 2021/2085 establishing Joint Undertakings, IHI drafted a plan for the **phasing-out of the JU from Horizon Europe funding**, focusing on the main administrative and operational adaptation needed. Further elements of the phasing-out plan will be completed during 2024.
- **Back-office arrangements** (BOA) were further developed in the area of procurement and ICT with IHI as co-lead in the latter. IHI JU continued to exercise the back-up role for the HR BOA.
- IHI worked on improving its procedures related to receiving and reviewing applications from legal entities interested in becoming IHI **contributing partners**.
- The Internal Audit Service (IAS) carried out a preliminary survey and series of interviews in the context of its audit on ***'IHI JU Governance and relations with stakeholders'.***
- IAS performed a follow up audit on the remaining open recommendation related to **fraud risk assessment** and **anti-fraud actions** and concluded that the recommendation had been adequately and effectively implemented and was therefore closed.
- In its '*Annual report on the EU Joint Undertakings for the financial year 2022'*, the European Court of Auditors (ECA) gave a clean bill of health for IHI JU, issuing an **unqualified ('clean') opinion** on the reliability of the accounts as well as on the legality and regularity of the revenue and payments underlying the annual accounts.
- The CAAR 2023 provides information on the effectiveness of the **internal controls** implemented and on the main results of monitoring and supervision controls. The JU internal control systems are working as intended.
- IHI JU continued to execute its budget applying the principles of **sound financial management**, which resulted in several budget transfers between budget chapters, in line with operational needs. In 2023, there were no budget transfers between titles.

The Governing Board recognises the setting up of IHI and notes in particular that:

- Results from IMI projects continue to highlight the ability of **public-private partnerships** to deliver results in challenging areas and create **long-lasting networks** that continue to collaborate long after the end of the funding period.
- In the summer of 2023, IHI announced that a new **Executive Director** had been appointed with a start date in January 2024.
- 2023 was a pivotal year where IHI went from an ambition to reality. With the implementation of IHI, **three programmes** are running in parallel, with different sets of rules, as an important number of projects launched under IMI / IMI2 are still ongoing.
- In 2023, the **total budget for IHI** was **EUR 223,231,575** in commitment appropriations and **EUR 225,848,975** in payment appropriations. The budget execution of the commitment appropriations and the payment appropriations reached **92.65%** and **90.29%** respectively.
- As the first IHI projects only started in 2023, they have yet to hit any significant milestones. Their first reporting period is in 2024 and therefore minimal progress at the moment to report against the IHI specific **key performance indicators** (KPIs).
- The **16 IHI projects** launched cover all objectives outlined in the SRIA and address diverse **unmet public health needs**. They also contribute to the EU's green deal and digital health political priorities.
- IHI is very **unique** and there is no other programme worldwide driving **interdisciplinary research** and bringing together diverse experts, including medical researchers, healthcare practitioners, patients, and health industry representatives.
- As the IHI portfolio continues to grow, ensuring the long-term **uptake of project outcomes** while deepening connections with important actors such as regulatory, **regional health actors** and health technology assessment bodies will be key to its success.

- The **States Representatives Group** (SRG) and **Science and Innovation Panel** (SIP) are important advisory bodies and provide valuable input on IHI activities and future direction.
- The first **IHI staff engagement survey** was launched and showed an overall satisfaction and commitment to the work. However, some actions are needed to further improve IHI staff work-life balance and balance the workload.
- Strong **gender balance** is observed in IHI governance bodies.
- The full **list of GB decisions** adopted in 2023 can be found on the IHI website as well as the GB platform. In the spirit of **transparency**, other documents are made public on the IHI website such as the agendas of the Science and Innovation Panel and States Representatives Group meetings, annual IHI activity reports and work programmes, and budgetary and financial management reports.

Assessment

The declaration of the Executive Director and the Consolidated AAR 2023 give 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 JU in the year 2023.

The Governing Board notes that the management of the JU has reasonable **assurance** that, overall, **suitable controls** are in place and working as intended, **risks** are being appropriately assessed, monitored and mitigated, and necessary process improvements and reinforcements recommended by the auditors are being implemented.

The Governing Board notes the implementation of the IHI programme in alignment with **Strategic Research Agenda** priorities, bringing together the different stakeholders involved in health research, fostering cross-project collaboration while focusing on **high unmet medical and societal needs**.

Therefore, the IHI JU Governing Board hereby adopts this analysis and assessment of the Consolidated AAR 2023 of the authorising officer. This analysis and assessment will be included in the Consolidated AAR 2023.

Done at Brussels, on _____

For the Innovative Health Initiative Joint Undertaking,

_____

Irene Norstedt
Chairperson of the Governing Board

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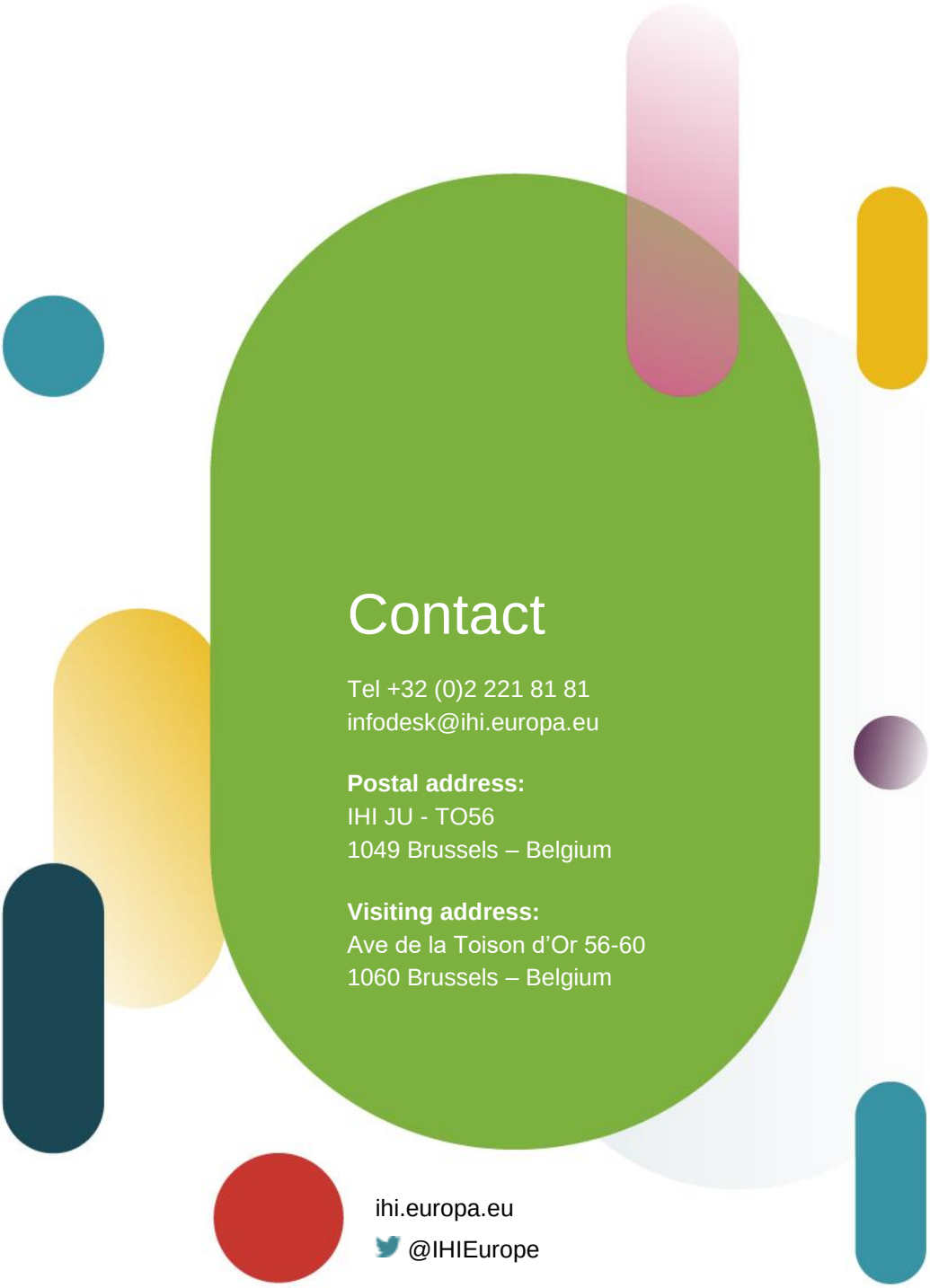

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