

# 2019 Annual Work Plan and Budget

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In accordance with Article 16 of the Statutes of the IMI2 JU annexed to Council Regulation (EU) No 557/2014 of 6 May 2014 and with Article 31 of the Financial Rules of the IMI2 JU.  
The Annual Work Plan will be made publicly available after its adoption by the Governing Board.

**Annex to the Decision of the IMI2 JU Governing Board  
No. IMI2-GB-DEC-2018-32 adopted on 12.12.2018  
IMI reference: IMI2/INT/2018-00001**

**Corrigendum of 18 January 2019, page 64**

## NOTICE

Please note that until the UK leaves the EU, EU law continues to apply to and within the UK, when it comes to rights and obligations; this includes the eligibility of UK legal entities to fully participate and receive funding in Horizon 2020 actions such as those called for in this work plan. Please be aware however that the eligibility criteria must be complied with for the entire duration of the grant. If the UK withdraws from the EU during the grant period without concluding an agreement with the EU ensuring in particular that British applicants continue to be eligible, they will no longer be eligible to receive EU/JU funding and their participation may be terminated on the basis of Article 50 of the grant agreement.

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## Chronology and list of reviews

Version	Date of the adoption by the Governing Board	Items
Version 1.0	12.12.2018	Annual Work Plan and Budget for 2019
Version 1.1	18.01.2019	Corrigendum of Annex I – page 64 4th bullet point under Scope of topic 1 has been updated to clarify the objective

# 1 Introduction

In 2019, IMI2 JU will continue to focus on its core activity of launching Calls for proposals for projects that address key challenges highlighted in the IMI Strategic Research Agenda in areas such as diabetes/metabolic disorders, neurodegeneration, immunology, infection control (including vaccines), translational safety, digital health, and oncology.

In addition, the IMI2 JU Programme Office will continue implementing the recommendations of the experts' panel on the interim evaluation of IMI2 JU. This will include continuing with the strategy to attract more small and medium-sized enterprises (SMEs) to IMI2 JU, as well as putting greater efforts into identifying our projects' most important outputs and communicating on them to a wider audience.

To ensure that IMI2 JU projects include a broad range of stakeholders, IMI2 JU will continue to reach out to priority groups like SMEs, patients, and regulators. IMI2 JU will also engage proactively with potential Associated Partners from the philanthropic and public sectors, as well as companies from other industry sectors (e.g. ICT, imaging, medical technology, animal health, nutrition, etc.).

Throughout the year, the IMI2 JU Programme Office will strive to deliver work of the highest quality, following strict ethical standards, adhering to the principle of sound financial management and within the context of a robust internal control framework.

In the long term, these activities will help IMI2 JU to achieve its goals of accelerating and improving medicines development and ensuring that new discoveries are rapidly transformed into benefits for both the wider medical research community, and healthcare systems and patients.

Pierre Meulien

Executive Director

## 2 Annual Work Plan Year 2019

### 2.1 Executive Summary

The main goals of IMI2 JU in 2019 are set out as follows.

- Launch three new Calls for proposals based on scientific priorities set out in section 2.2.2. Additional call topics might be considered according to very urgent public-health needs.
- Successfully manage and connect a growing portfolio of projects.
- Expand the basis of external collaborations and partnerships to best meet the challenges of speeding up the development of, and patient access to, innovative medicines and optimise the innovation framework.
- Implement an ambitious communication strategy to demonstrate, in a spirit of openness and transparency, the added value of the partnership to EU citizens. Our focus on the impacts of our projects and the results of the socio-economic impact study on completed IMI1 projects will contribute to meeting this objective.
- Improve and upgrade various aspects of our operating systems, including efficient management of IMI2 project cycle using common Horizon 2020 IT tools.
- Carry out and implement audits and controls over beneficiaries that receive IMI2 JU funding and companies' in-kind contributions.

### 2.2 Operations

#### 2.2.1 Objectives & indicators - risks & mitigations

The key objectives for IMI2 JU operations in 2019 are identified by the Governing Board in the Annual Work Plan and by the Management at operational level.

Key operational objectives for 2019 are as follows:

- 1. execute Strategic Research Agenda priorities by initiating competitive Calls for proposals bringing together the different stakeholders involved in health research (including SMEs, regulators and patient organisations) and by fostering cross-project collaboration;**
- 2. ensure sound budget implementation through the effective and efficient management of Calls for proposals, grant award process, close monitoring of projects and error rate;**
- 3. demonstrate the EU added value of IMI2 JU through assertive communication to target audiences with emphasis on the openness, transparency, relevance, and coherence of IMI2 JU activities;**
- 4. involve industry from related sectors other than the pharmaceutical industry (diagnostics, medical technologies industry, imaging, digital industry, food and nutrition, etc.) in IMI2 JU projects through proactive outreach strategies;**
- 5. ensure IMI2 JU internationalisation and build productive linkages to major international efforts to address Global Challenges (AMR, Alzheimer and other dementias, autism, cancer, diabetes, emerging infectious diseases, etc.);**
- 6. improve and broaden access to IMI project outcomes in collaboration with IMI2 projects by embedding dissemination in all stages of the project lifecycle.**

## IMI2 KPIs

Reporting on measuring and outcomes on the following ten Key Performance Indicators will be provided yearly as part of the IMI2 JU Annual Activity Reports for year 2019 and beyond.

KPI	Definition	Comment	Relates to	Baseline	Target
1	Number of relevant priority areas in the WHO 'Priority Medicines for Europe and the World 2013 Update' reflected in the IMI2 Strategic Research Agenda (SRA) and addressed by IMI2 projects.	Based on the SRA and including the WHO priority medicines therapeutic areas: - expressed as a number of areas reflected in the IMI2 portfolio; - complemented by the number and budget of grant agreements that delivered them.	IMI2 Regulation objective b1:  b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'	0	12
2	The number of project-developed assets which complete 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 objective b1, b2, b4, b5 and b6:  b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'  b2: 'reduce the time to reach clinical proof of concept in medicine development...'  b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators'  b5: 'reduce the failure rate of vaccine candidates in phase III of clinical trials through new biomarkers for initial efficacy and safety checks'  b6: 'improve the current drug development process by providing the support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products'	0	50



KPI	Definition	Comment	Relates to	Baseline	Target
3	<p>New or improved guidelines, methodologies, tools, technologies or solutions accepted by regulatory authorities for use in the context of R&amp;D, specifically for:</p> <ul style="list-style-type: none"> <li>- new tools for preclinical drug development;</li> <li>- biomarkers and tools developed to predict clinical outcomes;</li> <li>- improved protocols to design and process of clinical trials;</li> <li>- new biomarkers developed for the efficacy and safety of vaccine candidates.</li> </ul>	<ul style="list-style-type: none"> <li>- Measured by the number of the formal qualification procedures completed (letters of support, qualification opinions received).</li> <li>- Complemented by number of qualification procedures launched.</li> <li>- Expressed as net figure.</li> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> </ul>	<p>IMI2 Regulation objective b1, b2, b4, b5 and b6:</p> <p>b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'</p> <p>b2: 'reduce the time to reach clinical proof of concept in medicine development...'</p> <p>b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators'</p> <p>b5: 'reduce the failure rate of vaccine candidates in phase III of clinical trials through new biomarkers for initial efficacy and safety checks'</p> <p>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'</p>	0	10 (for completed procedures)

KPI	Definition	Comment	Relates to	Baseline	Target
4	New taxonomies of diseases and new stratifications (such as the definition of patient subpopulations, development, validation and use of new diagnostics) developed.	<ul style="list-style-type: none"> <li>- Expressed as net figure.</li> <li>- As published and/or implemented by industrial partners and evidenced in annual reporting.</li> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> </ul>	<p>IMI2 Regulation objective b3 and b4:</p> <p>b3: 'develop new therapies for diseases for which there is a high unmet need...'</p> <p>b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators'</p>	0	30
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.	<p>IMI2 Regulation objective a:</p> <p>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...';</p> <p>and IMI2 Regulation recital 8:</p> <p>'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.'</p>	0	EUR 300 Million

KPI	Definition	Comment	Relates to	Baseline	Target
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, <i>in silico</i> tools, training materials, clinical trial networks, guidance etc.	<ul style="list-style-type: none"> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> <li>- Accessibility to be evidenced by online availability (with or without fee), and documented by project reports.</li> </ul>	<p>IMI2 Regulation objective a, b2 and b6:</p> <p>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...'</p> <p>b2: 'reduce the time to reach clinical proof of concept in medicine development'</p> <p>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'</p>	0	50%
7	Co-authorships and cross-sector publications between European researchers on IMI2 projects (sectors include academia, small and mid-sized companies, pharma, regulators, patient organisations, etc.).	<ul style="list-style-type: none"> <li>- Expressed as net figure</li> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> </ul>	<p>IMI2 Regulation objective a:</p> <p>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...'</p>	0	1500

KPI	Definition	Comment	Relates to	Baseline	Target
8	New tools and processes generated by IMI2 projects that have been implemented by the industry participants of IMI projects.	<ul style="list-style-type: none"> <li>- New tools and processes: e.g. animal models, standards, biomarkers, SOPs, use of screening platforms and clinical trial networks.</li> <li>- Expressed as net figure.</li> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> <li>- Assessment based on yearly reporting by industrial partners until the project close-out meetings.</li> </ul>	<p>IMI2 Regulation objective a, b2 and b6:</p> <p>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...'</p> <p>b2: 'reduce the time to reach clinical proof of concept in medicine development'</p> <p>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'</p>	0	50
9	Share of projects involving patient organisations and healthcare professionals' associations (as consortium partners, members of advisory boards, members of stakeholder groups etc.).	<ul style="list-style-type: none"> <li>- Complemented by the number and budget of grant agreements that delivered them.</li> </ul>	<p>IMI2 Regulation objective a, and b1:</p> <p>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...'</p> <p>b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'</p>	Share of IMI1 projects involving patient organisations: (participants /advisory boards etc. 40%)	80%

10	Support to SMEs: share of SMEs participating as formal IMI project beneficiaries.	- To be complemented by the number of SMEs benefitting from IMI project support in other ways.	H2020 priority; IMI2 Regulation recital 9  '(...) should seek to foster the capacity of smaller actors such as research organisations, universities and SMEs for participating in open innovation models and to promote the involvement of SMEs in its activities, in line with its objectives'	Share of SMEs participating as formal IMI1 project beneficiaries: 15.96%	20%
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To ensure the monitoring of the above-mentioned 10 Key Performance Indicators, IMI2 JU has established a performance evaluation plan which aims at identifying appropriate sources of information, a suitable framework as well as consistent processes and tools.

## Risks & mitigations

Risks are a strategic element of planning activities as their identification enables management to customise the objectives and prioritise actions.

The annual risk assessment exercise towards the Annual Work Plan (AWP) 2019 objectives has identified 8 corporate risks that might potentially challenge their achievement. These risks are documented in the internal Risk Register of the IMI2 JU, which incorporates a description of the respective action plans, detailing the action owners and individual deadlines. In practice, the outcome of the risks assessment indicates that:

1. Some risk factors persist, as they are typically associated with IMI2 JU nature of public-private partnership and its mission – which aim at supporting volatile activities such as the development and implementation of pre-competitive research and innovation in the pharmaceutical sector. For these risks, the mitigating actions envisaged in the past will continue to be applied in 2019.
2. On the other hand, the 2019 annual objectives could be challenged by some specific risks, whose factors will be continuously monitored and mitigated by the Programme Office where needed. These relate to:
  - the impact of the external environment (e.g. Brexit) on programme implementation and operational activities<sup>1</sup>;
  - the implementation of IMI2 JU communications strategy to demonstrate, in a spirit of openness and transparency, the benefit of the partnership to EU citizens; this should contribute to mitigating possible negative perception or misconceptions about IMI2 JU objectives;
  - avoiding delays in defining annual scientific priorities and call topics through a fixed plan of call development stages, as well as the enhancement of the quality of key operations (i.e. Horizon 2020 implementation, project extension, etc. ), financial management and staff allocation; this should avoid any mismatch between the ambition of the programme and limited resources available affecting the implementation of the programme;
  - ensuring proactive outreach strategies and exploring alternative approaches to ensure and boost industry participation and contribution;
  - carrying on with the new SME strategy, and exploring and drafting potential call topics adapted to SME needs and activities to address the low rate of SME participation.

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<sup>1</sup> The plans/activities of the year will take into account and reflect the needs which are related to Brexit. Notwithstanding the need to cater for individual specificities to the Joint Undertaking, these actions are being coordinated by the Secretariat-General of the European Commission with a view to ensuring coherence in the design and timing of these measures.

## 2.2.2 Scientific priorities for 2019

The IMI2 JU activities for 2019 are fully in line with the objectives as set out in Article 2 of the IMI2 JU Regulation. In particular, they aim at the development and implementation of pre-competitive research and innovation activities of strategic importance to the EU's competitiveness and industrial leadership, and address specific Horizon 2020 societal challenges, in particular improving European citizens' health and well-being.

These activities will be developed within the general framework of the Scientific Research Agenda (SRA) for IMI2 JU (see <http://www.imi.europa.eu/about-imi/strategic-research-agenda>). The SRA identifies a set of scientific priorities, where IMI2 JU attempts to pilot new ideas in a real life, safe harbour environment. The IMI2 JU model maximises collaboration and synergies among all stakeholders; drives innovation in business models to support the transition from blockbusters to personalised medicines by testing new approaches across multiple companies and projects simultaneously; and it pilots new types of collaboration between companies with different innovation cycles to optimise the success in delivering IMI2 JU objectives. The SRA furthermore identifies data and knowledge management as key enabling technologies, as well as education and training, and excellence in clinical trial implementation as key implementation strategies.

In order to achieve its objectives, IMI2 JU continues to seek the involvement of a broader range of partners from different sectors (e.g. biomedical imaging, medical information technology, diagnostics and/or animal health industries among others). The actions resulting from the 2019 priorities will generate results that will have a high impact and facilitate the maximum number of stakeholders to join forces. The outcome and impact of these actions should bring great benefits to patients and society-at-large. There will also be engagement with regulatory agencies and other health bodies fostering the approval of research outcomes. Involving the wider community in this way should help to advance the development of new approaches and technologies for the prevention, diagnosis and treatment of diseases with an expected high impact on public health.

SMEs have an important role in strengthening the competitiveness and industrial leadership in the EU. In addition, SME involvement might offer a complementary perspective to industry and the academia, and help deliver the long-term impact of IMI2 JU. Thus, in 2019, IMI2 JU will continue its efforts to increase the engagement of SMEs in all its activities and to encourage their involvement in applicant consortia.

For 2019, IMI2 JU has identified ten scientific priorities, broken down into several topics, taking into account the advice that the Strategic Governing Groups (SGGs) provided to the IMI2 JU Governing Board. As described in the following pages, each priority area will be implemented via the launch of one or more topics, which will generate multi-stakeholder actions, potentially including (or even driven by) Associated Partners. Further details regarding the expected multi-stakeholder actions are elaborated under the individual topics. Topics for 2019 have been prioritised based on criteria that include the highest impact on reducing attrition in drug development, speeding up patient access, improving health outcomes and enhancing the biomedical research ecosystem.

Additional topics for 2019 might also be considered at a later stage in the case of very urgent public health needs, such as rapid response to emerging diseases. The Annual Work Plan 2019 would then be updated accordingly.

To implement the 2019 priorities, IMI2 JU will initiate three competitive Calls for proposals, each covering several topics (see table at the end of this section), with indicative predefined launch dates foreseen for Q1 and Q2 in 2019.<sup>2</sup>

Topics launched based on this Annual Work Plan 2019 will seek synergies with other ongoing initiatives especially those funded under Horizon 2020 and at the national level, and those identified by the European Strategy Forum on Research Infrastructures (ESFRI), to ensure the consistency of approaches, to leverage other funding initiatives and to avoid duplication of effort and funding.

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<sup>2</sup> Please see Article 1 (f) and (g) of the Statutes, annexed to the IMI2 JU Council Regulation

## A. Diabetes/Metabolic disorders

Activities in 2019 will address the following topic.

- 1. Optimising future obesity treatment.** This topic focuses on multifaceted profiling of patients with obesity in order to define clinically meaningful and relevant subgroups as a premise for optimising future prevention and treatment of obesity and its complications. The aim is to pool pre-existing observational and/or clinical data to establish a federated database with enough phenotypic granularity for a data-driven stratification of obesity into subgroups based on a set of operational parameters including subject characteristics, biomarkers and questionnaires. In addition, activities will address specifically type 1 and type 2 diabetes (T1D and T2D) as examples of co-morbid conditions in which obesity influences both clinical phenotype and treatment.

### Expected impact:

- a common understanding and vocabulary among stakeholders to facilitate scientific, medical and political acknowledgement of obesity as a disease and the importance of prevention, personalising health and lifestyle interventions and weight management;
- potential high impact on future guidelines to treat diabetic and obese individuals;
- potential high impact on public health regarding population morbidity, co-morbidity and mortality, and public healthcare costs.

### Type of actions:

Research and innovation actions



## B. Neurodegeneration and other neuroscience priorities

Activities in 2019 will address the following topics.

### Pain

- 2. Digital transformation of clinical trial endpoints in pain.** As part of the programme on digital endpoints, started in 2018, with a specific focus on different diseases, the objective is to develop objective, continuous or high-frequency digital measures of clinical efficacy and disability experienced by patients with pain. Digital endpoints relevant to clinical pain (e.g. pain severity, daily activity, quality of life, sleep) will be validated in selected pain conditions with the goal of obtaining acceptance of digital endpoints by regulators and HTA bodies as primary or key secondary endpoints for use in pivotal pain trials.
- 3. Placebo effect in pain.** The placebo response in clinical trials in pain can be substantial, and high placebo effect is associated with reduced drug-placebo difference, which, in turn, interferes with signal detection for new therapies. This topic aims to develop and validate effective methods for reduction of placebo response in randomised controlled trials in pain. It will support the identification of factors influencing the magnitude of the placebo response by analysing patient clinical data and site characteristics.

### Psychiatry

- 4. Psychiatric ratings using intermediate stratified markers -2 (PRISM-2).** This topic supports activities to further progress on delivery of a quantitative biological approach to the stratification of neuropsychiatric disorders, specifically Alzheimer's dementia and schizophrenia while also considering a wider application. Activities will focus on understanding neural substrates of the symptoms of social withdrawal and both the identification of biomarkers and clinical rating tools that can be proposed for regulatory validation.

#### Expected impact:

- novel drug pathways for neurodegenerative and psychiatric disease interception and for pain, including validated biomarkers and clinical trial endpoints ;
- accelerate patient access to innovative medical treatments for neurological, psychiatric disorders and for pain;
- reduce the patient burden due to mental health disorders;
- enable more efficient and cost-effective clinical trials and real-world studies.

#### Type of actions:

Research and innovation actions

## C. Immunology

Activities in 2019 will address the following topic.

- 5. Psoriatic arthritis:** Early diagnosis, prediction of radiographic outcomes and the development of rational, personalised treatment strategies to improve outcomes in psoriatic arthritis (PsA). This topic will address the major unmet need to identify early predictors of progression to PsA in patients with skin psoriasis, thereby enabling earlier intervention and possibly even preventing development of PsA. The results will provide stratification of PsA patients in clinical trials and allow a potential reduction of the clinical and economic burden of disease for patients by postponing the start of the PsA symptoms.

### Expected impact:

- improved methods for recognition and diagnosis of autoimmune and inflammatory disorders and a range of treatment options;
- earlier availability of new, more cost-effective therapies for patients most likely to benefit;
- expanding our current knowledge will give rise to more precise, targeted treatments yielding long-lived reductions in disease and improved patient quality of life, and fulfilling unmet medical needs in patient care.

### Type of actions:

Research and innovation actions

## D. Infection control including vaccines

Activities in 2019 will address the following topic.

- 6. New topic(s) under the AMR accelerator platform.** The objective is to expand the AMR Accelerator Programme launched in 2018, in particular under the Pillars A and C to expand activities and accelerate scientific discoveries in antimicrobial resistance (AMR) and to progress a pipeline of potential therapeutic, biologic and preventive medicines & procedures, e.g. diagnostics, to manage patients and/or populations with resistant bacterial infections in Europe and across the globe.

### Expected impact:

- a pipeline of promising new agents for tackling antibiotic-resistant bacterial infections;
- a significant contribution to the development of a vibrant AMR research environment in the EU and to the strengthening of its competitiveness and industrial leadership;
- major impact on the improvement of public health.

### Type of actions:

Research and innovation actions

## E. Translational safety

Activities in 2019 will address the following topics.

- 7. Dosing in specific populations.** The term specific population has been used to describe patient attributes that may require alterations in the course of therapy when compared to typical patients; examples include renal and hepatic-impaired patients, children, the elderly and pregnant women. These populations are often excluded or under-represented in pivotal trials. 50% to 80% of new molecular entities do not have explicit dosing recommendations for severe renal and hepatic impairment, respectively. Therefore, the objective of this topic is to establish a framework for developing models, criteria for establishing adequacy of predictions, and a drug-development-regulatory framework for incorporation of derived dosing recommendations into product labels.
- 8. Digital pathology** Pathology is the cornerstone of the workup of many diseases such as cancer, autoimmune diseases, transplant rejection, but still relies on the interpretation of a tissue section by a qualified pathologist. Although the pathologist's report is currently the only accessible pathology data, slide scanners can capture the data of the entire tissue sections digitally. The systematic digitization of slides opens the field of digital pathology. It facilitates the consultations with expert pathologists and the search or review of large collections of slides. As digital modality, it allows to quantify features from tissues. The recent development of deep learning has propelled the field of digital pathology even further, opening the way to computer-assisted diagnosis. This has the potential to revolutionize medicine by allowing to discover new clinic-pathological entities and better identify treatments for specific groups of patients.  
In drug development, digital pathology would apply to unbiased evaluation of preclinical safety or clinical efficacy. Regulators could conduct faster review of pathology data and could have a transversal view across projects/sponsors.  
The proposal would comprise: (1) centralised repository for digitalized slides, including secured archival of pathology data (2) the initial population of such a repository with preclinical safety studies, clinical trials, and clinical collections, (3) a legal and regulatory framework to enable exchange of studies and cases series while preserving patient's privacy, and (4) tools for access, visualisation, quality control (QC) and data mining (open source).

The slides would be collected from preclinical safety studies and clinical trials (source: industrial and Academic partners) and could be associated with clinical findings and biomarkers. The partners would provide electronic versions (scans) of pathology slides used in upcoming preclinical safety studies, and clinical trials.

### Expected impact:

- better prediction and understanding of toxicities of drugs;
- reduce use of animals in toxicology studies;
- accelerate clinical development programmes and better identify treatments for specific groups of patients;
- reduced costs and enhanced commercial viability of drug development.

### Types of action:

Research and innovation actions

## F. Big data, digital health, clinical trials and regulatory research

Activities in 2019 will address the following topics.

- 9. ROADMAP 2: need and opportunity for public-private collaborative research to continue the RoadMap efforts:** This topic will leverage prior phase I work of the project 'Real-world outcomes across the Alzheimer's disease (AD) spectrum for better care: multi-modal data access platform', ROADMAP. The objective is to validate the outcomes of interest with a broader range of stakeholders including clinical experts and AD clinical centres, patient organisations, regulatory and national health authorities and payers across the EU. This should result in a standardised data set to be collected via a proof-of-concept study for real-world (RW) standardised prospective data collection in patients with AD.
- 10. Independent observatories of health outcomes for patients being the guardians of health data.** This topic will support activities to provide a legal and ethical framework for the management of patient reported outcomes (PROs), collect process, integrate and make health data available in an ethical manner, and contribute to standardising and integrating health data. The objective of this project is to work collaboratively with patient associations and empower individual patients to monitor their outcomes in a standardised manner. The data, when collected, will provide transparency of patient outcomes on specific diseases on a per country or regional basis. This will provide the evidence required for making informed decisions on resource allocation. At the same time, it will also create a unique value proposition for patients to collect their health data.
- 11. E-product information. Leveraging digital technology to drive the correct use and understanding of medicines: a user-centric approach to adherence and risk minimisation.** This topic addresses two critical challenges associated with the use of medicinal products in Europe: lack of adherence to the health-authority-approved product information, and poor understanding of this information in relation to treatment. Such challenges affect multiple stakeholders across Europe, and it is of utmost importance that these diverse perspectives are captured to ensure that any future solution is fit-for-purpose for citizens, healthcare providers, health authorities and industry alike. It embraces all medicinal products registered in European Member States. It is assumed that the paper version of the package leaflet (PL) will continue to exist according to current legislation. However, the delivery method for the product information will be examined (e.g. printing the PL at the pharmacy instead of always in the pack) as well as options for reconstruction of the health-authority-approved text in ways which are more personalised to an individual's needs. The overall objective is to optimise provision of information on medicines to users across the EU so that adherence to the product information is improved, and users' understanding of their medicine is increased. These two challenges are related and have profound implications for patient safety and well-being, as well as widespread effects within healthcare systems and industry across the EU.

Digital priorities are also addressed in the "Digital Transformation of Clinical Trial Endpoints in pain" topic in section B-Neurodegeneration above.

### Expected impact:

- improved transparency of data reuse and of its impact on research & development;
- faster translation of insights from real-world health data to biomedical research and development approaches;
- enable more efficient and cost-effective clinical trials and real-world studies;
- enhanced drug efficacy and effectiveness via a better understanding and adherence to medicines.

### Type of actions:

Research and innovation actions

## G. Oncology

Activities in 2019 will address the following topic.

**12. Patient-reported outcomes and quality of life endpoints.** There is an increased emphasis on patient-centred care, health-related quality of life (HRQL), and other patient-reported outcomes (PRO), that quantify how a patient feels and/or functions. These parameters may acquire an even more prominent role as important endpoints in cancer clinical trials. However, so far, no standardization in the use and analysis of HRQoL and PRO data in cancer clinical trials is given. Such a lack of standardisation can lead to variations in the analysis of data and could result in two identical trials being analysed in different ways, leading to different conclusions. In particular, in oncology such a lack of standardization can undermine the credibility of the HRQoL and PROs since this can lead to differences in interpretation of the findings depending on how the data were analysed. Thus, this topic aims to develop and recommend international standards for the analysis of HRQOL data from cancer clinical trials.

Expected impact:

- better assessment of the risks and benefits of cancer therapies and fostering of patient-centred cancer care.
- a large positive impact on treatment outcomes, to support the adequate reimbursement of innovations in this field.

The Oncology area is also addressed in the CAR-T topic in the “H. Facilitating the translation of advanced therapies to patients in Europe” section below.

Type of actions:

Research and Innovation Actions

## H. Facilitating the translation of advanced therapies to patients in Europe

Activities in 2019 will address the following topics.

- 13. Accelerating research and development of Advanced Therapies.** There are key research and regulatory issues in gene therapy development. The objective of this topic is to provide the research data, mechanism and a pathway with the view of improving the available research tools and developing recommendations for a unified regulatory approach accepted by global health authorities. Sustained therapeutic efficacy is key to the success of gene therapy. However, there are risks around the persistence of the effect and re-dosing the vector. Understanding these factors could allow us to (1) treat a broader population and (2) design protocols to overcome existing limitations as may be relevant to research and development and clinical trial activities, exploring use cases including ultra-rare diseases.
  
- 14. ATMP Patient Registries Outcomes Data and Evidence.** This topic aims to: (1) pilot the benefits of a holistic, pan-EU registry for a specific rare disease (e.g. Duchene muscular dystrophy; haemophilia) serving the needs of academia, scientific associations, industry, patient organisations and healthcare payers; (2) to directly address the current gap in patient centricity and patient perspectives in advanced therapies medicinal products (ATMPs), which are not recorded in any existing efforts. Once completed, the pilot could potentially serve as a model for other rare diseases and provide optimal access of innovative medicines to patients.
  
- 15. CAR-Ts.** CAR-T cell therapies (chimeric antigen receptor T-cell therapy) are complex medicinal products. Their translation from basic and pre-clinical research to clinical trials therefore poses many challenges that slow down clinical development. The objective of the topic is to develop pre-clinical models to better predict safety and efficacy. Definition of a regulatory frame for the translation of pre-clinical findings into the clinic and standardisation of monitoring methods will be also addressed.

### Expected impact:

- to enhance research and development of advanced therapies in the EU and the Horizon 2020 Associated Countries as a fully-fledged industrial activity to make the EU more competitive and make advanced therapy products available to all patients in need;
- a powerful public-private innovation platform for efficiently addressing all challenges in the pathway from science to healthcare systems and patients including those with rare diseases.

### Type of action:

Research and innovation actions

## I. Other enablers of research topics

Activities in 2019 will address the following topics.

- 16. Open access chemogenomics library and chemical probes for the druggable genome.** The objective is to generate potent, well-characterised functional modulators for a significant number of targets from the human druggable genome and, at the same time, lay the foundation for identifying an entire set of open-access tool compounds for the entire druggable human genome, which is currently estimated to consist of at least 3000 genes.
  
- 17. Intelligent prediction and identification of environmental risks posed by human medicinal products.** Building on *in silico*, *in vitro* and *in vivo* tools and models developed in the project 'Intelligent assessment of pharmaceuticals in the environment', this topic aims to upgrade them to include other targets and endpoints. The aim is to maximise their predictive capability through machine learning and artificial intelligence approaches, including validation of their capacity to identify environmental concerns much earlier than within the current models in order to inform greener medicines development.
  
- 18. Handling of biologic drug products.** The objective is to get insight into the impact of the handling of biologic drug products – after they are released by the manufacturer and up to their administration – on the stability of the drug. Routine handling or unintentional mishandling of therapeutic protein products may cause degradation that can potentially compromise the clinical safety and efficacy of the product. This topic supports activities that should allow for identification of the risk factors and addressing them in drug production and supply processes.

### Expected impact:

- a resource for the entire chemical biology community;
- access to the highest quality tool compounds as starting points for probe development or drug discovery.
- seeding a massive community target prioritisation and target deconvolution effort via the availability of an unprecedented high-quality broader compound library;
- innovative approaches to ensure the environmental safety of human medicinal products;
- increased safety and efficacy of biological drug products;
- reduction of costs via increased efficiency of drug discovery and drug production.

### Type of action:

Research and innovation actions



## J. Restricted Call to maximise the impact of IMI2 JU objectives and scientific priorities

The drug development process is a highly challenging field of research which can only be tackled using a sequential approach where the next step can only be decided on the basis of the results of the previous one.

At the same time, it is also paramount that each step seamlessly follows the next one to achieve full impact. Accordingly, certain IMI2 JU topics – launched under now closed IMI2 JU Calls for proposals – recognised the need for a stepwise approach already at the topic stage, by including the information for potential applicants, that the IMI2 JU could publish at a later stage a subsequent Call for proposals restricted to consortia selected under the initial topics.

The scope of the restricted Call will be to support further activities in only exceptional cases necessary to enable successful consortia to build upon the achievements of their initial action, move onto the next step of the challenge seamlessly, and maximise the impacts of the initial action results. Activities supported by this Call will fall beyond the scope of the initial actions and could not be implemented within the financial and temporal framework of the initial actions. The applicants will need to demonstrate the uniqueness of the initial consortium that justifies the need to restrict the Call to this original consortium (with some limited modifications to the list of partners, if any, according to the expertise needed for the new proposed activities) to carry out follow-up activities successfully. For instance: the original consortium represents a unique partnership as expertise, equipment or methodologies, or access to unique resources and intellectual properties (IP) rights are not available from another consortium; the implementation of follow up activities through an open competitive Call would jeopardise the timely and seamless building on the unique results from the original project, including IP and ethical considerations, as relevant. The applicants will also need to justify that follow-up activities are needed to further maximise the public-private partnership value of IMI2 JU as demonstrated by a substantial amount of in-kind and financial contributions brought by EFPIA constituent and affiliated entities and when relevant by IMI2 JU Associated Partners, and that will be complemented by the expected IMI2 JU contribution.

The restricted Call will be published as a single-stage Call in the second quarter of 2019. This Call will be:

- restricted to the original consortia of actions funded under topics published in the IMI2 JU Annual Work Plan of 2014 and of 2015, since only these actions are sufficiently advanced in their implementation to be considered for follow-up activities, and;
- limited to those topics which already pre-informed potential applicants about the possibility for a later restricted Call.

Applicant consortia will be competing for a maximum total EU contribution as indicated in the Calls for proposal table at the end of this section.

### Expected impact:

- accelerate the impact of action breakthroughs to the next stage of drug development;
- significant impact on patients as novel treatments and patient pathways emerge;
- significant impact on EU industrial leadership;
- significant benefit for society and EU added value;
- further maximisation of the IMI2 JU public-private partnership value proposition.

### Type of action:

Research and innovation actions

## Calls for Proposals

Call number and topics	Indicative Call launch timing	Indicative IMI2 JU funding (in EUR) <sup>3,4</sup>	Indicative in-kind contribution from EFPIA entities and Associated Partners (in EUR)
<p style="text-align: center;"><b><u>IMI2 Call 17</u></b></p> <p><i>Diabetes/Metabolic disorders</i></p> <ul style="list-style-type: none"> <li>▪ Optimising future obesity treatment</li> </ul> <p><i>Other enablers of research topics</i></p> <ul style="list-style-type: none"> <li>▪ Open access chemogenomics library and chemical probes for the druggable genome</li> <li>▪ Intelligent prediction and identification of environmental risks posed by human medicinal products</li> </ul>	22 January 2019	40,786,000	43,108,139
<b>IMI2 Call 17 process</b>			
<p>Two-stage call with predefined submission deadline.            Indicative Call deadline for <b>short proposals: 25 April 2019</b>            Indicative Call deadline for <b>full proposals: 7 November 2019</b>            Research and innovation actions (RIA)</p>			

Call number and indicative topics	Indicative Call launch timing	Indicative IMI2 JU funding (in EUR) <sup>5,6</sup>	Indicative in-kind contribution from EFPIA entities and Associated Partners (in EUR)
<p style="text-align: center;"><b><u>IMI2 Call 18</u></b></p> <p><i>Neurodegeneration and other neuroscience priorities</i></p> <ul style="list-style-type: none"> <li>▪ Digital transformation of clinical trial endpoints in pain</li> <li>▪ Placebo effect in pain</li> <li>▪ Psychiatric ratings using intermediate stratified markers -2 (PRISM-2)</li> </ul> <hr/> <p><i>Immunology</i></p> <ul style="list-style-type: none"> <li>▪ Psoriatic arthritis</li> </ul> <hr/> <p><i>Infection control including vaccines</i></p> <ul style="list-style-type: none"> <li>▪ New topic(s) under the AMR Accelerator platform</li> </ul> <hr/> <p><i>Translational safety</i></p> <ul style="list-style-type: none"> <li>▪ Dosing in specific populations</li> <li>▪ Digital pathology</li> </ul>	26 June 2019	201,426,585	199,104,446

<sup>3</sup> Based on estimate of total operational commitment appropriations available in 2019. This is without prejudice to commitment appropriations to be carried over from 2018 to 2019 (to be determined early 2019).

<sup>4</sup> The maximum possible rate of co-financing is 100 %.

<sup>5</sup> Based on estimate of total operational commitment appropriations available in 2019. This is without prejudice to commitment appropriations to be carried over from 2018 to 2019 (to be determined early 2019).

<sup>6</sup> The maximum possible rate of co-financing is 100 %.

Call number and indicative topics	Indicative Call launch timing	Indicative IMI2 JU funding (in EUR) <sup>5,6</sup>	Indicative in-kind contribution from EFPIA entities and Associated Partners (in EUR)
<p><i>Big data, digital health, clinical trials and regulatory research</i></p> <ul style="list-style-type: none"> <li>▪ ROADMAP 2: need and opportunity for public-private collaborative research to continue the RoadMap efforts</li> <li>▪ Independent observatories of health outcomes for patients being the guardians of health data</li> <li>▪ E-product information. Leveraging digital technology to drive the correct use and understanding of medicines: a user-centric approach to adherence and risk minimisation</li> </ul> <hr/> <p><i>Oncology</i></p> <ul style="list-style-type: none"> <li>▪ Patient-reported outcomes and quality of life endpoints</li> </ul> <hr/> <p><i>Facilitating the translation of advanced therapies to patients in Europe</i></p> <ul style="list-style-type: none"> <li>▪ Accelerating research and development of advanced therapies</li> <li>▪ ATMP Patient Registries Outcomes Data and Evidence.</li> <li>▪ CAR-Ts</li> </ul> <hr/> <p><i>Other enablers of research topics</i></p> <ul style="list-style-type: none"> <li>▪ Handling of biologic drug products</li> </ul>			

IMI2 Call 18 process
<p>Two-stage call with predefined submission deadline.  Indicative Call deadline for <b>short proposals: 26 September 2019</b>  Indicative Call deadline for <b>full proposals: 26 March 2020</b>  Research and innovation actions (RIA) &amp; coordination and support actions (CSA)</p>

Call number and indicative topics	Indicative Call launch timing	Indicative IMI2 JU funding (in EUR) <sup>7, 8</sup>	Indicative in-kind contribution from EFPIA entities and Associated Partners (in EUR)
<b><u>IMI2 Call 19</u></b> <i>Restricted Call</i> Restricted Call to maximise impact of IMI2 JU objectives and scientific priorities	26 June 2019	20,000,000	20,000,000
<b>IMI2 Call 19 process</b>			
One-stage call with predefined submission deadline. Indicative Call deadline for <b>full proposals: 26 September 2019</b> Research and innovation actions (RIA) Restricted Call			
<b>Overall total IMI2 Calls</b>		<b>262,212,585</b>	<b>262,212,585</b>

<sup>7</sup> Based on estimate of total operational commitment appropriations available in 2019. This is without prejudice to commitment appropriations to be carried over from 2018 to 2019 (to be determined early 2019).

<sup>8</sup> The maximum possible rate of co-financing is 100 %.

## Budget

The budget for the financial year 2019 is based on the currently available information.

A table overview of the operational budget for 2019 is set out below.

Chapter	Heading Title 3	Financial year 2019		Comments
		Commitment Appropriation (CA)	Payment Appropriation (PA)	
30	Implementing the research agenda of IMI2 JU	262,212,585	186,910,765	Grant agreements - Payments
30	Implementing the research agenda of IMI JU - carry over from 2018	114,341,000		The amount carried over from 2018
	<b>Total operational costs Title 3</b>	<b>376,553,585</b>	<b>186,910,765</b>	

The difference between the total budget available for Title 3 and the budget available for fresh Calls in 2019 is EUR 114 341 000. This amount represents the unused commitment appropriations carried over to the 2019 budget, to conclude Grant Agreements for IMI2 - Call 13.

A table overview of the 2019 Budget is set out in Chapter 3 to this Annual Work Plan.

### **2.2.3 Call management (planning, evaluation, selection...)**

Key activities in 2019 will comprise the launch of three competitive Calls for proposals implementing the 2019 scientific priorities with indicative launch dates on 22 January 2019 for the first call of the year and 26 June 2019 for the other two calls.

In the single-stage submission evaluation procedure, the submission deadline will be approximately three months from the publication of the Calls for proposals.

In the two-stage submission evaluation procedure, the submission deadline will be:

- for stage 1: approximately three months from the publication of the Calls for proposals;
- for stage 2: approximately eight months from the publication of the Calls for proposals.

In addition, the evaluation of short proposals and full proposals submitted in response to Calls launched under the AWP 2019 will be held according to the predefined timelines established in the relevant Call for proposals.

Timelines for the completion of the evaluation process and of preparation will be kept as lean as possible with the aim of completing the signature of the Grant Agreements within applicable time to grant (TTG), in compliance with the Horizon 2020 framework, i.e. a maximum of eight months from the final date of submission of the full proposals.<sup>9</sup>

For Call management, IMI2 JU will utilise the Horizon 2020 IT infrastructure available under Funding & tender opportunities - Single Electronic Data Interchange Area (SEDIA).

To maximise the efficiency of the calls management, the IMI2 JU will continuously explore and implement simplification and improved processes while maintaining the highest standards of the evaluation process.

### **2.2.4 Activities to support and monitor ongoing projects**

In 2019, IMI will have 70 ongoing projects at different stages of their life cycle in 2019. In addition, 32 new projects that will start during the year when the IMI2 Calls launched in 2017 (IMI2 - Call 13), and 2018 (IMI2 - Calls 14, 15 and 16) complete the evaluation cycle and their Grant Agreements are signed. . Most projects will submit to IMI2 JU a periodic report for the previous year summarising their progress and costs incurred. These reports form the basis for the Programme Office's ex-ante controls.

In addition to periodic reporting and associated feedback, IMI2 JU will continue to provide support and advice to the consortia, including on amendments to Grant Agreements.

Given the current planning and project durations, it is expected that IMI2 JU will organise 20 reviews for IMI2 projects.

The following table presents the number of ongoing projects per Call as well as a forecast of the reporting expected for 2019.

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<sup>9</sup> Article 20 of the Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in 'Horizon 2020'

The following table presents a forecast of the reporting expected for 2019.

IMI Calls	ongoing in 2019	Project periodic report due in 2019						Of which		
		1st RP <sup>10</sup> in 2019	2nd RP in 2019	3rd RP in 2019	4th RP in 2019	5th to 7th RP in 2019	Total reports	Reports due after 31/10/2018	finishing in 2019	Final report due 2019
IMI1 C1	0	0	0	0	0	0	0	0	0	0
IMI1 C2	0	0	0	0	0	0	0	0	0	0
IMI1 C3	0	0	0	0	0	0	0	0	0	0
IMI1 C4	0	0	0	0	0	0	0	0	0	0
IMI1 C5	0	0	0	0	0	0	0	0	0	0
IMI1 C6	0	0	0	0	0	1	1	0	0	0
IMI1 C7	1	0	0	0	0	1	1	0	0	1
IMI1 C8	2	0	0	0	0	3	3	0	0	1
IMI1 C9	2	0	0	0	1	1	2	0	0	1
IMI1 C10	1	0	0	0	1	1	2	0	0	0
IMI1 C11	9	0	0	0	1	7	8	0	0	1
<b>Total IMI1</b>	<b>15</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>3</b>	<b>14</b>	<b>17</b>	<b>0</b>	<b>0</b>	<b>4</b>
IMI2 C1	1	0	0	0	1	0	1	0	0	0
IMI2 C2	4	0	0	0	4	0	4	3	4	1
IMI2 C3	5	0	0	5	0	0	5	1	1	1
IMI2 C4	0	0	0	0	0	0	0	0	0	0
IMI2 C5	6	0	0	6	0	0	6	0	2	2
IMI2 C6	3	0	3	0	0	0	3	3	0	0
IMI2 C7	7	0	7	0	0	0	7	2	1	1
IMI2 C8	4	1	1	0	0	0	2	0	0	0
IMI2 C9	6	1	5	0	0	0	6	1	0	0
IMI2 C10	8	8	0	0	0	0	8	0	0	0
IMI2 C11	3	2	0	0	0	0	2	0	0	0
IMI2 C12	7	0	0	0	0	0	0	0	0	0
IMI2 C13	13	0	0	0	0	0	0	0	0	0
IMI2 C14*	4	0	0	0	0	0	0	0	0	0
IMI2 C15*	8	0	0	0	0	0	0	0	0	0
IMI2 C16*	7	0	0	0	0	0	0	0	0	0
<b>Total IMI2</b>	<b>86</b>	<b>12</b>	<b>16</b>	<b>11</b>	<b>5</b>	<b>0</b>	<b>44</b>	<b>10</b>	<b>8</b>	<b>5</b>
<b>Total IMI</b>	<b>101</b>	<b>12</b>	<b>16</b>	<b>11</b>	<b>8</b>	<b>14</b>	<b>61</b>	<b>10</b>	<b>8</b>	<b>9</b>

\* For IMI2 – Calls 13 to 16, the number of projects is an estimate based on the number of topics included in the ongoing IMI2 Calls.

<sup>10</sup> Reporting Period

A key task will be to continue maximising efficiency, as well as facilitating, optimising, and monitoring the implementation of all these projects and seeking feedback for continuous improvement to IMI2 JU operations. To this end, further workshops to provide guidance on the management of financial and administrative aspects of the projects will be held for IMI2 JU beneficiaries. In addition, the IMI2 JU Programme Office will work with consortia to help them communicate on project progress and disseminate achievements.

## **2.2.5 Monitoring and analysis of projects' results**

67 project periodic reports will be submitted in 2019 (for ongoing projects and those finalised in 2018 see column 8 in the table above – 'Project periodic report due in 2019 – Total reports'). These reports will be used to track progress against their stated objectives and deliverables as laid out in the relevant description of the action.

This reporting will also allow for an assessment of project achievements and the impact of results. In addition to the usual ex-ante controls, a combination of internal management information systems, external databases, independent evaluations and, if necessary, commissioned studies and surveys will be used to measure the progress and identify significant achievements of IMI projects.

In 2019, the analysis of the IMI2 JU project scientific outputs in terms of publications and collaboration among IMI researchers will be continued. Where feasible, monitoring and analysis approaches will be refined in line with observations from the European Court of Auditors (ECA) to ensure the highest possible standards.

## **2.2.6 Stakeholders' engagement and external collaborations**

In 2019, IMI2 JU will continue to develop its relationships and engagement with key stakeholders such as patients, SMEs, regulators, payers and healthcare professions to ensure that its outputs are aligned with and address the needs of the society.

### **Patient engagement**

Building on the experience of patient engagement so far, the IMI2 JU Programme Office will continue to work on developing an open and transparent system of patient engagement at all levels. The need for a consolidated framework for interaction with patients has been highlighted as one of the key elements reflecting IMI2 JU's patient engagement strategy. In this respect, IMI2 JU will create an IMI Patient Community, a pool of patient experts that will assist the JU to better include patients' perspectives in its activities and become more patient-centric.

Therefore, IMI2 JU foresees the launch of a Call for Expressions of Interest via its website in Q1 2019 to identify patient experts (approx. 50) who will be involved in IMI2 JU's activities. The members of the IMI Patient Community will provide resources to the Governing Board, the SGGs and to consortia, depending on the need and topics discussed.

To facilitate the full engagement of the Patient Community, the Programme Office will hold at least two meetings aiming at providing the IMI Patient Community members with relevant information and guidance about IMI2 JU's cycle of activities.

Additionally, the Programme Office will continue to enhance, support and facilitate patient involvement in IMI2 JU projects and develop guidance for patients taking part in IMI2 JU activities. The JU will also lead efforts to ensure that patient engagement is embedded in procedures surrounding the preparation of Call topics, proposal evaluation as well as project reviews.

### **SMEs**

Given their importance in driving employment and innovation in the EU and the Horizon 2020 Associated Countries, the IMI2 JU will remain engaged with SMEs and encourage their participation in IMI2 JU projects. In 2019, the IMI2 JU will continue to highlight SME opportunities in all topic texts and also embed SME participation at the earliest stages of topic development, for example through exploring call designs more appealing to SMEs.



The IMI2 JU will also continue to develop and disseminate targeted materials for SMEs and continue the SME outreach programme outlined in the IMI2 JU SME strategy. This includes partnering with other European, national and regional clusters to participate in events aimed at encouraging SMEs to apply and participate in IMI2 JU projects.

### **Regulators**

The regulatory environment is key to ensuring that safe and effective medicines reach the market for the benefit of patients. IMI2 JU will continue to engage with all relevant regulatory authorities, in particular, the European Medicines Agency (EMA). When possible and relevant, IMI2 JU will continue to strengthen engagement with other international agencies and competent national authorities, through for instance interactions with the heads of agencies. Similarly, IMI2 JU will continue to strengthen engagement with relevant health technology assessment (HTA) bodies, through interactions with EUnetHTA for instance in order to progress the goal of end-to-end integration in medicine development. In addition, IMI2 JU will organise its 6<sup>th</sup> Regulatory Science Summit in 2019 to ensure that our projects have a real impact on patients' lives and global health.

### **Other industries and stakeholders**

IMI2 JU will continue to explore how to mobilise industries and stakeholders outside of the pharmaceutical sectors. Through face-to-face meetings, workshops and presentations at conferences, IMI2 JU will engage with players in the ICT, imaging, diagnostic and health technology areas, to mention but a few. Likewise, important steps will continue to engage major players in the food and nutrition sector into discussions around potential programmes under the IMI2 JU umbrella. In addition to other industrial sectors, IMI2 JU will encourage the participation of charities and charitable foundations in its work programmes.

IMI2 JU and ECSEL JU ([www.ecsel.eu](http://www.ecsel.eu)) initiated in 2017 the first discussions to explore possibilities for cooperation between both JUs in the domain of smart health along three thematic areas: sensors and diagnostics, imaging, and patient monitoring platforms. As a continuation of the first concrete interactions set up in 2018, participation of both JUs in their respective governance bodies (e.g. participation of ECSEL in SGG Digital Health & Patient Centric Evidence Generation, Immunology, etc.), interactions during topics design and consultation process, as well as dedicated workshops, are planned in 2019. The objective is to further support synergies between the JUs' activities and potential collaborations between projects of the respective JUs.

As the healthcare challenges faced by society are global, IMI2 JU will continue exploring interactions and seeking synergies with EU and non-EU organisations (including technology hubs at national or regional level) when appropriate, for example in the area of antimicrobial resistance, mental health/neuroscience, microbiome, ATMP vaccines, bio preparedness or oncology. Where necessary, a workshop with IMI founding members and relevant experts will be organised in order to identify gaps and bring new ideas for future topics.

In order to share best practices between projects and develop potential synergies, IMI2 JU will encourage its projects to organise cross-project meetings for both IMI2-JU-funded and other initiatives. This is particularly important in helping disseminate information about IMI2 JU and ensuring harmonisation of approaches at both a European and global level.

IMI2 JU will host a workshop organised by the SGG oncology where experts will be invited to brainstorm on pre-identified themes in order to identify gaps and bring new ideas for future topics in oncology to be launched in upcoming Calls for proposals.

## **2.2.7 Dissemination and information about projects results**

Although the responsibility for maximising the impact of their own research and innovation lies primarily with the project consortia, promoting the successes of IMI2 JU projects is a core element of both the IMI2 JU communications and dissemination strategies.

The IMI2 JU Programme Office identifies results and successes in a variety of ways, including through formal routes (project periodic reports, interim reviews) and informal routes (direct contacts with project participants, monitoring of project websites and social media, etc.). IMI2 JU will continue to support and supplement the dissemination of projects' public deliverables via a variety of channels, including the IMI2 JU and projects' websites, newsletter, social media (Twitter and LinkedIn), the press and events. Particular efforts will be invested in scaling up the online catalogue of accessible tools generated by our projects on the JU website.

In addition, IMI2 JU will continue to explore how to make better use of EU specific dissemination channels for the promotion of projects and their results by actively participating in the European Commission's Dissemination and Exploitation Network (D&E Net).

In 2019, the IMI2 JU expects to receive 13 final project reports. These reports will come from projects finishing in 2018 but reporting in 2019 (2 projects) and those finishing and reporting in 2019 (11 projects). In addition, 3 projects reaching their end date in 2019 will report in 2020. Capturing the outcomes and impacts of these projects presents IMI2 JU with a continuing challenge of ensuring that project results are disseminated widely and taken up by researchers in the field.

It is expected that at least 13 close-out meetings will be organised around the time of the final report submission. The IMI2 JU will prepare specific communication materials for each project based upon information provided in the respective final report and close out meeting.

Lastly, IMI2 JU will continue to fulfil its role/obligation to look after policy conformity, effectiveness and efficiency of the dissemination and exploitation at the level of each project.

### **2.2.8 Socio-economic impact study**

An important part of evaluating the performance of IMI JU will be an assessment of the socio-economic impacts of the projects supported by the IMI1 programme. The efforts to assess this socio-economic impact will be continued using the previously developed methodology.

The final report will be ready for publication by the end of 2019 and will be disseminated to all stakeholders, including policymakers at the European level.

## 2.3 Call management rules

All proposals must conform to the conditions set out in the Horizon 2020 Rules for Participation ([http://ec.europa.eu/research/participants/data/ref/h2020/legal\\_basis/rules\\_participation/h2020-rules-participation\\_en.pdf](http://ec.europa.eu/research/participants/data/ref/h2020/legal_basis/rules_participation/h2020-rules-participation_en.pdf)) and the Commission Delegated Regulation with regard to IMI2 JU <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0622&from=EN>.

The following general conditions shall apply to the IMI2 JU Calls for Proposals. They are based on the General Annexes to the Horizon 2020 Work Programme 2018-2020<sup>11</sup>.

### LIST OF COUNTRIES AND APPLICABLE RULES FOR FUNDING

By way of derogation<sup>12</sup> from Article 10(1) of Regulation (EU) No 1290/2013, only the following participants shall be eligible for funding from the Innovative Medicines Initiative 2 Joint Undertaking:

(a) legal entities established in a Member State or an associated country, or created under Union law; and

(b) which fall within one of the following categories:

(i) micro, small and medium-sized enterprises and other companies with an annual turnover of EUR 500 million or less, the latter not being affiliated entities of companies with an annual turnover of more than 500 million; the definition of 'affiliated entities' within the meaning of Article 2(1)(2) of Regulation (EU) No 1290/2013 shall apply *mutatis mutandis*,

(ii) secondary and higher education establishments,

(iii) non-profit organisations, including those carrying out research or technological development as one of their main objectives or those that are patient organisations;

(c) the Joint Research Centre;

(d) international European interest organisations.

Participating legal entities listed in (b) above established in a third country may receive funding from the IMI2 JU provided their participation is deemed essential for carrying out the action by the IMI2 JU or when such funding is provided for under a bilateral scientific and technological agreement or any other arrangement between the Union and the country in which the legal entity is established<sup>13</sup>.

### STANDARD ADMISSIBILITY CONDITIONS, PAGES LIMITS AND SUPPORTING DOCUMENTS

Part B of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan.

In addition, page limits will apply to proposals as follows:

- at stage 1 of a two-stage call, the limit for RIA/IA short proposals is 30 pages and for CSA short proposals is 20 pages;
- for a single-stage call, as well as at stage 2 of a two-stage call, the limit for RIA/IA full proposals is 70 pages and for CSA full proposals is 50 pages.

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<sup>11</sup> [http://ec.europa.eu/research/participants/data/ref/h2020/other/wp/2018-2020/annexes/h2020-wp1820-annex-ga\\_en.pdf](http://ec.europa.eu/research/participants/data/ref/h2020/other/wp/2018-2020/annexes/h2020-wp1820-annex-ga_en.pdf)

<sup>12</sup> Pursuant to the Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014 establishing a derogation from Regulation (EU) No 1290/2013 of the European Parliament and of the Council laying down the rules for participation and dissemination in 'Horizon 2020 — the Framework Programme for Research and Innovation (2014-2020)' with regard to the Innovative Medicines Initiative 2 Joint Undertaking

<sup>13</sup> In accordance with Article 10(2) of the Regulation (EU) No 1290/2013 and Article 1 of Commission Delegated Regulation (EU) No 622/2014

## STANDARD ELIGIBILITY CONDITIONS

Part C of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall *apply mutatis mutandis* for the actions covered by this Work Plan.

In addition, under all two-stage submission procedures the following additional condition applies:

The participants from EFPIA constituent entities and affiliated entities and Associated Partners which are pre-defined in the topics – under the section ‘Industry consortium’ – of a call for proposals do not apply at the stage 1 of the call. The applicant consortium selected from the stage 1 of the Call for proposals is merged at the stage 2 with the EFPIA constituent entities or their affiliated entities and Associated Partners.<sup>14</sup>

## TYPES OF ACTION: SPECIFIC PROVISIONS AND FUNDING RATES

Part D of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan.

## TECHNOLOGY READINESS LEVELS (TRL)

Part G of the General Annexes to Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan.

## EVALUATION RULES

Part H of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan with the following additions:

The relevant call texts launched under this Work Plan must specify whether the Call for proposals is a single-stage or two-stage Call, and the predefined submission deadline.

### Award criteria and scores:

Experts will evaluate the proposals on the basis of criteria of ‘Excellence’, ‘Impact’ and ‘Quality and efficiency of the implementation’ according to the submission stage and type of action, as follows:

Type of action	Excellence	Impact	Quality and efficiency of the implementation
RIA and IA 1st stage evaluation	<p>The following aspects will be taken into account, to the extent that the proposed work corresponds to the topic description in the call for proposals and referred to in the IMI2 annual work plan:</p> <p>Clarity and pertinence of the proposal to meet all key objectives of the topic;</p> <p>Credibility of the proposed approach;</p> <p>Soundness of the concept, including trans-disciplinary considerations, where relevant;</p>	<p>The following aspects will be taken into account, to the extent to which the outputs of the project should contribute at the European and/or international level:</p> <p>The expected impacts of the proposed approach as mentioned in the Call for proposals</p> <p>Added value from the public-private partnership approach on R&amp;D, regulatory, clinical and healthcare practice as relevant;</p> <p>Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges;</p>	<p>The following aspects will be taken into account:</p> <p>Coherence and effectiveness of the outline of the project work plan, including appropriateness of the roles and allocation of tasks, resources, timelines and approximate budget;</p> <p>Complementarity of the participants within the consortium (where relevant) and strategy to create a successful partnership with the industry consortium as</p>

<sup>14</sup> Article 9(5) of the Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in “Horizon 2020”

Type of action	Excellence	Impact	Quality and efficiency of the implementation
	<p>Extent that proposed work is ambitious, has innovation potential, and is beyond the state of the art;</p> <p>Mobilisation of the necessary expertise to achieve the objectives of the topic, ensure engagement of all relevant key stakeholders</p>	<p>Improving European citizens' health and wellbeing and contribute to the IMI2 objectives<sup>15</sup>.</p>	<p>mentioned in the topic description in the Call for proposal;</p> <p>Appropriateness of the proposed management structures and procedures, including manageability of the consortium.</p>
<p>RIA and IA</p> <p>Single stage, and 2nd stage evaluation</p>	<p>The following aspects will be taken into account, to the extent that the proposed work corresponds to the topic description in the Call for proposals and referred to in the IMI2 annual work plan and is consistent with the stage 1 proposal:</p> <p>Clarity and pertinence of the proposal to meet all key objectives of the topic;</p> <p>Credibility of the proposed approach;</p> <p>Soundness of the concept, including trans-disciplinary considerations, where relevant;</p> <p>Extent that proposed work is ambitious, has innovation potential, and is beyond the state of the art;</p> <p>Mobilisation of the necessary expertise to achieve the objectives of the topic, ensure engagement of all relevant key stakeholders.</p>	<p>The following aspects will be taken into account, to the extent to which the outputs of the project should contribute at the European and/or international level:</p> <p>The expected impacts of the proposed approach as mentioned in the Call for proposals;</p> <p>Added value from the public-private partnership approach on R&amp;D, regulatory, clinical and healthcare practice as relevant;</p> <p>Enhancing innovation capacity and integration of new knowledge;</p> <p>Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges; Improving European citizens' health and wellbeing and contribute to the IMI2 objectives;<sup>15</sup></p> <p>Any other environmental and socially important impacts;</p> <p>Effectiveness of the proposed measures to exploit and disseminate the project results (including management of IPR), to communicate the project, and to manage research data where relevant.</p>	<p>The following aspects will be taken into account:</p> <p>Coherence and effectiveness of the project work plan, including appropriateness of the roles and allocation of tasks, resources, timelines and budget;</p> <p>Complementarity of the participants within the consortium (where relevant);</p> <p>Clearly defined contribution to the project plan of the industrial partners (where relevant);</p> <p>Appropriateness of the management structures and procedures, including manageability of the consortium, risk and innovation management and sustainability plan.</p>

<sup>15</sup> Article 2 of the Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking (O.J. L169 of 7.6.2014)

Type of action	Excellence	Impact	Quality and efficiency of the implementation
CSA 1st stage evaluation	<p>The following aspects will be taken into account, to the extent that the proposed work corresponds to the topic description in the Call for proposal and referred to in the IMI2 annual work plan:</p> <p>Clarity and pertinence of the proposal to meet all key objectives of the topic;</p> <p>Credibility of the proposed approach;</p> <p>Soundness of the concept, including trans-disciplinary considerations, where relevant;</p> <p>Quality of the proposed coordination and/or support measures;</p> <p>Mobilisation of the necessary expertise to achieve the objectives of the topic, ensure engagement of all relevant key stakeholders.</p>	<p>The following aspects will be taken into account, to the extent to which the outputs of the project should contribute at the European and/or international level:</p> <p>The expected impacts of the proposed approach as mentioned in the Call for proposal;</p> <p>Added value from the public-private partnership approach on R&amp;D, regulatory, clinical and healthcare practice as relevant.</p> <p>Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges;</p> <p>Improving European citizens' health and wellbeing and contribute to the IMI2 objectives<sup>16</sup>.</p>	<p>The following aspects will be taken into account:</p> <p>Coherence and effectiveness of the outline of the project work plan, including appropriateness of the roles and allocation of tasks, resources, timelines and approximate budget;</p> <p>Complementarity of the participants within the consortium (where relevant) and strategy to create a successful partnership with the industry consortium as mentioned in the topic description in the Call for proposal.</p> <p>Appropriateness of the proposed management structures and procedures, including manageability of the consortium.</p>
CSA Single stage and 2nd stage evaluation	<p>The following aspects will be taken into account, to the extent that the proposed work corresponds to the topic description in the Call for proposal and referred to in the IMI2 annual work plan and is consistent with the stage 1 proposal:</p> <p>Clarity and pertinence of the proposal to meet all key objectives of the topic;</p>	<p>The following aspects will be taken into account, to the extent to which the outputs of the project should contribute at the European and/or international level:</p> <p>The expected impacts of the proposed approach as mentioned in the Call for proposal;</p> <p>Added value from the public-private partnership approach on R&amp;D, regulatory, clinical and health care practice as relevant</p>	<p>The following aspects will be taken into account:</p> <p>Coherence and effectiveness of the project work plan, including appropriateness of the roles and allocation of tasks, resources, timelines and budget;</p> <p>Complementarity of the participants within the consortium (where relevant);</p>

<sup>16</sup> Article 2 of the Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking (O.J. L169 of 7.6.2014)



Type of action	Excellence	Impact	Quality and efficiency of the implementation
	<p>Credibility of the proposed approach;</p> <p>Soundness of the concept, including trans-disciplinary considerations, where relevant;</p> <p>Quality of the proposed coordination and/or support measures;</p> <p>Mobilisation of the necessary expertise to achieve the objectives of the topic and to ensure engagement of all relevant key stakeholders.</p>	<p>Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges;</p> <p>Improving European citizens' health and wellbeing and contribute to the IMI2 objectives<sup>17</sup>.</p> <p>Effectiveness of the proposed measures to exploit and disseminate the project results (including management of IPR), to communicate the project, and to manage research data where relevant.</p>	<p>Clearly defined contribution to the project plan of the industrial partners (where relevant);</p> <p>Appropriateness of the management structures and procedures, including manageability of the consortium, risk and innovation management and sustainability plan.</p>

The scheme above is applicable to a proposal in a single-stage submission procedure, as well as in a two-stage submission procedure. At each evaluation stage of the two-stage submission procedure, the relevant evaluation criteria and threshold apply.

These evaluation criteria include scores and thresholds. Evaluation scores will be awarded for the criteria, and not for the different aspects listed in the above table. For all evaluated proposals, each criterion will be scored out of 5. Half marks may be given.

For the evaluation of first-stage proposals under a two-stage submission procedure, the threshold for each one of the two first criteria ('excellence' and 'impact') will be 3. There is no overall threshold. For the evaluation of second-stage proposals under a two-stage submission procedure; the threshold for individual criteria will be 3. The overall threshold, applying to the sum of the three individual scores, will be 10. For the evaluation of proposals under a single-stage submission procedure, the threshold for individual criteria is 3. The overall threshold, applying to the sum of the three individual scores is 10.

Following each evaluation stage, applicants will receive an ESR (Evaluation Summary Report) regarding the respective evaluated proposal.

The full evaluation procedure is described in the IMI2 JU Manual for submission, evaluation and grant award in line with the Horizon 2020 Rules for Participation.<sup>18</sup>

Where appropriate and duly justified, IMI2 JU Calls for proposals may follow a two-stage process.

Under the single-stage evaluation process, evaluated proposals will be ranked in one single list. The best-ranked proposals, in the framework of the available budget, will be invited to prepare a Grant Agreement.

<sup>17</sup> Article 2 of the Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking (O.J. L169 of 7.6.2014)

<sup>18</sup> [http://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/IMI2JU\\_AWP%26Budget\\_2018\\_approved\\_15Dec2017.pdf](http://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/IMI2JU_AWP%26Budget_2018_approved_15Dec2017.pdf)

Under the two-stage evaluation procedure, and on the basis of the outcome of the first stage evaluation, the applicant consortium of the highest ranked short proposal (first stage) for each topic<sup>19</sup> will be invited to discuss with the relevant industry consortium the feasibility of jointly developing a full proposal (second stage).

Under the stage 2 preparation process, the applicant consortia of the second and third-ranked short proposals (stage 1) for each topic may be invited by the IMI2 JU, in priority order, for preliminary discussions with the industry consortium if the preliminary discussions with the higher ranked proposal and the industry consortium fail. The IMI2 JU may explore this possibility if the first ranked applicant consortium and the industry consortium jointly notify the IMI2 JU that the preparation of a joint full proposal is not feasible. If this is the case, the first ranked consortium and the industry consortium shall notify IMI2 JU without delay, not later than within 30 days from the invitation to submit the stage 2 proposal. This notification must be accompanied by a joint report clearly stating the reasons why a stage 2 proposal is considered not feasible in order for the IMI2 JU to take the decision whether to invite the lower ranked consortium. In the absence of a joint notification within the deadline, it is deemed that the first ranked applicant consortium and the industry consortium are going to submit the joint stage 2 proposal. Accordingly, the second and third-ranked short proposals will be formally rejected.

Under the two-stage evaluation procedure, contacts or discussions about a given topic between potential applicant consortia (or any of their members) and any member of the relevant industry consortium are prohibited throughout the procedure until the results of the first stage evaluation are communicated to the applicants.

As part of the panel deliberations, the IMI2 JU may organise hearings with the applicants to:

- clarify the proposals and help the panel establish their final assessment and scores, or
- improve the experts' understanding of the proposal.

IMI2 JU evaluation procedure is confidential. The members of the applicant consortia shall avoid taking any actions that could jeopardise confidentiality.

#### INDICATIVE TIMETABLE FOR EVALUATION AND GRANT AGREEMENT

	Information on the outcome of the evaluation  (single stage, or first stage of a two-stages)	Information on the outcome of the evaluation  (second stage of a two stages)	Indicative date for the signing of grant agreement
Single-stage	Maximum 5 months from the submission deadline at the single stage.	N/A	Maximum 8 months from the submission deadline.
Two-stages	Maximum 5 months from the submission deadline at the first stage.	Maximum 5 months from the submission deadline at the second stage.	Maximum 8 months from the submission deadline at the second stage.

#### BUDGET FLEXIBILITY

Part I of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan.

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<sup>19</sup> In cases clearly identified in the relevant call for proposals where a given topic is composed of two or more sub-topics, one short proposal per sub-topic will be invited



## ACTIONS INVOLVING FINANCIAL SUPPORT TO THIRD PARTIES

Part K of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions selected under topics covered by this Work Plan.

## CONDITIONS RELATED TO OPEN ACCESS TO RESEARCH DATA

Part L of the General Annexes to the Horizon 2020 Work Programme 2018-2020 shall apply *mutatis mutandis* for the actions covered by this Work Plan.

However, should a project 'opt-out' of these provisions, a Data Management Plan must still be prepared. A template for the Data Management Plan is available on the [IMI2 JU website](#).

## SUBMISSION TOOL

Proposals in response to a topic of the IMI2 JU Call for proposals must be submitted online, before the call deadline, by the coordinator via the Submission Service section of the relevant topic page available under Funding & tender opportunities - Single Electronic Data Interchange Area (SEDIA).

No other means of submission will be accepted.

## OTHERS

For proposals including clinical trials/studies/investigations, a specific template to help applicants to provide essential information on clinical studies in a standardised format is available under:

<http://www.imi.europa.eu/apply-funding/call-documents/imi2-call-documents#imi2-call-documents-collapsible-1>.

In the first stage of a two-stage evaluation procedure, this template should not be submitted. However, applicants may integrate relevant aspects of this information in their short proposal (within the page limit). In the second stage of two-stage evaluation procedure involving clinical studies, the use of this template is mandatory in order to provide experts with the necessary information to evaluate the proposals. The template may be submitted as a separate document.

Ethical issues should be duly addressed in each submitted proposal to ensure that the proposed activities comply with ethical principles and relevant national, Union and international legislation. Any proposal that contravenes ethical principles or which does not fulfil the conditions set out in the H2020 Rules for Participation, or in the IMI2 JU Call for proposals shall not be selected.<sup>20</sup>

In order to ensure excellence in data and knowledge management consortia will be requested to Disseminate scientific publications on the basis of open access<sup>21</sup> (see 'Guidelines on Open Access to Scientific Publications and Research Data in Horizon 2020').

To ensure actions are implemented properly, at the time of the signature of the grant agreement, each selected consortia must have agreed upon a consortium agreement, i.e. the internal arrangements regarding their operation and co-ordination.

Single-stage proposals and two-stage full proposals must contain a draft plan for the exploitation and dissemination of the results.

Applicants intending to submit a proposal in response to the IMI2 JU Calls should also read the topic text, the IMI2 JU Manual for submission, evaluation and grant award, and other relevant documents<sup>22</sup> (e.g. IMI2 JU model Grant Agreement).

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<sup>20</sup> Article 19 of Horizon 2020 Framework Programme and Articles 13 and 14 of the Horizon 2020 Rules for Participation.

<sup>21</sup> Article 43.2 of Regulation (EU) No 1290/2013 of the European Parliament and of the Council laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" and repealing Regulation (EC) No 1906/2006

<sup>22</sup> <http://www.imi.europa.eu/apply-funding/call-documents/imi2-call-documents>

## 2.4 Support to Operations

### 2.4.1 Communication and events

#### Communication objectives

IMI2 JU has set up a communications strategy aiming to pursue five main strategic goals:

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

The year 2019 will be dedicated to consolidating the communication of IMI project results, building on the 10<sup>th</sup> anniversary communication campaign launched in 2018. The main objective in the area of communication will be to demonstrate the EU-added value of IMI2 JU: to what extent IMI2 JU is delivering results in the field of health that are tangible and translate into concrete benefits for European citizens.

As a follow up of the 2018 Stakeholder Forum, the Communications team will also focus its activities on the current and future cross-sectoral collaboration in IMI projects.

#### Communication support to IMI2 JU stakeholder strategies: patients and SMEs

As the IMI2 JU patient strategy keeps evolving with patients and carers reaching new ways of meaningful involvement in IMI projects, the Communications team will continue to support awareness-raising activities and to encourage patients to get involved in both IMI's projects and its broader activities.

In line with Horizon 2020, IMI2 JU will be expected to ensure 20% of its budget goes to SMEs. Yet the JU is competing with other funding programmes to attract SME participation, some of them SME tailored. The Communications team will continue to focus on a comprehensive outreach and support strategy by (i) improving communication on IMI2 JU through SRGs/regional contact points/clusters, (ii) by participating in partnering events and investor conferences and (iii) by providing specific resources for SMEs such as dedicated webinars or new content for the dedicated SME webpage in the JU website.

#### Further develop IMI success stories

IMI2 JU now holds close-out meetings with the representatives of projects that have finished, learning about what the projects have achieved and their legacy. These meetings are providing IMI2 JU with a wealth of success stories that can be adapted for different audiences and channels and back up IMI2 JU's key messages. IMI2 JU will also continue to maintain close contacts with ongoing projects to gather and promote their latest news and results.

In order to amplify the reach of project success stories and results, IMI2 JU will continue to work in close collaboration with the communication unit of the European Commission's Directorate-General for Research and Innovation, responsible for services such as the Horizon Magazine and the webpage for EU research success stories.

#### Media outreach

The coverage of IMI2 JU in both the general and specialist press tends to be either neutral or positive in tone. In 2019, IMI2 JU will work to ensure that this trend continues by building and maintaining links with journalists, issuing regular press releases, organising press interviews, and inviting journalists to IMI2 JU events.

At the same time, IMI2 JU will remain alert to issues that could damage IMI2 JU's reputation and respond accordingly, for example by preparing briefings or sets of questions and answers.

## Communication channels

IMI2 JU will continue to develop the following channels:

- events (both IMI2 JU and external);
- website;
- newsletter;
- social media (LinkedIn, Twitter);
- multipliers (e.g. European Commission & EFPIA, States Representatives Group (SRG), SC, National Contact Points, relevant scientific associations, patient organisations, etc.);
- media (general and specialist, mainly in Europe but also elsewhere);
- direct mailings;
- publications;
- videos;
- direct contacts with opinion leaders.

## Social media

Building on the success of the IMI 10th anniversary campaign in 2018, in 2019 IMI2 JU will continue to develop its brand on social media, especially Twitter. This will include developing engaging content with strong visuals and using promoted / sponsored tweets at key moments of the year.

## Key events in 2019

Event	Timeline
Promote IMI2 JU projects	Throughout year
IMI2 JU presence in the European Parliament	Throughout year
IMI2 JU presence at relevant external events, e.g. BIO, BIO-Europe, EAPM, BioFIT	Throughout year
Follow up meeting SF2018	Q4
Promote IMI2 JU Calls for proposals (webinars, info days, website, etc.)	Q2, Q4
IMI2 JU Stakeholder Forum 2019	Q4
Organise a coordination meeting with IMI project partners responsible for communications	Q1/Q2

### 2.4.2 Procurement and contracts

In order to reach its objectives and adequately support its operations and infrastructures, IMI2 JU will allocate funds to procure the necessary services and supplies. To make tender and contract management as effective and efficient as possible, IMI2 JU resorts extensively to multi-annual framework contracts and EU inter-institutional tenders. Most essential framework contracts are already in place and will be renewed beyond 2019.

### 2.4.3 IT and logistics

IMI2 JU information technologies (IT) strategic objective is to deliver value to the business and to be a key enabler of new business initiatives with the goal of supporting and shaping the present and future of the JU. Operations and administration information systems and infrastructure aim at making all IMI2 JU processes simpler and more efficient.

In order to achieve the afore-mentioned goal, the IMI2 JU IT team will focus its 2019 activities on three areas:

- business operations information systems;
- collaboration, communication and administration management information systems and;
- infrastructure, security and office automation support.

#### 2.4.3.1 Business operations information systems

In 2017, IMI2 JU's business operations started utilising the full suite of Horizon 2020 IT tools for the management of IMI2 JU calls, applications, evaluations and grants. In 2018, all projects under IMI2 JU started reporting under those tools. The IT team will monitor satisfactory functioning for all end-users, in close liaison with the European Commission services.

To provide reliable reporting and statistics for the benefit of all stakeholders, the IMI2 JU Programme Office is working on a new data warehouse project, combining various data sources (eGrants/CORDA, Submission OF Information Application (SOFIA), and other reference data). The first release (planned for the beginning of 2019) will include entirely new business intelligence environment based on QlikSense, which will gradually replace existing Qlikview reports and dashboards. It will also automatically feed the JU website with projects and participants' data and provide a possibility for embedding dashboards on the Intranet.

Since IMI1 projects go on until at least 2020 and some of the IMI2 JU specific requirements (e.g. EFPIA and Associated Partners annual reporting of in-kind contributions) are not available in eGrants, we will continue the maintenance and development of the in-house SOFIA.

#### 2.4.3.2 Collaboration, communication and administration management information systems

IMI2 JU Programme Office has well established collaborative platforms to provide support to the governance bodies, namely the Governing Board, the SC, the SRG and the SGGs. These platforms will be maintained and updated both from a content and operations point of view.

Planned implementation of the European Commission document management and human resources systems (Hermes-Ares-NomCom HAN and SYSPER2) will lead to the phaseout of relevant in-house Liferay applications.

In order to facilitate internal communication, we foresee a complete revamp of the Intranet with improved structure and usability.

#### 2.4.3.3 Infrastructure, security and office automation support

IMI2 JU shares IT infrastructure, related IT operations and office automation support with other JUs that are also located in the same premises. In the context of the common infrastructure, the following activities are foreseen for 2019 and are expected to provide efficiency gains in the operation of the organisation:

- monitoring and maintenance of the common infrastructure and end-user office-automation support covering incidents, service requests and improvements (Q1 – Q4 2019);
- implementation of the new common framework contract for the provision of IT services.

## 2.4.4 Human Resources

The 2019 objective for HR shall be: recruit, train, assess, motivate and retain highly qualified staff with a view to ensure effective and efficient operation of the JU, as well as equal opportunities. This objective will be implemented through the following four main themes.

### Staffing

The staffing needs of IMI2 JU will be the same as in 2018. The total number of staff remains at 54 temporary and contract agents (of which 39 temporary agents and 15 contract agents), as well as two additional seconded national experts.

In accordance with the Staff Regulations, technical adaptations have been made to the Staff Establishment Plan in order to create a margin for reclassification (promotions) of staff. Those adaptations do not affect the total number of staff.

### Organisation development

The human resources team will advise management on means and actions to enhance operational efficiency and effectiveness. The main action shall be the oversight of duties and responsibilities assigned to staff in order to achieve the fulfilment of IMI2 JU objectives and tasks.

### HR management

Human resources will deal with core functions such as: day-to-day management of administrative workflows and processes; performance management and assessment; safety and wellbeing at work; salary, compensation and benefits; employee motivation, communication, and training. It is expected that during 2019 IMI2 JU will start working in the European Commission human-resource IT system, SYSPER II, which will help in the personnel administration.

### Inter-JU cooperation

The efficiency and cost-effective management of IMI2 JU resources is also based on a close collaboration with other Joint Undertakings through arrangements and mechanisms of pooling expertise for specific time-bound tasks. In 2019, the JUs will continue to share the human-resource IT tools where necessary, common Calls for tender, as well as a common approach to implementing rules of the EU staff regulations.

## 2.4.5 Administrative budget and finance

### Budget 2019

The budget forecast 2019 for staff (Title 1) and administrative activities (Title 2) has been defined in line with the planning of the year. The increase of 6.86% in 2019 compared to 2018, is mainly due to staff management as well as increasing meetings costs related to experts and close out projects. A comparison table of the financial years 2018 and 2019 is set out below.

	Heading Title 1	Financial year 2018	Financial year 2019	Evolution	Comments
Chapter		Budget EUR	Budget EUR	%	
11	Staff in active employment	5,425,000	5,740,000	5.8	3.5% standard annual promotion and indexation set out in the EU Financial Regulation. 2 positions of Seconded National Experts
12	Staff recruitments - miscellaneous expenditure	20,000	20,000	0.0	
13	Missions and duty travels	190,000	190,000	0.0	
14	Socio-medical structure	360,000	360,000	0.0	
17	Entertainment and representation	20,000	20,000	0.0	
	<b>Title 1 - Total</b>	<b>6,015,000</b>	<b>6,330,000</b>	<b>5.24</b>	
	Heading Title 2	Financial year 2018	Financial year 2019	Evolution	
Chapter		Budget EUR	Budget EUR	%	
20	Office building and associated costs	729,000	756,000	3.7	Additional costs with newly rented space and cleaning.
21	Information technology purchases	712,000	779,000	9.4	Additional recurrent license, maintenance of paperless system and new Intranet.
22	Office equipment (movable property and associated costs)	153,000	153,000	0.0	
23	Current administrative expenditure	123,000	123,000	0.0	
24	Telecommunication and postal expenses	68,000	78,000	14.7	Increase due to higher number of teleconferences
25	Expenditure on formal meetings	158,000	158,000	0.0	
26	Administrative costs in connection with operational activities	300,000	388,154	29.4	Increase in the activities such as SGG, projects close out meetings.
27	External communication, information and publicity	625,000	625,000	0.0	
28	Service contracts	730,000	730,000	0.0	
29	Expert contracts and cost of evaluations	700,000	900,000	28.6	Increase in number of Calls' topics.
	<b>Title 2 - Total</b>	<b>4,298,000</b>	<b>4,690,154</b>	<b>9.12</b>	
	<b>Total Administrative Costs</b>	<b>10,313,000</b>	<b>11,020,154</b>	<b>6.86</b>	

The operational budget is covered under section 2.2.2. Scientific priorities for 2019. For an overview of the Budget Plan 2019 – see Chapter 3.

## **Financial Management**

During 2019, the Programme Office will implement the updated IMI2 JU Financial Rules in line with the 2018 revised Regulation (EU, Euratom) 2018/1046 on the financial rules applicable to the general budget of the Union, repealing Regulation (EU, Euratom) No 966/2012 (2012 Financial Regulation).

In addition, the finance team will continue with its day-to-day activities of initiation, verification and payments of invoices and cost claims, creation of commitments, recovery orders, and analysis of periodic reports and negotiations of financial and administrative parts of projects. These activities will be conducted in a timely manner that will be monitored through corporate KPIs, in particular payment times and budget execution.

Best practice and highest quality standards will be ensured through the Financial Circuits Manual and a set of standard operating procedures and workflows. In addition, knowledge dissemination will be further developed through the development of further guidance and the tenure of several financial workshops, in particular targeting beneficiaries, with the aim to reduce errors in financial reporting.

### **2.4.6 Data protection**

The IMI2 JU will continue its efforts undertaken in the wake of the entry into effect of the General Data Protection Regulation, following the adoption of the successor regulation to 'Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data'.

The IMI2 JU, with the active involvement of its Data Protection Officer, will continue to implement the changes brought about by the overhaul of the EU data protection regime. This will include finalising the update of the JU's internal data protection rules, guidelines and practices, raising awareness among IMI2 JU staff and stakeholders, and contributing to the activities of the inter-institutional data protection networks and working groups in which the JU participates.

### **2.4.7 Access to documents**

IMI2 JU will continue to address requests for access to IMI2 JU documents according to Regulation (EC) No 1049/2001, in a spirit of openness and transparency in order to bring its activities and outputs closer to the public. In this context, the Programme Office will further develop a transparency policy on activities of its governance bodies in accordance with the Council Regulation setting up IMI2 JU. In particular, IMI2 JU will continue the implementation of the standard operating procedure (SOP) on Access to documents and the training of the staff on access to documents issues.

Furthermore, the objectives of actions in this field will continue, as a means to keep a high-level of public confidence in IMI2 JU by giving the opportunity to the public to monitor its work. In addition, this will bring additional benefits such as:

- improving public awareness of IMI2 JU activities and processes;
- stimulating the interaction on key issues.



## 2.5 Governance

### Key objectives

- Further develop an IMI2 JU strategic orientation and related objectives.
- Ensure that activities are in line with and support IMI2 JU strategic orientation.
- Further improve the efficiency and effectiveness of the IMI2 JU's governance activities.
- Promote and maintain a positive reputation among stakeholders and partners as a key facilitator of healthcare research.

### Planned activities

- Support to the Governing Board, the SC, the SRG and management.
- Align planning activities (strategy, annual work plans and related budget) and the associated monitoring and reporting activities.
- Improve responsibilities and accountability.
- Enhance communication and transparency.

IMI2 JU will continue to provide support to the Governing Board, the SC, the SRG, and the Stakeholder Forum and their working groups.

The **Governing Board** gathers representatives of IMI2 JU members. It has the responsibility for overseeing the operations of the IMI2 JU and the implementation of its activities. It will meet at least twice.

The **Scientific Committee** (SC) will continue in its advisory role to the IMI2 JU and will notably be consulted on the scientific priorities to be addressed in Annual Work Plans and on the scientific achievements to be described in the Annual Activity Report. Three meetings of the SC are planned for 2019. The Chair will participate in the Governing Board meetings as an observer. Information can be found at: <http://www.imi.europa.eu/about-imi/governance/scientific-committee>

The **States Representatives Group** (SRG) will be consulted on the Annual Work Plan (and subsequent amendment(s)) and will receive information on Calls outcomes and evaluation process. At least two meetings of the SRG are planned for 2019. The Chair will participate in Governing Board meetings as an observer. Information can be found at: <http://www.imi.europa.eu/about-imi/governance/states-representatives-group>

In addition, a joint meeting between the SC and the SRG is planned in order to support the activities initiated to strengthen the synergies between the two advisory bodies and exchange on topics of common interest.

In order to cover all areas of life science research and innovation of public health interest and to further support the IMI2 JU objectives, the JU will pursue its action to attract a wide range of stakeholders from various sectors, notably by promoting the possibility to become **Associated Partners** at programme or topic level and supporting such an involvement. Practical information can be found at: <http://www.imi.europa.eu/get-involved>.

The SGGs continue to ensure the coordination of IMI2 JU's work in seven strategic areas and work to make the development of new topics more transparent and effective. The SGGs are made up of representatives from companies active or interested in the area covered by the scope of the SGG as well as representatives from the European Commission, the IMI2 JU Programme Office and the SC. Currently, the seven established SGGs focus on the following areas: immunology; diabetes / metabolic disorders; neurodegeneration; translational safety; infections control; oncology; and digital health and patient-centric evidence generation (which replaced the data and knowledge management in 2018).

In 2019 the SGGs will continue to develop comprehensive strategies for future projects for their specific areas.

Each SGG will meet at least 2 to 3 times a year to discuss their portfolio of projects and ensure synergies with ongoing projects, both projects within IMI2 JU and those outside. They may engage with external parties to consult on topic development or key challenges in specific areas as required. Efforts will be made to enhance communication with these bodies as well as seek feedback on any significant IMI2 JU activities and developments.



In 2019, facilitation of better cross-SGGs coordination will continue, notably through the dedicated IT platform set up in 2017, as well as a series of dedicated cross-SGGs meetings. These improved efficiency mechanisms will facilitate the increased flow of information not only within a given SGG, but also with IMI2 JU governance bodies (Governing Board, SC, SRG). Therefore, the SGG meeting agendas, publishable minutes and attendance lists will be more readily available. In addition, they will be called upon to advise on how best to exploit IMI2 JU projects' outputs, enhance cross-projects' collaboration, as well as explore synergies with similar or complementary activities at national and global level.

In line with article 13.3 (b) of IMI2 JU Regulation, costs of activities related to allowing the SGGs perform these tasks and achieve their objectives are considered as eligible in-kind contributions under the conditions set out in the SGG charter.<sup>23</sup>

### ***Expected results***

- Streamlined governance activities

Actions:

- Preparation of plans, reports, briefings, decisions
- Organisation of consultations and assessment of the input
- Organisation of meetings and presentations
- Implementation of decisions and recommendations
- Coordinate information across governance structures.

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<sup>23</sup> [http://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/IMI2\\_GB\\_DEC\\_2016\\_21\\_Decision\\_on\\_new\\_SGGs\\_Charter\\_SIGNED\\_30SEP2016.pdf](http://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/IMI2_GB_DEC_2016_21_Decision_on_new_SGGs_Charter_SIGNED_30SEP2016.pdf)

## 2.6 Internal Control framework

In 2019, the IMI2 JU will continue working on the improvement of its internal operational and financial processes and procedures. In particular, the new Internal Control Framework (ICF) – aligned with the revised control framework adopted by the European Commission – will be fully implemented based on the characteristics, indicators and targets developed during 2018 and adapted to the specific IMI2 JU environment.

In parallel, the Programme Office will: ensure the alignment with and implementation of the Horizon 2020 legal framework and programme management tools; develop guidance materials; and keep its financial procedures effective and up to date.

Another relevant element of the control strategy operated by IMI2 JU will be the revision – in line with the European Commission and DG RTD – of its Antifraud Strategy with the appropriate communication and training measures to staff and beneficiaries.

The specific target set by the IMI2 JU on internal control is to sustain the IMI2 JU operational and financial performance<sup>24</sup> in order to ensure the achievement of its objectives.

### 2.6.1 Ex-ante and ex-post controls

#### Ex-ante controls

During 2019, the IMI2 JU Programme Office will continue to work effectively in its day-to-day activities of initiation, verification and payments of invoices and cost claims, creation of commitments, recovery orders, validation of financial and technical reports and following-up on other financial and administrative aspects of the projects.

These activities will be conducted in a timely and efficient manner according to the principle of sound financial management. All activities will be monitored through the defined set KPIs, in particular, the time to pay and the budget and work plan execution. Best practice and highest quality standards will be ensured through the availability of the newly adopted Horizon 2020 Vademecum on Grant Agreement Preparation (GAP, the Vademecum on monitoring and reporting and the Vademecum on Amendments). These procedures will complement the existing set of financial manuals, SOPs and workflows.

Specific attention will be placed on:

- implementation of the joint guidance on Horizon 2020 ex-ante controls for interim and final payments;
- increased financial checks during the GAP phase;
- raising the awareness of beneficiaries on financial and administrative aspects of Horizon 2020 rules and how to avoid errors in cost reporting.

#### Ex-post controls

For projects running under the IMI1 programme, the Programme Office will carry on with the implementation of its ex-post audits strategy as a means to ensure the legality and regularity of operational expenditure. This strategy complements ex-ante controls embedded in IMI's management processes and includes the correction of any amounts found to have been paid in excess. Errors of a systematic nature will also continue to be extended to cover unaudited financial statements ('Form C') of the same participants.

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<sup>24</sup> Effectiveness, efficiency and economy of operations; reliability of reporting; safeguarding of assets and information; prevention, detection, correction and follow-up of fraud and irregularities; and adequate management of the risks relating to the legality and regularity of the underlying transactions, taking into account the multiannual character of programmes as well as the nature of the payments (IMI2 JU Financial Rules, Art 12.2).

Representative and, if necessary, risk-based audits of beneficiaries will be launched during the year to cover new cost claims received and validated by IMI2 JU since the last audited period. Systematic risk-based audits of accepted declarations of in-kind contributions by EFPIA companies will not be continued in 2019, as the programme is reaching its end and the planned, near totality of the companies' contributions will have been covered by audits. Risk-based audits may nevertheless be initiated should a specific need arise.

As regards the IMI2 JU programme, the JU's ex-ante and ex-post controls of grants are both aligned with the harmonised strategies adopted for the entire Horizon 2020 Programme. The IMI2 JU Programme Office will carry out the ex-ante checks as prescribed in the Horizon 2020 Control strategy. As for ex-post controls, the Commission Common Audit Service (CAS) will carry out the Horizon 2020 audits in accordance with the common Horizon 2020 audit strategy. IMI2 JU contributes to the implementation of the audit strategy in close cooperation with the CAS. The harmonised legal framework will enable IMI2 JU to draw an additional element of assurance from extension of audit results on shared beneficiaries across the Horizon 2020 programme as well as from audits sampled by CAS in line with the overall programme objectives.

In line with the IMI2 JU Regulation, controls of in-kind contributions by EFPIA companies will be based essentially on review of audit certificates provided annually by independent auditors.

## **2.6.2 Internal and External audits**

The audit environment is an assurance and accountability pillar within the IMI2 JU internal control framework since it provides reasonable assurance about the state of effectiveness of risk management and control processes and serves as a building block for the annual Declaration of Assurance of the Executive Director.

The Audit Manager will coordinate audits carried out by IMI2 JU's internal and external auditors and will follow up and assess the implementation of the Internal Audit Service (IAS) of the European Commission and the European Court of Auditors (ECA) audit recommendations with the objective to confirm the effective implementation.

Internal audits are carried out by the IAS in liaison with the Audit Manager.

In 2019, the focus will be put on:

- coordination of the new risk assessment to be carried out by the IAS in view of the strategic internal audit plan for 2019 – 2021 and the approval of the new multiannual audit plan by the Governing Board.

External audits are carried out by ECA. ECA will audit and issue opinions on the legality and regularity of the underlying transactions, revenue, and reliability of accounts. In accordance with the IMI2 JU Financial rules, IMI2 JU's 2018 annual accounts will be audited by an external audit company while the Court will draw an opinion on the basis of their work.

In view of the overall corporate objective of receiving an unqualified ('clean') ECA audit opinion and positive statement of assurance, the key activities will focus on:

- liaising and supporting ECA auditors throughout the audit on 2018 and 2019 accounts and a possible performance audit;
- liaising with an independent financial audit firm (contracted in 2018 under the EC (DG BUDG) framework contract) throughout the audit of accounts for financial year 2018 and 2019.

### 3 Budget 2019

An overview of the 2019 budget per chapters is set out below.

STATEMENT OF REVENUE				
	Heading Revenue	Financial year 2019		Comments
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
10	European Commission contribution (including EFTA contribution/Draft Budget 2019) <sup>25</sup>	267,722,662	190,575,842	Commitment appropriations include EUR 5,510,077 for administrative costs and EUR 262,212,585 for operational costs. Payment appropriations include administrative costs of EUR 5,510,077 and operational costs of EUR 185,065,765 (of which 50,405,301 for FP7 actions).
C2	Appropriations carried over	114,341,000		The amount carried over from previous year. Operational expenditure - commitment appropriation.
	<b>Title 1 - Total</b>	<b>382,063,662</b>	<b>190,575,842</b>	
20	EFPIA contribution	5,510,077	5,510,077	EFPIA contribution to IMI JU administrative costs.
21	Subsidy from other Members other than the Union and the Associated Partners, or their constituent entities or their affiliated entities		1,000,000	Four EFPIA companies contribution to operational payment appropriations
	<b>Title 2 - Total</b>	<b>5,510,077</b>	<b>6,510,077</b>	
30	Associated Partners contributions		845,000	Bill and Melinda Gates Foundation contribution to operational payment appropriations
	<b>Title 3 - Total</b>		<b>845,000</b>	
	<b>Total contributions</b>	<b>387,573,739</b>	<b>197,930,919</b>	

<sup>25</sup> Subject to approval of European Union Draft Budget (DB) for 2019 by the Budgetary Authority (comprised of the Council of the European Union and the European Parliament) as proposed by the European Commission.

STATEMENT OF EXPENDITURE				
	Heading Title 1	Financial year 2019		Comments
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
11	Staff in active employment	5,740,000	5,740,000	Salaries
12	Staff recruitments - miscellaneous expenditure	20,000	20,000	Miscellaneous expenditure on staff recruitment: travel expenses, etc.
13	Missions and duty travels	190,000	190,000	Mission expenses
14	Socio-medical structure	360,000	360,000	Other staff costs: training, language classes, medical service, interim staff
17	Representation	20,000	20,000	Representation, receptions and internal meetings
	<b>Title 1 - Total</b>	<b>6,330,000</b>	<b>6,330,000</b>	
	Heading Title 2	Financial year 2019		Comments
Chapter		Commitment Appropriations (CA)	Payment Appropriations (PA)	
20	Office building and associated costs	756,000	756,000	Rent, works, common/IMI charges and parking. Additional costs: indexation, insurance, water/gas, electricity, heating, maintenance + repairs, security and surveillance.
21	Information technology purchases	779,000	779,000	IT purchases, software licences, software development, IMI website.
22	Office equipment (movable property and associated costs)	153,000	153,000	Purchases and rental of office equipment, maintenance and repair.
23	Current administrative expenditure	123,000	123,000	Office supply. Literature, subscriptions, translation services, bank charges and miscellaneous office expenditure.
24	Telecommunication and postal expenses	78,000	78,000	Data communication such as telephone, video conferences and postal services.
25	Expenditure on formal meetings	158,000	158,000	Official meetings such as SRG, Scientific committee, Governing Board and working groups created by GB.
26	Administrative costs in connection with operational activities	388,154	388,154	Expenditure in connection with research activities and objectives of IMI (workshops, meetings and events targeting IMI projects).

	Heading Title 2	Financial year 2019		Comments
Chapter		Commitment Appropriations (CA)	Payment Appropriations (PA)	
27	External communication, information and publicity	625,000	625,000	External communication and events such as Info Days, stakeholder forums.
28	Service contracts	730,000	730,000	Studies, audits.
29	Expert contracts and cost of evaluations	900,000	900,000	Costs linked to evaluations, expert contracts.
	<b>Title 2 - Total</b>	<b>4,690,154</b>	<b>4,690,154</b>	
	<b>Total administrative costs Title 1 + Title 2</b>	<b>11,020,154</b>	<b>11,020,154</b>	

	Heading Title 3	Financial year 2019		Comments
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
30	Implementing the research agenda of IMI2 JU	262,212,585	186,910,765	Grant agreements - Payments
C2	Appropriations carried over from 2018	114,341,000		The amount carried over from 2018
	<b>Total operational costs Title 3</b>	<b>376,553,585</b>	<b>186,910,765</b>	
	<b>Total contributions</b>	<b>387,573,739</b>	<b>197,930,919</b>	

An overview of the 2019 budget and structure per budget lines is set out in the table below:

Expense budget line	Description	Commitment appropriations	Payment appropriations
A01100	Staff in active employment and costs linked to employment	3,959,000	3,959,000
A01101	Family Allowances	374,000	374,000
A01102	Transfer and expatriation allowance	405,000	405,000
A01110	Contract Agents	636,000	636,000
A01111	Seconded National Experts	0	0
A01130	Insurance against sickness	98,000	98,000
A01131	Insurance against accidents and occupational diseases	15,000	15,000
A01132	Unemployment insurance for temporary staff	39,000	39,000
A01133	Pension	0	0
A01140	Birth and death allowance	10,000	10,000
A01141	Annual travel costs from the place of employment to place of origins	59,000	59,000
A01144	Fixed local travel allowances	3,000	3,000
A01149	Other allowances	0	0
A01172	Cost of organising traineeships within IMI2 JU	32,000	32,000
A01175	Translation and typing services and work to be contracted	0	0
A01177	Other services rendered	5,000	5,000
A01178	PMO fees	45,000	45,000
A01180	Sundry recruitment expenses	0	0
A01181	Travelling expenses (taking up duty)	5,000	5,000
A01182	Installation allowance	43,000	43,000
A01183	Moving expenses	0	0
A01184	Temporary daily allowance	10,000	10,000
A01190	Weightings (correction coefficient)	2,000	2,000
A01191	Salaries adaptation	0	0
<b>11</b>	<b>Staff in active employment</b>	<b>5,740,000</b>	<b>5,740,000</b>
A01200	Miscellaneous expenditure on staff recruitment	20,000	20,000
<b>12</b>	<b>Staff recruitments - miscellaneous expenditure</b>	<b>20,000</b>	<b>20,000</b>
A01300	Mission expenses	190,000	190,000

Expense budget line	Description	Commitment appropriations	Payment appropriations
<b>13</b>	<b>Missions and duty travels</b>	<b>190,000</b>	<b>190,000</b>
A01401	Socio-medical structure, EU school	80,000	80,000
A01410	Other trainings	110,000	110,000
A01430	Medical service	5,000	5,000
A01440	Trainings covered by the SLA	6,000	6,000
A01490	Other interventions	159,000	159,000
<b>14</b>	<b>Socio-medical structure</b>	<b>360,000</b>	<b>360,000</b>
A01700	Representation expenses	20,000	20,000
<b>17</b>	<b>Representation</b>	<b>20,000</b>	<b>20,000</b>
	<b>Title 1 - Total</b>	<b>6,330,000</b>	<b>6,330,000</b>
A02000	Rentals	586,000	586,000
A02001	Guarantees	0	0
A02002	Contributions	0	0
A02010	Insurance	0	0
A02020	Water gas electricity and charges	131,000	131,000
A02030	Cleaning and maintenance	10,000	10,000
A02040	Furnishing of premises (works)	10,000	10,000
A02050	Security and surveillance	19,000	19,000
A02090	Other expenditure on buildings	0	0
<b>20</b>	<b>Office building and associated costs</b>	<b>756,000</b>	<b>756,000</b>
A02101	Hardware, infrastructure and related services	255,000	255,000
A02102	Software development, licenses and related services	524,000	524,000
A02103	Other expenses maintenance and repair	0	0
<b>21</b>	<b>Information technology purchases</b>	<b>779,000</b>	<b>779,000</b>
A02200	Purchase	123,000	123,000
A02201	Rentals	10,000	10,000
A02202	Maintenance utilisation and repair	20,000	20,000
A02203	Other office equipment	0	0
<b>22</b>	<b>Office equipment (movable property and associated costs)</b>	<b>153,000</b>	<b>153,000</b>
A02300	Stationery and office supply	40,000	40,000
A02320	Bank charges	0	0
A02321	Exchange rate losses	0	0
A02329	Other financial charges	0	0



Expense budget line	Description	Commitment appropriations	Payment appropriations
A02330	Legal expenses	0	0
A02350	Other operating expenditure	13,000	13,000
A02351	Petty expenses	0	0
A02360	Library stocks purchase of books and subscriptions	44,000	44,000
A02370	Translation interpretation	26,000	26,000
<b>23</b>	<b>Current administrative expenditure</b>	<b>123,000</b>	<b>123,000</b>
A02400	Correspondence and communication expenses	78,000	78,000
<b>24</b>	<b>Telecommunication and postal expenses</b>	<b>78,000</b>	<b>78,000</b>
A02500	Formal meetings	158,000	158,000
<b>25</b>	<b>Expenditure on formal meetings</b>	<b>158,000</b>	<b>158,000</b>
A02600	Administrative costs in connection with operational activities	47,154	47.154
A02601	Events	10,000	10,000
A02602	Workshops	325,000	325,000
A02603	Knowledge Management	6,000	6,000
<b>26</b>	<b>Administrative costs in connection with operational activities</b>	<b>388,154</b>	<b>388.154</b>
A02700	External communication	225,000	225,000
A02701	Events	300,000	300,000
A02702	Material	100,000	100,000
<b>27</b>	<b>External communication, information and publicity</b>	<b>625,000</b>	<b>625,000</b>
A02800	Ex-post Audits	536,000	536,000
A02801	Studies, consultancy	114,000	114,000
A02802	Audit services	80,000	80,000
<b>28</b>	<b>Service contracts</b>	<b>730,000</b>	<b>730,000</b>
A02900	Evaluation Experts meetings	750,000	750,000
A02901	Evaluation Facilities	150,000	150,000
A02902	Evaluations ENSO	0	0
<b>29</b>	<b>Expert contracts and cost of evaluations</b>	<b>900,000</b>	<b>900,000</b>
	<b>Title 2 - Total</b>	<b>4,690,154</b>	<b>4,690,154</b>
B03000	Implementing the research agenda of IMI1 JU	0	0
B03001	Call 1	0	0
B03002	Call 2	0	700,000
B03003	Call 3	0	1,000,000
B03004	Call 4	0	1,495,000
B03005	Call 5	0	7,000,000

Expense budget line	Description	Commitment appropriations	Payment appropriations
B03006	Call 6	0	6,350,000
B03007	Call 7	0	500,000
B03008	Call 8	0	7,000,000
B03009	Call 9	0	3,000,000
B03010	Call 10	0	800,000
B03011	Call 11	0	14,000,000
B03012	ENSO 2012	0	0
B03013	ENSO 2013	0	0
B03020	Implementing the research agenda of IMI2 JU	0	0
B03021	IMI2 Call 1	0	1,000,000
B03022	IMI2 Call 2	0	17,000,000
B03023	IMI2 Call 3	0	4,000,000
B03024	IMI2 Call 4	0	0
B03025	IMI2 Call 5	0	5,000,000
B03026	IMI2 Call 6	0	6,000,000
B03027	IMI2 Call 7	0	4,000,000
B03028	IMI2 Call 8	0	3,000,000
B03029	IMI2 Call 9	0	3,700,000
B03030	IMI2 Call 10	0	6,000,000
B03031	IMI2 Call 11	0	300,000
B03032	IMI2 Call 12	0	0
B03033	IMI2 Call 13	0	30,065,765
B03034	IMI2 Call 14	0	15,000,000
B03035	IMI2 Call 15	0	35,000,000
B03036	IMI2 Call 16	0	15,000,000
B03037	IMI2 Call 17	40,786,000	0
B03038	IMI2 Call 18	201,426,585	0
B03039	IMI2 Call 19	20,000,000	0
B03999	Recovery Ex-post audit	0	0
<b>30-C1</b>	<b>Implementing the research agenda of IMI2 JU</b>	<b>262,212,585</b>	<b>186,910,765</b>
B03033 - C2	IMI2 Call 13	114,341,000	
<b>30-C2</b>	<b>Implementing the research agenda of IMI2 JU</b>	<b>262,212,585</b>	
	<b>Title 3 - Total</b>	<b>376,553,585</b>	<b>186,910,765</b>
	<b>Total expenditures</b>	<b>387,573,739</b>	<b>197,930,919</b>

### 3.1 Staff Establishment Plan 2019

Grade	Establishment Plan 2018			Year 2019											
				Posts evolution						Organisational evolution			Establishment Plan 2019		
				Promotion / Career advancement			Turn-over (departures/arrivals)			New posts (per grade)			Requested (Budget)		
				PERM	TEMP	TOTAL	Officials	TA - LT	TA - ST	Officials	TA - LT	TA - ST	Perm	TA - LT	TA - ST
AD16															
AD15															
AD14		1	1											1	1
AD13															
AD12		2	2											2	2
AD11		2	2											2	2
AD10															
AD9		5	5		+1									6	6
AD8		7	7		-1	+1								7	7
AD7		4	4		-1									3	3
AD6		2	2		+2									4	4
AD5		10	10		-2									8	8
Total AD		33	33											33	33
AST11															
AST10															
AST9															
AST8		1	1											1	1
AST7															
AST6															
AST5															
AST4		2	2		+2									4	4
AST3		2	2		-2									0	0
AST2															
AST1		1	1											1	1
Total AST		6	6											6	6
SC6															
SC5															
SC4															
SC3															
SC2															
SC1															
Total SC		0	0											0	0
Overall Total		39	39											39	39

<b>Contract Agents Grade</b>	<b>2018</b>	<b>2019</b>
<b>FG IV</b>	2	2
<b>FG III</b>	12	12
<b>FG II</b>	1	1
<b>FG I</b>	0	0
<b>Total CA</b>	<b>15</b>	<b>15</b>

<b>Seconded National Experts</b>	<b>2018</b>	<b>2019</b>
	2	2

# Annex I - IMI2 Call 17 topics text

## Introduction

The Innovative Medicines Initiative is a jointly funded partnership between the European Union, represented by the European Commission, and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

The Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) has been created<sup>26</sup> following the principles below:

Research related to the future of medicine should be undertaken in areas where societal, public health and biomedical industry competitiveness goals are aligned and require the pooling of resources and greater collaboration between the public and private sectors, with the involvement of Small- and Medium-sized Enterprises (SMEs).

The scope of the initiative should be expanded to all areas of life science research and innovation.

The areas should be of public health interest, as identified by the World Health Organisation (WHO) report on priority medicines for Europe and the World<sup>27</sup>.

The IMI2 JU objectives are usually implemented through research and innovation actions (RIAs), and coordination and support actions (CSAs) where public and private partners collaborate, joining their expertise, knowledge and resources.

The initiative should therefore seek to involve a broader range of partners, including mid-sized companies<sup>28</sup>, from different sectors e.g. biomedical imaging, medical information technology, diagnostic and/or animal health industries. Involving the wider community in this way should help to advance the development of new approaches and technologies for the prevention, diagnosis and treatment of diseases with high impact on public health.

The IMI2 Strategic Research Agenda (SRA)<sup>29</sup> is the main reference for the implementation of research priorities for IMI2 JU. The scientific priorities for 2018 for IMI2 JU have been prepared based on the SRA.

Applicant consortia are invited to submit a proposal for each of the topics that are relevant for them. These proposals should address all aspects of the topic to which the applicant consortia are applying. The size and composition of each consortium should be adapted so as to respond to the scientific goals and the expected key deliverables.

Applicant consortia, during all stages of the evaluation process, must consider the nature and dimension of the IMI2 JU programme as a public-private collaboration.

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<sup>26</sup> Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU), OJ L 169, 7.6.2014, p. 54–76.

<sup>27</sup> [http://www.who.int/medicines/areas/priority\\_medicines/en/](http://www.who.int/medicines/areas/priority_medicines/en/)

<sup>28</sup> Under IMI2 JU, mid-sized companies having an annual turnover of EUR 500 million or less not being affiliated entities of companies with an annual turnover of more than 500 million; the definition of 'affiliated entities' within the meaning of Article 2(1)(2) of Regulation (EU) No 1290/2013 applies mutatis mutandis. Where established in an EU Member State or an associated country, are eligible for funding.

<sup>29</sup> [http://www.imi.europa.eu/sites/default/files/uploads/documents/About-IMI/research-agenda/IMI2\\_SRA\\_March2014.pdf](http://www.imi.europa.eu/sites/default/files/uploads/documents/About-IMI/research-agenda/IMI2_SRA_March2014.pdf)

While preparing their proposals, applicant consortia should ensure that the needs of patients are adequately addressed and, where appropriate, patient involvement is encouraged. Applicants should ensure that gender dimensions are also considered. Synergies and complementarities with other national and international projects and initiatives should be explored in order to avoid duplication of efforts and to create collaboration at a global level to maximise the European Union's added value in health research. Where appropriate, the involvement of regulators is also strongly encouraged.

Applicant consortia shall ensure that where relevant their proposals are in compliance with the General Data Protection Regulation (EU) 2016/679<sup>30</sup> and Clinical Trial Regulation (EU) 536/2014<sup>31</sup> (and/or Directive 2001/20/EC<sup>32</sup>) and any relevant legislation<sup>33</sup>.

Before submitting a proposal, applicant consortia should familiarise themselves with all Call documents such as the IMI2 JU Manual for submission, evaluation and grant award<sup>34</sup>, and the IMI2 evaluation criteria. Applicants should refer to the specific templates and evaluation procedures associated with the topic type Research and Innovation Actions (RIA).

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<sup>30</sup> Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), OJ L 119, 4.5.2016, p. 1–88.

<sup>31</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, OJ L 158, 27.5.2014, p. 1-76.

<sup>32</sup> Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (the "Clinical Trials Directive"), OJ L 121, 1.5.2001, p. 34.

<sup>33</sup> Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and the free movement of such data and implementing national laws, OJ L 281, 23.11.1995, p. 31–50.

<sup>34</sup> [https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2\\_ManualForSubmission\\_v1.7\\_November2018.pdf](https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2_ManualForSubmission_v1.7_November2018.pdf)

# Topic 1: Optimising future obesity treatment

## Topic details

Topic code	IMI2-2019-17-01
Action type	Research and innovation action (RIA)
Submission and evaluation process	2 stages

## Specific challenges to be addressed

The prevalence of obesity is increasing and affects more than 650 million people of all ages to become one of the foremost global health threats [3]. Obesity is complex. We only have a crude understanding of its underlying causes and biology, how to best describe and define it. Defining obesity as a disease has been debated over the past years and it is still not recognised as such in many countries. However, obesity is included in the WHO classification system ICD10 under 'Endocrine, nutritional and metabolic diseases' [2][3]. Obesity can be preventable, but once it has occurred it is considered a chronic disease for which treatments/interventions are often inadequate. Currently we have no way of predicting who will respond to or benefit from what kind of treatment or intervention [4]<sup>35</sup>.

Obesity can seriously impair health through a broad range of complications such as cardiovascular disease, type 1 and 2 diabetes (T1D and T2D), cancer, musculoskeletal disorders, psychosocial imbalances, and reduced quality of life, and impacts the treatment of other conditions [5]. Weight reduction has been shown to have a positive effect on these co-morbidities and may increase the effectiveness of treatments specific for other co-morbidities. Lifestyle modification is an integral part of the weight management journey, but is often insufficient on its own, and can be complimented by pharmacological and surgical add-on treatments to achieve greater and more sustainable weight loss, as appropriate. It is likely that there are subgroups of patients that are more suited to certain types of treatment and results risk dilution of perceived efficacy unless these groups are identified and treatment is personalised. People with T1D have traditionally been thought to have low body mass index (BMI), but current research has shown otherwise [6]. The obesity prevalence in T1D is increasing faster than in the general population [7].

This topic focuses on multifaceted profiling of patients with obesity in order to define clinically meaningful and relevant subgroups as a premise for optimising future prevention and treatment of obesity and its complications. Stakeholders are expected to pool pre-existing observational and/or clinical data to establish a database with enough phenotypic granularity for a data-driven stratification of obesity into subgroups based on a set of operational parameters including subject characteristics, biomarkers<sup>36</sup> and questionnaires. The outcome of this proposal should work towards a common understanding and an aligned vocabulary among stakeholders to facilitate scientific, medical, economic, and political acknowledgement of obesity as a disease and the importance of weight loss and weight maintenance.

## Need and opportunity for public-private collaborative research

This initiative, based on a public-private partnership, provides a unique scientific opportunity to address the challenges of maximising the efficacy of preventing and treating obesity. The major advantages of using the IMI platform are the ability to address these challenges in an independent effort, to engage with multiple stakeholders that otherwise might not interact in this context such as academia, patient organisations, clinical researchers, pharmaceutical industry, food, diagnostic companies including small and medium-sized enterprises (SMEs) with knowledge and interest in obesity and its complications. Recognised academics in this field and a range of companies with expertise in obesity and its complications approaching this topic from each their own individual angle would be needed to optimally analyse and interpret the large pool of data and impact the obesity landscape. The industry partners contribute with the necessary expertise to ensure that the scope

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<sup>35</sup> In the context of this topic, treatment refers in a broad sense to a variety of different interventions for patients with obesity including lifestyle advice on appropriate diet and exercise alone or in combination with drugs or obesity surgery.

<sup>36</sup> Biomarkers should be understood in a wide sense, i.e. any measure that can be used for clinically meaningful and operational sub-classification of obesity, e.g. including the microbiome, should such data exist.

of the analysis is fit for the purpose of developing innovative treatment paradigms and medicines. The participation of patient organisations will ensure the relevance for patients and they should be actively consulted as a source of unique knowledge. Therefore, to ensure success of the action, it is important to engage with a broad range of stakeholders including patients, clinicians and decision makers.

## Scope

The scope of the topic is to identify pathophysiologically and clinically meaningful subgroups of obesity that will allow for optimisation of prevention and treatment of obesity and its complications. Establishing (or revisiting) a robust sub-classification may include the current use of body mass index as the best anthropometric measure, or alternatively waist circumference or waist-to-hip ratio; it may include a direct or indirect measure for the duration of disease (e.g. acknowledging the difference between paediatric onset obesity and decades of metabolic insult); genetics, phenotypes, markers of fatty liver disease, characteristics of the gut microbiota, and epigenetics, to name a few.

More specifically the objectives of the topic are to:

- establish a federated database by pooling of the baseline data from pre-existing cohorts from observational or interventional studies to achieve as broad and detailed information on patients with obesity as possible, including sufficient clinical phenotyping and multi-omics data;
- perform data-driven analysis of the federated database to identify and characterise patient subgroups and potential biomarkers for diagnosis, prediction of the development of complications, and potentially inform on appropriate type of and response to treatment as well as identifying markers for effective weight management;
- fill the gaps of information regarding selected biomarkers by reanalysing pre-existing biobank samples. Such biomarkers should be affordable and operational in the context of real-world clinical practise and clinical development of innovative medicines and other treatments;
- address specifically type 1 diabetes (T1D) and type 2 diabetes (T2D) as examples of conditions in which both clinical phenotype and treatment is influenced by obesity in an intricate manner, including public education about obesity in T1D. While there is a lot of data available on obesity in relation to T2D, there is little on T1D and obesity, therefore one focus will be on generating new knowledge on T1D<sup>37</sup>. As part of this, data sets from the T1D Exchange programme will be available;
- collect and integrate patient perspectives in relation to diagnosis and treatment of obesity to understand the need, perceived barriers and value of determining medical treatment for patients with obesity;
- conduct a shared value analysis among key stakeholders reflecting values and challenges within the obesity landscape for optimising treatment and prevention. Engagement of external stakeholders is encouraged to generate educational material to support a common understanding of obesity. The content could include determinants and consequences of obesity including weight management.
- establish a Patient Advisory Board including representatives from patient organisations in order to ensure that patient-driven research and insights relevant for the project are identified and considered within and across the different work packages.

## Expected key deliverables

The ambition is that the proposed topic should lead to:

- a federated database of pre-existing phenotypic characterisation that can be used for the funded action and sustained for future analysis (see below on estimate on size of database);
- a set of operational variables that can be used for stratification of obesity into clinically meaningful patient subgroups, i.e. subgroups that may require different or respond differently to treatment of obesity and its complications;

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<sup>37</sup> Corrigendum: applicants should note that the text under this bullet point has been updated to clarify the objective.



- a detailed description of the clinical characteristics and manifestations of the identified patients subgroups, and wherever possible any existing or expected differences in treatment preference, effect, size, and sustainability of the effect and safety;
- an algorithm based on the set of operational variables that can be used to identify subjects that require and respond differently to prevention and/or treatment of obesity in clinical practice;
- description of the impact of obesity on T1D and T2D in terms of patient characteristics, clinical manifestation, treatment and outcomes, whether similar or different from non-obese patients with T1D or T2D. Use of corresponding data from the federated database is expected to be very useful to contrast or balance these findings;
- documentation of patient preferences regarding diagnosis and treatment of obesity;
- a shared value analysis among key stakeholders and the establishment of a common understanding and vocabulary about obesity as a disease.

## Expected impact

Paving the way for an optimised and more personalised future obesity treatment, the identified patient subgroups should, where data are available, be analysed for treatment results, including weight loss and weight maintenance, and prevention and/or development of complications. Importantly, novel ways of defining and diagnosing obesity may also develop and detail the classification of obesity, and contribute to improving prevention, personalising health and lifestyle interventions, and weight management as well as the precision of evidence-based medicine and development of novel treatments. Deciphering the heterogeneity of obesity and the potentially differential effect of weight loss and weight maintenance should lead to:

- novel ways of describing and defining the obesity disease;
- potential for novel and innovative diagnostics for classification and evaluation of the obesity disease;
- increased understanding and respect for obesity as a chronic disease entity;
- increased potential to contribute to the development of more targeted prevention and lifestyle interventions;
- increased potential to develop targeted delivery of safe and effective treatments to clinically meaningful subgroups of patients with obesity;
- reducing the barrier of entry for innovative translational research and medicines development;
- improved clinical trial design;
- increased precision of evidence-based obesity medicine;
- better understanding of how to design effective measures to prevent and treat obesity based on its stratification into patient subgroups;
- increased understanding of the effect or lack of effect of weight loss on a broad range of obesity related complications;
- increased understanding of how obesity impacts other diseases as exemplified by impact on incidence, characteristics, treatment, costs, and outcomes of e.g. T1D.

Applicants should also demonstrate how their proposal will impact the competitiveness and industrial leadership of the European Union by, for example, engaging suitable SMEs.

## Potential synergies with existing consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap, duplication of efforts and funding.

The action generated by this topic should consider initiatives such as previous IMI projects and other projects, consortia that have addressed the compilation of cohorts from legal/ethical and technical/analytical perspectives e.g:

**EMIF** (European Medical Information Framework) <http://www.emif.eu/>,

**DIRECT** (Diabetes Research on patient stratification) <https://www.direct-diabetes.org/>

**RHAPSODY** (for precision therapy and prevention of diabetes) <https://imi-rhapsody.eu/>

**MetaCardis** (the role of gut microbes in cardiometabolic diseases) <http://www.metacardis.net/>

**Diogenes** (Diet, Obesity and Genes)

<http://www.diogenes-eu.org/>; [https://cordis.europa.eu/result/rcn/51783\\_en.html](https://cordis.europa.eu/result/rcn/51783_en.html)

**Joint Programming Initiative Healthy Diet for Healthy Life** (<https://www.healthydietforhealthylife.eu/>) with European Nutritional Phenotype Assessment and Data Sharing Initiative (<http://www.enpadasi.eu/index.html>) and the two projects: Confronting Obesity: Co-creating policy with youth: [https://cordis.europa.eu/project/rcn/216413\\_en.html](https://cordis.europa.eu/project/rcn/216413_en.html) and Science and Technology in childhood Obesity Policy: [https://cordis.europa.eu/project/rcn/214762\\_en.html](https://cordis.europa.eu/project/rcn/214762_en.html)

Data from these projects within the obesity and diabetes areas could also be of importance for the current topic.

In order to have the same federated database platform, the applicants should also consider interacting with the project **EHDEN** resulting from the topic European Health Data Network IMI2 – Call 12<sup>38</sup>, which will deliver an operational, federated network in order to have direct access to RWD for developing new or incremental services in healthcare area.

Likewise, IMI2 **PREFER** project should be considered regarding patient preference for preventive measures and treatment <https://www.imi-prefer.eu/>.

## Industry consortium

The industry consortium is composed of the following EFPIA partners:

- Novo Nordisk A/S (lead)
- Boehringer Ingelheim
- Sanofi

In addition, the industry consortium includes the following IMI2 Associated Partners:

- Juvenile Diabetes Research Foundation (JDRF)
- Obesity Action Coalition (OAC)
- T1D Exchange

The industry partners will bring in-depth knowledge in the fields of clinical pharmacology and translational medicine, clinical data management, bioinformatics analysis, and of obesity. The industry partners will also provide know-how and means to support the establishment of the federated database including legal advice, setting up the database, and making analysis feasible, accessible and sustainable over time.

Limited supplementary funding could be made available for supporting further analysis of biobanked samples and development of digital tools to assist physicians in subgrouping of patients based on the outcome of the analysis (to be discussed by the full consortium).

The industry consortium will provide access to the following observational cohorts:

### **Gutenberg Health Study (Univ. Med. Center Mainz, Germany)**

The Gutenberg Health Study (<http://www.gutenberg-gesundheitsstudie.de/ghs/willkommen.html>) [8] is a population-based, prospective, single-center cohort study including more than 15 000 subjects with 5- (completed) and 10 year (planned) follow-up that started in 2007 at the University Medical Center Mainz and is supported by Boehringer Ingelheim. Approximately 3 500 subjects with a BMI >30 kg/m<sup>2</sup> at baseline have

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<sup>38</sup> [http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2Call12/IMI2\\_Call12\\_CallText.pdf](http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2Call12/IMI2_Call12_CallText.pdf)

been included. The study focuses on cardiovascular diseases, cancer, eye diseases, metabolic diseases, diseases of the immune system and mental diseases. The study aims at improving the individual risk prediction for diseases, and includes a comprehensive data set comprising anthropomorphic characteristics, general health status, disease status, and clinical chemistry parameters. In addition, DNA, citrate/EDTA plasma samples, serum and urine samples have been banked and are available for -omics analyses. Access is granted to the Gutenberg Health data after review of specific research studies proposed by the selected consortium and release by the GH Steering Committee. Support for data analysis of the Gutenberg Health Study, as well as further biomarker research/validation by omics methods analysis of bio-banked samples, will be provided by Boehringer Ingelheim.

### **The T1D Exchange database**

The T1D Exchange clinical registry comprises data from about 35 000 children and adults with T1D in the U.S.; about 2/3 of adults and close to half of youth being overweight or obese. There is prospective 5-year-follow-up data and biosamples are available for a subset of the subjects [9][10]. The registry's aim is to characterise the population of adults and children with T1D in the U.S. with respect to diabetes history and medical history. The registry includes a comprehensive data set of anthropomorphic characteristics, general health status, disease and treatment status, and clinical chemistry parameters.

Anonymised data from clinical trial cohorts from industry partners can be made available supplementing the academic cohorts, e.g. for validation of findings or addressing specific research questions.

### **Indicative duration of the action**

The indicative duration of the action is 60 months.

### **Indicative budget**

The indicative in-kind and financial contribution from EFPIA partners and IMI2 JU Associated Partners is EUR 8 301 139.

This contribution comprises an indicative EFPIA in-kind contribution of EUR 7 100 000 and an indicative IMI2 JU Associated Partners in-kind contribution of EUR 1 201 139. The latter includes EUR 1 000 000 financial contribution provided by JDRF whose allocation will be decided by the full consortium at stage 2 when preparing the full proposal.

The financial contribution from IMI2 JU is a maximum of EUR 8 301 000.

### **Applicant consortium**

The applicant consortium will be selected on the basis of the submitted short proposals. The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium, which will join the selected applicant consortium in preparation of the full proposal for stage 2. This may require mobilising, as appropriate, the following:

- existing research activities either within public health or clinical services in the field of obesity treatment with interests in better defining phenotypes of obesity and their responses to treatment, and;
- expertise in e.g. anthropology, epidemiology, public health, health economics, data management and harmonisation, bioinformatics, systems medicine or multi-omics analysis, lifestyle treatment, public relations; healthcare professionals skilled in obesity care and/or research;
- access to general databases of obesity including both obese with or without T1D and T2D. In addition, since T1D is often juvenile onset and T2D is now becoming more frequent in adolescents, special attention should be paid to including childhood obesity cohorts;
- access to pre-existing clinical cohorts (expected total number from public and private data sets n=50 000) with as broad and detailed relevant phenotyping as possible and access to biobanked specimens for selected biomarker analysis wherever available (including documented informed consent), ideally including both childhood and adult cohorts across different ranges of obesity and when relevant different treatment approaches

The involvement of patient organisations is imperative to making findings relevant. They should be involved at least as advisors to the analysis and interpretation, and as advocates for the community outreach. In addition, the results from the project should be discussed in a dialogue with regulators.

Relevant SMEs with proven expertise are encouraged to participate in the applicant consortium. SMEs can be of great benefit to IMI projects and, inter-alia strengthen the competitiveness and industrial leadership of the European Union. Their involvement might offer a complementary perspective to industry and academia, and strengthen the long-term impact of the project. For these reasons, applicants should consider engaging SMEs throughout the proposal. Under this topic, the contribution of SMEs could be considered in providing expertise and activities such as data and knowledge management; project management with expertise and experience relevant to IMI2 JU/H2020 projects.

## Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the industry contributions and expertise provided below.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

The below architecture for the full proposal is a suggestion. The architecture of the full proposal should be designed to fulfil the objectives and key deliverables within the scope of this proposal. However, there are already from the participating partners some cohorts and data available that the applicants may want to consider how to include and analyse. A plan for aspects related to sustainability, facilitating continuation beyond the duration of the action should also be proposed.

In addition to being an active contributor to the key deliverables of the relevant work packages, the participating patient organisations will support communication internally and help disseminate information externally. The Patient Advisory Board is expected to meet with work package leads four times a year, either in person or via a teleconference. Both industry and academic partners are expected to contribute to Patient Advisory Board activities, and thus funds should be reserved for this purpose.

### **Work package 1 – Project management**

The goal of this work package is the overall project coordination including:

- financial management and monitoring of deliverables and milestones;
- legal and contractual management;
- ethics management.

### **Work package 2 – Data federation and database management**

The goals of this work package are as follows:

- provision of pre-existing observational and/or clinical data from obese and obesity-risk cohorts;
- provision of multi-omics data, where possible;
- converting data from different cohorts into a standard format;
- perform a quality control of biobanked cohort samples, before these are analysed for additional biomarkers (i.e. ensure standardised quality and fitness-for-purpose of the samples);
- harmonisation of anonymised and converted data into a common structure to be able to be pooled;

- making data accessible to database for analysis;
- construction of a federated database and establishment of suitable database analysis tools;
- database management and administration of users, permissions and security;
- ensure legal issues including data sharing agreements;
- develop plan for sustainability of database and ways to ensure creation of value from the project results beyond the project period.

### **Work package 3 – Systems biology and data analysis**

The goals of this work package are as follows:

- setup of a web portal and tools enabling analysis and visualisation of data, including an Application Programming Interface (API) for programmatic access for data analysis;
- perform integrative analysis across data sets and cohorts to identify the patient sub-groups;
- comparison of patient cohorts and identifying relevant gaps and biosamples for analysis;
- perform additional biomarker analysis in bio-banked samples for relevant gaps identified;
- identify and/or establish assays for analysis of biosamples.

### **Work package 4 – Analysis of T1D, T2D and obesity**

The goals of this work package are as follows:

- epidemiology: determine prevalence of overweight/obesity among people with T1D, T2D and obesity in general population, by demographic group (age, income, ethnicity), by lifestyle (diet, exercise frequency, etc.);
- characterisation of the obese phenotype in T1D, T2D and obesity;
- determine how obesity and its converse, weight loss, affect T1D, T2D and obesity disease characteristics, treatment effectiveness, clinical outcomes;
- identify mechanisms underlying the effect of obesity on T1D, T2D and obesity metabolism and outcomes toward the goal of developing improved treatments in the future;
- assess the effects of long-term obesity in people with T1D, T2D and obesity, and ‘metabolic memory’ phenotypes conferred by obesity that may persist even after weight loss;
- assess whether any of the above is distinct for T1D due to the autoimmune milieu and whether specific therapeutic strategies should be targeted or not;
- weight management in T1D, T2D and obesity: determination of effective therapeutic and lifestyle interventions for obesity prevention and weight loss in people with T1D, T2D and obesity;
- communication of findings to the public to educate all customers about T1D, T2D and obesity and to increase citizen and patient involvement in identifying relevant approaches and optimising study design.

### **Work package 5 – Patient preferences**

The goals of this work package are as follows:

- collection and generation of information on patient preferences in relation to the need, value and assessment of obesity treatment, taking the social, cultural and other environment of the patient into account;
- apply an analytic mindset and tools to synthesise a patient perspective to ensure the relevance and value to patients across the project. Liaise and collaborate with patients and key stakeholders to facilitate outcomes and learnings including educational material with relevant patient organisations.

### **Work package 6 – Shared value analysis and communication**

The goals of this work package are as follows:

- establish a network consisting of key internal and external stakeholders to engage in collaboration around obesity from public health and payers' perspective;
- conduct a shared value analysis to extract common values and challenges. Based on this analysis, generate a shared value package/communication to reflect current thinking among stakeholders;
- engage across work packages to shape communication and deliverables as relevant to address public health perspectives and support knowledge about obesity, prevention and treatment opportunities.

### **Industry contribution**

In summary, the industry consortium will provide the following to the project:

- access and support for analysis of the Gutenberg Health Study;
- access to the T1D Exchange data;
- anonymised data from clinical trial cohorts from industry partners supplementing the academic cohorts;
- in-depth knowledge in the fields of clinical pharmacology and translational medicine, clinical data management, bioinformatics analysis, and of obesity;
- know-how and means to support the establishment of the federated database including legal advice, setting up the database, and making analysis feasible, accessible and sustainable over time;
- limited supplementary funding for supporting further analysis of biobanked samples;
- limited supplementary funding of development of digital tools to assist physicians in subgrouping of patients based on the outcome of the analysis;
- management of the consortium including the Patient Advocacy Board.

### **Expected Applicant consortium contribution:**

In summary, the applicant consortium is expected to provide the following:

- pre-existing cohort data from patients with obesity and data from comparative non-obese patients;
- biobanked samples for analysis;
- data-driven analysis tools and expertise;
- follow-up analysis of data and definition of further biomarker analysis needs;
- generation of a subgrouping tool, e.g. an application based on a diagnosis algorithm including a measure of the confidence level of the suggested subgroup;
- bioinformatic expertise;
- public-health and public relations skills;
- capability of omics analysis;
- access to validated platforms for analysis of bio-samples;
- assay development;
- data reformatting and harmonisation.

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## Topic 2: Open access chemogenomics library and chemical probes for the druggable genome

### Topic details

Topic code	IMI2-2019-17-02
Action type	Research and innovation action (RIA)
Submission and evaluation process	2 stages

### Background and specific challenges to be addressed

In biomedicine, discoveries arising from novel enabling technologies and reagents have garnered a quarter of the Nobel Prizes for chemistry and medicine in this century. Among the myriad of these transformative techniques and reagents, bibliometric evidence shows that pharmacological modulators (chemical and biological probes) have both the greatest scientific citation impact, the greatest sway on exploratory biomedical research, and provide the best mechanism to understand the relevance of a protein as a potential drug target [1][1]. Indeed, the field of drug discovery and the development of new molecular entities are predicated on the availability of sound mechanistic principles. Unfortunately, our understanding of human disease remains inadequate, and as a result clinical success rates for novel mechanisms remain low. Currently only one out of ten clinical drug candidates reaches the Open Access Chemogenomics Library and Chemical Probes for the Druggable Genome market after an average of 10 years and at a cost of at least EUR 2 billion in R&D expenses per drug.

Ultimately, the most effective method of dramatically improving the efficiency of R&D is to initiate studies on the 'right' target, and this is possible only if we dramatically increase our understanding of disease mechanisms. Experts agree that genetics and big data are promising approaches to select the right target, the appropriate biomarkers and the patients that are most likely to respond to any given treatment. However, this promise is a long way from reality in most cases; experience has shown there still remains a difficult path from prioritising a candidate gene with human genetics through to a successful R&D project [1][2].

We urgently need to close the gap between establishing a genetic link and the underlying disease mechanism for potential drug targets, and, to this end, we believe that there is an immediate need to design a set of open access (*i.e.* unencumbered and free of intellectual property restrictions) chemical compounds for the entire druggable genome. The set, which would comprise an openly accessible chemogenomics library and selected high-quality chemical probes will provide scientists across the world with the tools to interrogate and validate independently new candidate genes identified by modern genetic studies and bioinformatics in a variety of informative biological systems [1][3][1][4][1][5][1][6][1][7] among which advanced, patient-derived assays will be the most relevant.

### Need and opportunity for public-private collaborative research

The creation of an open access set of tools with which to interrogate the entire druggable genome is a challenge of scale and breadth that cannot be solved by a single institution. Moreover, a partnership between EFPIA members, mid-sized companies, Associated Partner organisations, academia and SMEs will be essential to achieve this goal, as these institutions have complementary resources and expertise necessary for success. For example, industry has extensive medicinal chemistry and screening facilities, but these capabilities must be used in the context of biological validation, most commonly performed in academia. Access to patient samples that are genotyped and accompanied by their clinical histories must be accessed by involving physician scientists in academic institutions. New technological and experimental approaches will also be needed to speed up the process of creating new tool compounds. We also believe that impact is dependent on open science because a pre-competitive, shared risk investment model will allow the partnership to provide the wider community access to the generated reagents quickly and with no strings attached, thus amplifying its impact. Moreover, open science also better assures adherence to high standards of quality and the reproducibility of results (a major issue in biological research), with concomitant increases in productivity and innovation. Finally, through a public-private partnership, both funding and expertise will be highly leveraged.



## Scope

Currently, the druggable human genome is estimated to consist of at least 3 000 genes. This topic aims to generate potent, well-characterised, functional, small-molecule modulators for a significant number of these and, at the same time, lay the foundation for identifying a set of openly accessible (i.e. unencumbered from restrictions on use) tool compounds for the entire druggable human genome. With this set of chemical tools available, scientists will be poised to interrogate the latest findings emerging from big data approaches and human genetic studies, thus compressing time from gene discovery to target prioritisation, and ultimately to patient benefits. Importantly, although we imagine the consortium can make great progress by assembling and characterising pre-existing compounds into an initial chemogenomics set, this is not enough. It is imperative to fill the significant gaps by discovering and developing novel chemical tools/probes against under-studied proteins (or protein families) that may be involved in the initiation and progression of disease.

The overall aim of this topic will be as follows:

- establish a framework to assemble an open-access chemogenomics library for the druggable genome – namely a physical library supported by compound meta-data;
- further enrich the open access library by inventing new, deeply characterised chemical probes to selected specific protein families;
- develop open-access assays from well characterised human disease tissue with a special emphasis on immunology, oncology (including immune-oncology) and neuroscience to profile the chemical tools and chemical probes;
- establish sustainable infrastructure, with high priority on accessible platforms and appropriate governance, for prolonged discovery and dissemination of tool compounds, assays, and associated data, beyond the lifetime of this project;
- develop a communication plan to facilitate the dissemination of the compound sets and to ensure their appropriate use.

N.B. A chemogenomics library describes the use of target family-directed chemical libraries in target or cell-based assays as a means of accessing new areas of biology and accelerating drug discovery research based on the assumption that similar receptors bind similar ligands. Such sets, although containing compounds that individually do not fulfill the stringent criteria of a chemical probe, can still be used to interrogate multiple members of protein families to help prioritise the most therapeutically relevant ones that could then form the basis of a chemical probe project. In contrast, a chemical probe is a small molecule that modulates the function of a protein in a specific and selective way. The compound must exhibit a defined *in vitro* potency for a single target and possess a minimum 30-fold selectivity relative to other sequence-related proteins of the same family. Furthermore, the probe must be profiled against a standard selection of other unrelated, pharmacologically relevant targets and large protein families of relevance to drug discovery (specificity), and, finally, have demonstrated on-target effects in cells (cellular activity).

## Expected key deliverables

The consortium will generate an open access chemogenomics library consisting of about 5 000 compounds that cover roughly 1 000 protein targets (i.e. one third of the current druggable genome). Here, the term open access includes not only the right to publish findings using these tools, but also includes the unencumbered and pre-publication dissemination of the results, the tools themselves, the assay protocols, and all the associated data packages. This open access chemogenomics set will serve as a substantial head start on generating a library covering the entire druggable genome. In addition, the consortium will develop chemical probes for two to three jointly agreed target families with an initial focus on E3 ligases and solute carriers (SLCs), which may be carried out in partnership with existing IMI consortia, such as ReSolute. For this component, up to 100 novel, well characterised, high-quality chemical probes, as defined by leaders in chemical biology [1][5][1][6][1][7][1][8] are intended to be generated. To achieve this goal, the consortium will generate recombinant proteins, solve crystal structures, and establish all biochemical and cellular assays needed to ensure that the probes meet the established stringent quality criteria, including target engagement in cells [1][9]. Finally, the consortium will develop scientific and sociological mechanisms to extract biological and disease information from the chemogenomics libraries and chemical probes – and their targets. Given the technical issues that plague interpretation of data from established cell lines, we strongly believe that this will depend on accessing more relevant assays through which to profile the compounds. These assays must be shown to be reproducible, to be derived from genotyped and deeply phenotyped patient-derived tissue and the results to be made available

broadly, so that biological data from all the assays can be combined and mined [1][10]. The partnership is expected to develop around 20 novel human tissue-derived assays in three major therapeutic areas of immunology, oncology (including immune-oncology) and neuroscience and test tool molecules and chemical probes in these assays.

Project success will require the partnership to establish enabling infrastructure to generate the probes. This includes cell and biochemical assay panels for characterisation of the compounds, including off-target analysis, a complementary database and a modern, scalable compound store and compound logistics. In addition, the partnership must explore new technologies in the field of fragment-based screening and high-throughput proteomics to accelerate the process of tool compound generation and characterisation. Finally, the consortium will set up platforms that permit broader access to these technologies both from within and outside the consortium – so the community can participate and help achieve, or exceed, the projects goals.

With this proposal, it is planned to lay the foundation on which to build and organise a worldwide network of laboratories to generate chemical tools for the entire druggable genome. Outstanding scientific leadership will be required in order to achieve this vision. It is also envisaged that this endeavor will help identify new scientific opportunities, identify and build strategic partnerships with other projects (e.g. patient groups, international consortia, other IMI projects), and promote truly openly accessible science.

The chemogenomics library, the chemical probes, and the accompanying metadata (potency, selectivity, activity in cell-based assays) are intended to be open access, i.e. use of the compounds will be made available unencumbered, in a pre-publication state and free from restrictions on use. After quality control, assays and data generated by the consortium will also be made publicly available without restrictions. In addition, technologies developed throughout the project must be likewise non-exclusive, platform-oriented, ready for application, openly and freely available for use, dissemination, and commercialisation during and following the completion of the project. Finally, as part of a sustainability concept, the partnership will provide non-exclusive access to the synthetic routes of these compounds to large and/or mid-size vendors that are willing to distribute the chemogenomics library and/or chemical probes and their controls worldwide.

## Expected impact

This project will provide the wider academic community with unencumbered access to the highest quality tool compounds for a large number of novel targets, and the expected impact should therefore be transformative. Presently, many companies and organisations are already in the process of setting up their own chemogenomics libraries. Although these have the potential to be phenomenal resources for the companies, their utility is also limited: they are not widely available to academia, they are likely to overlap, and each compound set is not as deeply characterised as could be managed within a larger, more focused, more resourced and more transparent project. By making a high-quality, broader compound set available, the consortium will seed a massive community target prioritisation and target deconvolution effort [1][2]. Moreover, in providing chemical tools without restriction, the consortium will also make available tools to invent new assays and unencumbered starting points for probe development or drug discovery. The consortium's centralised, cell-based and biochemical assay panels will serve as a resource for the entire chemical biology community. The ability to access these capabilities will provide significant incentives for external scientists to contribute innovative compounds to the network, thus expanding the impact with donated resources. The cell and tissue platform with the high-quality, patient-derived cell assays will provide the opportunity for clinical scientists to undertake translational medical research and biomarker discovery, and will provide the roadmap for other clinical centers to access the libraries and make important translatable discoveries.

The availability of chemical probes to unprecedented targets will also open up exciting new research avenues. As an example, open access, novel E3 ligase binders will provide much needed starting points for the development of new protein-targeting chimeras (PROTAC). In addition, the research strategies undertaken in this topic may serve as a template for the technology development to expand the project to include tool generation for areas of the genome currently not considered as druggable.

The management and data infrastructure and the assembled global collaborative network will lay the foundation for unparalleled progress in providing high-quality, open-access tool compounds as a basis for reproducible research. Indeed, this topic has the potential to cause a fundamental shift towards a more open and pre-competitive approach to the costly field of target prioritisation and discovery without compromising the proprietary research models required in industry. Finally, the significant amount of freely accessible, high-quality data generated within this consortium will be a rich source for future analyses by data scientists.

Artificial intelligence and machine learning applications using high-quality data on highly diverse compounds across many pharmacological mechanisms will spur research in new fields of biology and generate a source of targets for proprietary projects in various therapeutic areas.

## Open access – additional dissemination obligation

Considering the specific nature of this topic, it foresees application of an additional dissemination obligation (IMI2 JU MGA art. 29.1). All results of this project will be made available to the scientific community by open access (i.e. unencumbered, pre-publication, and free from restriction on use). Open access parameters include not only the right to publish findings using these tools, but also the right to disseminate the tools, results, assay protocols, and all the associated data packages, including cell-based assays.

## Potential synergies with existing Consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap and duplication of efforts.

Therefore, the synergies with the following past and ongoing IMI1 & IMI2 projects could be considered by the applicants:

- Unrestricted Leveraging of Targets for Research Advancement and Drug Discovery (ULTRA-DD): <https://www.imi.europa.eu/projects-results/project-factsheets/ultra-dd>
- Research Empowerment on Solute carriers (ReSOLUTE): <https://re-solute.eu/>
- Open PHACTS (terminated): <https://www.imi.europa.eu/projects-results/project-factsheets/open-phacts>

Please note that during the project implementation phase the applicants could also consider other potential knowledge generated by the forthcoming projects under IMI2 JU:

- European Screening Centre: unique library for attractive biology (ESCuLab): [https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/open-calls/IMI2\\_Call12\\_CallText.pdf](https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/open-calls/IMI2_Call12_CallText.pdf)
- Development of a platform for federated and privacy-preserving machine learning in support of drug discovery: [https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2%20CALL%202014%20TOPICS%20TEXT\\_EN.PDF](https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2%20CALL%202014%20TOPICS%20TEXT_EN.PDF)

Synergies with the following European and international initiatives could also be highly relevant:

- Structural Genomics Consortium (SGC, <https://www.thesgc.org/>) that has in depth expertise concerning all aspects of this proposal;
- US National Institutes of Health initiative, Illuminating the Druggable Genome (<https://ncats.nih.gov/idg>), which will provide the bioinformatics tools to help improve the understanding of the properties and functions of proteins that are currently not well studied within commonly drug-targeted protein families;
- European Bioinformatics Institute (EMBL-EBI, <https://www.ebi.ac.uk/>) for data handling and analyses;
- Open Targets (<https://www.opentargets.org/>) for target identification;
- H2020 iNEXT consortium ([https://cordis.europa.eu/project/rcn/194892\\_fr.html](https://cordis.europa.eu/project/rcn/194892_fr.html)) for fragment screening;
- H2020 OpenRiskNet ([https://cordis.europa.eu/project/rcn/206759\\_fr.html](https://cordis.europa.eu/project/rcn/206759_fr.html)) for compound design;
- ERIC EU-OPENSREEN ([www.eu-openscreen.eu](http://www.eu-openscreen.eu)) for screening;
- ESFRI-consortium ELIXIR ([www.elixir-europe.org](http://www.elixir-europe.org)) for sustainable infrastructure for biological information;
- ERIC INSTRUCT ([www.instruct-eric.eu](http://www.instruct-eric.eu)) for structural biology infrastructure.

## Industry consortium

The industry consortium is composed of the following EFPIA companies:

- Bayer (project co-lead)
- Boehringer Ingelheim (project co-lead)
- Pfizer
- Servier
- Takeda

As part of this endeavour, each pharmaceutical industry partner is willing to contribute at least 10 high-quality chemical probe compounds from their current or previously terminated R&D projects; at least 50 chemogenomics tool compounds from their own compound collections; and support the development of a minimum of 5 chemical probes by in-kind (especially chemistry).

In addition, the industry consortium includes the following IMI2 Associated Partners:

- Diamond Light Source (UK)
- Ontario Institute for Cancer Research (Canada)
- The Montreal Neurological Institute at McGill University (Canada)
- The Royal Institute of Technology (Sweden)

## Indicative duration of the action

The indicative duration of the action is 60 months.

## Indicative budget

The indicative in-kind and financial contribution from EFPIA partners and IMI2 JU Associated Partners is EUR 30 257 000.

This contribution comprises an indicative EFPIA in-kind contribution of EUR 23 800 000, of which EUR 9 930 000 financial contribution to the beneficiaries receiving JU funding in the selected action and an indicative IMI2 JU Associated Partners in-kind contribution of EUR 6 457 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be non-EU/H2020 Associated Countries in-kind contributions.

The financial contribution from IMI2 JU is a maximum of EUR 27 935 000.

## Applicant consortium

The applicant consortium (academic groups and SMEs) is expected to demonstrate expertise, leadership and a proven track record in all scientific areas addressed in the topic, including:

- adherence to open-access principles, and expertise in developing and managing open-access projects, which are essential to provide unencumbered and pre-publication access to the chemogenomics tools, chemical probes, patient-derived assays, and associated data packages to the scientific community free of any restrictions on use;
- expression, characterisation and structure determination of soluble proteins, integral membrane proteins, and protein complexes in an integrated project at large scale;
- assay development across a large number of different proteins and protein classes, including cell-based target engagement assays;

- screening compound libraries at scale, using a variety of approaches including high-throughput, focused, computational, fragment and DNA-encoded libraries;
- 'hit-to-probe' capabilities, including using structure-guided methods to improve efficiency and systematic characterisation in relevant biophysical, biochemical, and especially cellular/phenotypic assays;
- strategies to systematically map the knowledge space of protein families, including developing computational approaches and physical reagents to facilitate cross-screening;
- generation, characterisation and dissemination of chemogenomics libraries, including systematic compound characterisation *in vitro* and in cells;
- establish quality-control metrics and both demonstrate and record their use in practice, including mechanisms to solicit independent input into quality;
- development of innovative technologies to speed up the generation of tool compounds, and innovative approaches to accelerate their wider adoption in academia and industry;
- development of strategies to ensure that chemical probes are appropriately used by the community in biological assays;
- track record of scientific success in partnerships with clinical centres, and success in managing contracts and ethical issues;
- track-record of obtaining project-specific ethical approvals for clinical research collaborations;
- using patient-derived samples to advance drug discovery in close cooperation with industrial partners, including the development of novel assays.

SMEs can be of great benefit to IMI2 JU actions and can strengthen the competitiveness and industrial leadership of the European Union. Their involvement in the action might offer a complementary perspective to industry and the academia, and help deliver the long-term impact of the funded action. For these reasons, applicants should consider engaging SMEs throughout the proposal. For example, under this topic, the contribution of SMEs would be considered beneficial for broad profiling of chemogenomics compounds and chemical probes.

Members of the applicant consortium are also expected to demonstrate excellence and a proven record of accomplishment (evidenced by collaborative publications) in establishing networks of recognised thought leaders in all relevant sectors indicated in the topic, including:

- a global network that spans medicinal chemistry, biological assays, human biology, experimental medicine and clinical research;
- proven track record of achieving high-value/high-impact outcomes catalysing research in pioneer target areas of drug discovery;
- ability and history of leveraging additional funds with diverse and international organisations, including patient groups, foundations, philanthropy and SMEs;
- history of making research output widely available and evidenced commitment to open science principles;
- mechanism in place to efficiently and effectively disseminate chemical and biological research materials (e.g. chemical probes, protein constructs, antibodies).

Members of the applicant consortium are expected to have successfully collaborated with a network of scientific researchers especially with industry and should demonstrate:

- previous impact on launching or adding value to internal drug discovery projects in the pharmaceutical industry;
- previous impact on providing the foundation for experimental medicine studies in the public sector;
- previous success in collaborations among networks of academics and SMEs – as evidenced through shared projects and co-authored publications;

- previous success in governing and managing large projects, including e.g. finance, intellectual property and inter-institutional contracts;
- a track record of consistently achieving (or even exceeding) milestones and deliverables on time and within budget;
- a track record of making new technologies widely available, for example as generally accessible platforms or commercial products;
- experience in managing varying interests of multiple stakeholders.

## Suggested architecture of the full proposal

The applicant consortium should submit a short proposal that includes their suggestions for creating the full proposal architecture, taking into consideration the industry contributions and expertise provided below.

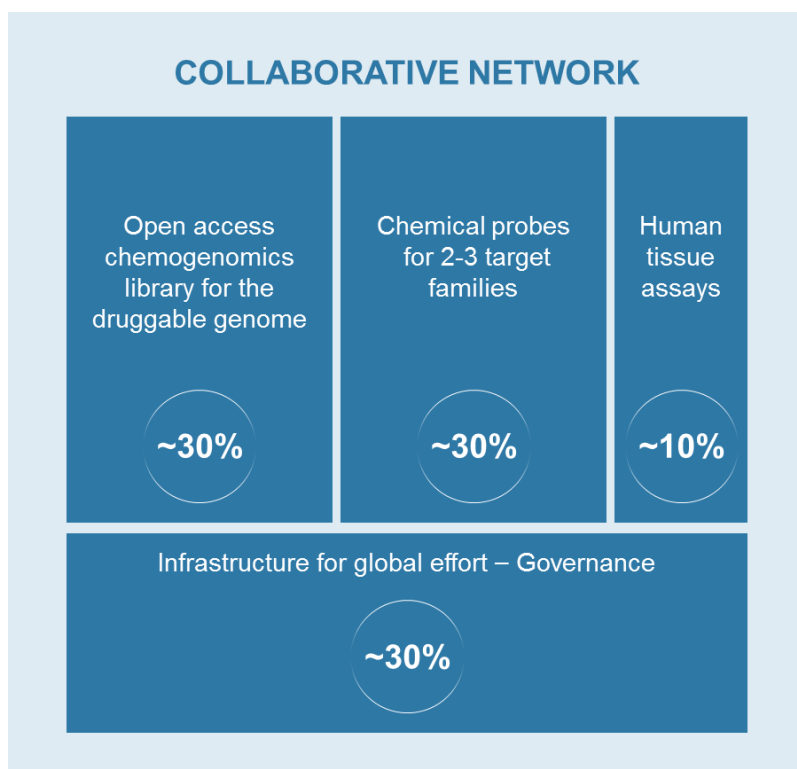
In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management.

The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

The full consortium will define project aspects such as governance, guiding principles and project plan. The architecture below for the full proposal is a suggestion.

A plan for aspects related to sustainability, facilitating continuation beyond the duration of the project should also be proposed.

The planned endeavour consists of four parallel pillars that include an underlying sustainable network infrastructure. The expected resource distribution to the four pillars is indicated below (% of overall resources):





## ***Pillar 1 – Open-access chemogenomics library for the druggable genome***

In the first pillar, it is planned to establish a chemogenomics library consisting of compounds meeting predefined target-specific criteria (biochemical activity, selectivity, physico-chemical profile sufficient for cell-based assays, evidence of cellular target engagement and no general cytotoxicity). To ensure transparency and quality, acceptance of compounds into this library will be governed by an arm's length committee of independent experts from academia. The acceptance criteria for Pillar 1 compounds (e.g. selectivity, potency) will not be as stringent as for chemical probes (Pillar 2 compounds), but because of the extensive annotation, Pillar 1 compounds will be very valuable for target prioritisation, target deconvolution, and as starting point for chemical probes. They will also enable a fast-track approach to develop drug leads for exciting new targets.

The following work packages are planned to achieve Pillar 1 goals:

### **Work package 1 – Collection of available compounds from academia and industry**

Deliverables: 30-100 mg of pure material for ~2 000 compounds identified and collected from the following sources meeting predefined criteria:

- compounds (1 000-2 000 compounds covering a variety of targets) identified and collected from known literature compounds;
- inclusion of openly available chemogenomics compound sets that fulfil stringent quality criteria;
- acquisition of compounds provided by participating pharmaceutical companies (at least 50 per participating EFPIA partner);
- compounds for selected target families generated within this IMI2 project (see Pillar 2);
- establish an independent review mechanism to assess the quality of the compound to be included in the set.

### **Work package 2 – Annotation of library compounds**

Deliverables:

- data packages necessary to enable use of the compounds in pre-clinical studies by scientists globally;
- making data available to the scientific community via a publicly accessible database (see Pillar 4, work package 10), either generated within the consortium, or in collaboration with an existing public partnership.

### **Work package 3 – New methods for chemogenomics compound generation and profiling**

Deliverables:

- protocols for novel and broadly applicable assay principles for biochemical, biophysical and cell-based assays to speed up generation of chemogenomics compounds and their characterisation;
- broadly applicable, novel technological and experimental approaches with the potential to speed up the hit-to-probe process by more than 6 months;
- generation of the remaining 2 000 to 3 000 compounds needed to cover one third of the druggable genome (assumption: 5 000 compounds needed to cover 1 000 targets, i.e. 1/3 of the druggable genome);
- establishing the strongest possible chemogenomics open source network of collaborations, allowing efficient sourcing of externally generated high-quality chemogenomics compounds and sets.

### **Industry and Associated Partner contribution to Pillar 1:**

- provide at least 50 chemogenomics compounds per EFPIA partner from proprietary compound collections as open access chemogenomics compounds; solid material for testing;
- compound profiling in established assay panels that are available within the companies;
- access (free of charge) to the Diamond Light Source (Associated Partner) platforms for external groups contributing to the project deliverables;
- membership in scientific and decision-making committees (e.g. definition of target family-specific criteria and assessment of candidate compounds).

### **Expected applicant consortium contribution to Pillar 1:**

- develop tools to identify chemogenomics compounds from patents, scientific publications and other sources;
- synthesis to provide solid material of chemogenomics compounds for testing;
- provide compound profiling to confirm that they meet the agreed upon criteria;
- experience in high-throughput, fragment-based screening;
- experience in covalent-ligand chemoproteomics approaches;
- assemble the remaining 2 000 to 3 000 chemogenomics compounds to cover one third of the druggable genome via internal activities or through collaborations and/or crowdsourcing;
- characterise selected compounds by determining three-dimensional protein-small molecule complex structures to high resolution and accuracy;
- membership in scientific and decision-making committees (definition of target family specific criteria; assessment of candidate compounds);
- manage independent peer-review mechanism to assess suitability of compounds for inclusion in the set.

### ***Pillar 2 – Chemical probes for 2 – 3 emerging target families***

For the second pillar, the aim will be to generate chemical probes for proteins within a minimum of 2-3 priority target families of high therapeutic interest. The initial priority will be on E3 ligases and solute carriers (SLCs), although we will not limit the scope to these target families. E3 ligases and SLCs were selected as initial priority families due to their high therapeutic importance, coupled with their relative intractability. This combination makes them ideally suited for a consortium-based approach for developing high-quality chemical tools. The inclusion of other target families will be agreed jointly by the consortium.

The number of chemical probes generated per family will depend on a number of considerations, including the strength of the genetic links to disease, experimental feasibility, therapeutic potential, as well as the number of members of the target family class. While working on probe projects, the consortium will also generate compounds that may not meet the stringent probe criteria but will be valuable as chemogenomics compounds thereby enriching the collection described in Pillar 1.

The following work packages are planned to achieve Pillar 2 goals:

#### **Work package 4 – Protein production**

##### Deliverables:

Validated protein expression clones, protein purification protocols, recombinant proteins for assay development and for 3D-structure determination; recombinant antibodies to facilitate assay development.



## **Work package 5 – Assay development for target engagement**

### Deliverables:

- protocols for target-specific biophysical, biochemical and cell-based assays and use of those assays for probe generation and confirming target engagement;
- genetically-engineered cell lines (such as knockout cells) to inform on target selectivity.

## **Work package 6 – Structure determination and chemical starting matter**

### Deliverables:

Generation of protein structures necessary to support probe generation. Depending on the target families selected, protein structures for both soluble and membrane proteins will be required. All protein structures generated in this project will be deposited in the Protein Data Bank (<https://www ww p d b . o r g />). In addition, fragment screens will be conducted to identify starting points for probe generation.

## **Work package 7 – Generation of chemical probes**

### Deliverable:

At least 100 well-characterised chemical probes, meeting stringent criteria for potency, selectivity and with demonstrated on-target effects in cells. This WP includes medicinal chemistry capabilities.

## **Work package 8 – Technology development**

### Deliverables:

Development of transferrable technologies for broadly applicable methods to speed up probe development and characterisation along the whole value chain from target selection to probe characterisation. This will include (but not exclusively) automation approaches, cloud-computing platforms, algorithms, parallelisation, reagents, devices, protocols and documentation.

### **Industry and Associated Partner contribution to Pillar 2:**

- design and access to fragment or other bespoke libraries;
- access to larger compound screening collections;
- high-throughput screening (HTS) or focused screens to identify hits;
- crystal-based fragment screening at Diamond Light Source (Associated Partner);
- access (free of charge) to the Diamond platforms for external groups contributing to the project deliverables;
- expertise in triage and validation of screening hits;
- design and synthesis of research chemical probes;
- medicinal chemistry to optimise hits;
- protein expression and purification for selected priority targets;
- assays (e.g. selectivity screening panels) and structure determination to support probe development;
- establish quantitative chemical probe criteria, in conjunction with the applicant consortium.

### **Expected applicant consortium contribution to Pillar 2:**

- ability to access chemical libraries from leading academic chemists and chemical biologists;

- small- and medium-scale screening of EFPIA partner chemical libraries;
- secondary biochemical screens to validate and prioritise hits;
- off-target biochemical and cell-based screens;
- crystallographic fragment screening and protein-ligand structure determination to support probe development;
- design and synthesis of chemical probes;
- medicinal chemistry to optimise hits;
- assays (e.g. selectivity screening panels) and 3D-structure determination to support probe development;
- high-throughput cloning, expression, purification, and novel 3D structure solution (if necessary);
- established quantitative chemical probe criteria, in conjunction with industry;
- technology development to improve quality and speed up the development and dissemination of chemogenomics compounds and of chemical probes.

### ***Pillar 3 – Human tissue assays***

All chemical probes and selected chemical tools will be subjected to unbiased phenotypic screening in patient-cell-derived assays for target validation in the human disease context. Specific assays will be in new and emerging areas of immunology (e.g. inflammatory bowel disease, scleroderma, interstitial lung disease, lupus, arthritis, and fibrosis in different organs), oncology (including immuno-oncology) or neurological areas (e.g. neuroinflammation and neurodegeneration). Assays developed previously in the Ultra-DD and other IMI programs might be leveraged and expanded to include new and emerging areas of research.

The following work packages are planned to achieve Pillar 3 goals:

#### **Work package 9 – Human tissue assays**

##### Deliverables:

- develop at least 20 novel human tissue-derived assays in three major therapeutic areas of immunology, oncology (including immune-oncology) and neuroscience. Selected established high-quality translational assays will be optimised and miniaturised and others (such as more complex co-culture systems) will be developed within the project;
- validate these assays by using tool molecules and test chemical probes, including gold-standard positive and negative controls. The cell-based assays will be derived from human material, such as blood and tissue biopsies;
- when possible and if scientifically appropriate, the consortium will convert primary cells into a renewable resource, such as human stem cells and spheroids as well as organoids;
- both primary and stem-cell derived cells will be deeply characterised phenotypically, and to the extent possible within the funding frame, also characterised by deep -omics technologies.

#### **Industry and Associated Partner contribution to Pillar 3:**

- contribute high-quality compounds for screening in these biological assays;
- provide scientific expertise and advice to support setup and develop the human tissue assays (including details on protocols, throughput formats and patient-genetic stratification for sample collection as needed);
- access to patient-derived assays for neurodegeneration;
- profile the compounds emerging from Pillars 1 and 2 above into assays and generate target validation data packages collaboratively with the consortium partners.

### **Expected applicant consortium contribution to Pillar 3:**

- network of target and disease experts to profile each probe in disease-relevant assays (e.g. immunology, cancer and neurology);
- access to patient-derived human material (fluids, blood, tissue, other);
- ethical and legal frameworks to engage in such collaborations;
- strategies to include genotyping and deep phenotyping of patient-derived cells and tissue;
- mechanism to characterise probes in other consortia with panels of cell-based assays, e.g. Sanger Institute (<https://www.sanger.ac.uk/>)  
NCI panel ([https://dtp.cancer.gov/discovery\\_development/nci-60/cell\\_list.htm](https://dtp.cancer.gov/discovery_development/nci-60/cell_list.htm))  
BTCure (<https://www.imi.europa.eu/projects-results/project-factsheets/btcure>)  
STEMBANCC (<https://www.imi.europa.eu/projects-results/project-factsheets/stembancc>);
- engage additional collaborators who are leading the field in functional cell assays and disease models for particular targets;
- mechanism to access additional, relevant phenotypic assay panels in priority areas.

### ***Pillar 4 – Infrastructure and governance to lay the foundation for a global effort on the whole druggable genome***

To establish an efficient and coordinated effort within this project, an additional goal of the fourth pillar is to align this project with similar projects or individual efforts globally, in order to reduce duplication of effort and to leverage the IMI investment. The consortium will work with global efforts to adopt such standards, and to this end, will establish or implement standardised, broad cell-based and biochemical assay panels to characterise chemogenomics compounds and chemical probes. The consortium will also establish a database for all data generated, as well as a central compound store and compound logistics (e.g. via a contract service organisation). The intention is for the chemogenomics library and the corresponding sustainable infrastructure to form the nucleus of a coordinated, worldwide, open-access effort to put together a reference compound library covering the entire druggable genome. Consequently, an important aspect of this project will be to provide leadership and a governance structure for the network, which will include investigators not only within the IMI consortium but also from complementary projects around the world. Although many members of the network will be working independently, and with independent funding, the aim is for all partners within the network to follow a jointly agreed masterplan to maximise synergies. In addition to the network, the consortium will find innovative ways to add compounds to the library, including e.g. setting up competitions for young scientists via crowdsourcing to add to the project deliverables. In summary, it is essential for the consortium to develop an international partnership comprising screening centres and chemical biologists around the world. We plan to encourage open-access publication of the results of the research in open-access scientific journals, help create platforms to share results, and work with commercial vendors to make the physical samples of tool compounds available for years to come to the biomedical community.

The following work packages are planned to achieve Pillar 4 goals:

#### **Work package 10 – Infrastructure and platforms**

##### Deliverables:

- compound logistics to handle distribution of all chemogenomics compounds and probes as well as compound exchange between partners;
- more than 500 assays established/accessible to annotate chemogenomics compounds and probes generated within this project with a potential to test compounds from network;
- easily accessible database containing all data generated within this project with a potential to hold data from related endeavours; format suitable for chemists and biologists; these data will be generated and made accessible according to FAIR (findable, accessible, interoperable, reusable) principles;

- long-lived platforms and transferrable infrastructure (e.g. open source code, commercially available services, cloud-hosted servers) to make the new technologies available to a wide audience beyond the consortium;
- open access and dissemination framework established.

### **Work Package 11 – Global framework**

#### Deliverables:

- the framework for a global network with partners around the world that work on related goals, established with a governance structure that supports efficient collaboration and sustainability;
- partnership agreements with major European and international efforts in screening assay development; patient-derived cell assays, chemical screening, chemical probe generation and compound profiling;
- a process for recruitment and rigorous triage of external activity and contributions.

### **Work package 12 – Project management**

#### Deliverables:

A management and governance structure which ensures that the project completes all deliverables in a timely and efficient manner.

#### **Industry and Associated Partner contribution to Pillar 4:**

- director or senior scientist/manager to represent company on joint steering committee;
- experts in drug discovery to manage collaborations in specific scientific areas or on specific targets/target families;
- contributions to collaborative scientific meetings, management of internal versus external activities;
- advice, involvement or secondment on infrastructure development, e.g. compound management, database, platform technologies, partnering opportunities and governance framework.

#### **Expected Applicant consortium contribution to Pillar 4:**

- experienced managers to ensure that the key consortium deliverables are completed;
- senior scientists to manage project deliverables, to disseminate the project outputs and to engage in collaborations to maximise impact;
- database, loader and visualisation tools to enable open access use of all data generated in this project and within related initiatives; partnering with public databases (e.g. ChEMBL) if possible;
- development of compound logistics for this project and for related initiatives to enable easy access to the chemogenomics compounds and the chemical probes, e.g. in collaboration with established SMEs;
- management of finance, valuation of deliverables, communication etc;
- create international alliance of screening, probe generation and compound profiling initiatives and align toward consortium objectives;
- dissemination of results in the form of publications, meeting presentations, and via the consortium's website;
- screening assays for broad profiling, e.g. broad panels for kinases, G-protein-coupled receptors (GPCRs); assays for cell permeability and unspecific toxicity;
- plan for sustainability of infrastructure after the end of this project, e.g. via partnering with contract research organisations (CROs), national facilities and vendors.

## Sustainability

Sustainability measures beyond the duration of the proposed action should be considered based on the expected results generated by the action. At stage 2 the full consortium would have to propose a sustainability plan to be implemented during the project duration and including relevant resources and budget. Sustainability is of utmost importance for this project.

- The chemogenomics library and the chemical probes, and the existing and new data from their use, should be easily accessible on a continuous basis. The applicant consortium should have a convincing plan how to achieve this, e.g. via non-exclusive access to the synthetic routes of these compounds to vendors be they large, mid-size or even start-ups, that are willing to distribute the chemogenomics library and/or chemical probes and their controls.
- A significant investment in hardware, software and expertise for compound logistics, database and assay panels will be needed to make this project a success. To make best use of the investment, the applicant consortium should already have an initial plan for sustainability.
- This project is planned as part of a global initiative for creating an open-access chemogenomics library for the entire druggable genome. This ambitious goal, which is beyond the scope of this particular call, will not be achieved within the timeframe of this IMI project, thus, sustainability of the infrastructure and platforms is of utmost importance for the overall mission.

The applicant consortium should already have an initial plan for sustainability, e.g. via CROs that are interested to continue operations as part of their business or via letters of intent from universities or other research organisations concerning the continued use of the research tools and the infrastructure. A detailed plan will be developed and implemented within the project.

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## Topic 3: Intelligent prediction and identification of environmental risks posed by human medicinal products

### Topic details

Topic code	IMI2-2019-17-03
Action type	Research and innovation action (RIA)
Submission and evaluation process	2 stages

### Specific challenges to be addressed

Pharmaceuticals are present in the environment as a consequence of patient use, manufacture, and improper disposal. They predominantly enter the aquatic environment via patient use and are typically found in concentrations from sub-ng/l to a few µg/l [1].

In the European Union (EU) an environmental risk assessment (ERA) is required as part of the marketing application and approval for new drugs [2]. Currently the ERA is conducted late in drug development and often parallel to Phase III clinical trials and after significant investment. An ERA is triggered if the predicted environmental concentration (PEC) exceeds 0.01 µg/l. More focused, exposure-independent environmental assessments are also required if (i) the drug is highly lipophilic ( $\log D \geq 4.5$ ) and could fulfil the criteria for a persistent, bioaccumulative and toxic (PBT) chemical, and/or (ii) the drug is a potential endocrine disruptor that acts on the reproductive axis requiring tailored assessment. Chronic sub-lethal ecotoxicity testing has only been required since 2006 in the EU [2].

The growing regulatory and scientific concerns regarding pharmaceuticals in the environment have reached the point where some stakeholders are advocating:

- the inclusion of environmental hazard and risk within the patient-benefit evaluation that underpins the marketing authorisation of a drug;
- a catch-up scheme for medicines authorised for use prior to 2006 that lack comprehensive environmental assessments;
- increased transparency of environmental data;
- increased consideration of environmental properties in drug development (i.e. greener drug design).

The inclusion of environmental hazard and risks in the patient-benefit analysis challenges the current drug development paradigm where environmental testing is conducted parallel to Phase III clinical trials. Without validated tools to predict environmental risk earlier in drug development this could impact the availability of life-changing medicines to patients within Europe and impact the competitiveness of the industry. These tools can also be used to prioritise established pharmaceuticals for testing and tailor specific test requirements to conclude on environmental risk in an effective and efficient manner. Many of these concerns are captured within the current European Commission (EC) strategic review of pharmaceuticals in the environment (PiE) [3] and they form the foundation for this IMI2 JU topic.

Burns et al. (2018) [4] have already demonstrated that prioritisation approaches need to consider consumption, environmental exposure potential (generic and spatially explicit exposure), lipophilicity, mode of action, pharmacological potency, target conservation and read-across, in order to identify drugs of potential environmental concern and ensure that the right species are chosen for a tailored environmental assessment. The availability of tools and models to assist with the prioritisation of approximately 1500 legacy drugs that lack any environmental data for tailored ERAs has the potential to deliver significant animal welfare benefits and cost savings without compromising environmental protection. It is also important that a database of environmental information on active pharmaceutical ingredients (APIs) is maintained, developed and populated within iPiE-25 in a manner that maximises the transparency of ERA data to all external stakeholders, in order to help inform ongoing environmental monitoring campaigns and other scientific and regulatory activities. The availability of these data in the public domain would also reduce unnecessary

duplication of testing, including some vertebrate testing on fish, and reduce the number of conflicting environmental risk assessments that exist for some compounds. Additionally, the same tools and models used for prioritisation could be used to predict the risk of human metabolites of APIs.

## Need and opportunity for public-private collaborative research

A public-private collaborative research partnership is required to identify and manage the environmental risks of human medicinal products across the whole of their product life cycle as no single stakeholder can proactively manage and mitigate these risks alone. The holistic environmental stewardship of human medicines requires consensus across many stakeholders and technical experts, potentially including:

- regulatory agencies (i.e., European Medicines Agency (EMA), U.S. Food and Drug Administration (FDA), national environment agencies, European Commission's Directorate-General for Environment) may contribute publicly available information on registered APIs;
- EMA and the EC as key stakeholders can contribute to appropriate assessment designs to address the issue of PiE and deliver elements of the PiE strategy;
- inter-governmental organisations with responsibility for environmental health policy such as environmentally persistent pharmaceutical pollutants (e.g. United Nations Environmental Programme and the Strategic Approach to International Chemicals Management (SAICM), the Organisation for Economic Co-operation and Development (OECD));
- medicinal chemists and structural biologists to support ambitions for exploring the feasibility of greener drug design;
- specialised subject matter experts may identify and extract public data and populate a species diverse ecotoxicological database;
- academia may contribute by elaborating theoretical and hypothesis-driven experimental testing programmes to validate hazard or risk predictions, and define prioritisation parameters;
- experts in artificial intelligence and machine-learning specialists to support the identification of relationships at a systems-wide level that can act as predictors of environmental hazard and risk;
- environmental engineers including scientists from the waste water industry;
- social scientist community and socio-economists to determine the relative value society and patients place on safety, efficacy and environmental considerations versus access to medicines;
- patient-oriented organisations;
- physicians and pharmacists who have interests in the environmental impact of pharmaceuticals and association professional development training;
- independent consultants that may support the development of *in vivo*, *in vitro* and *in silico* tools for ecotox hazard identification, prioritisation and risk assessment;
- industry may provide input with reference to their large product portfolio, in particular test materials, pre-clinical and clinical data, unpublished ecological information, and contribute to experimental validation programmes.

## Scope

The overall objective of this project is to ensure the environmental safety of human medicinal products through patient use by providing innovative and predictive tools to:

- identify environmental hazards and risks associated with candidates in drug development;
- screen and prioritise established, 'legacy' pharmaceuticals for a tailored environmental assessment;
- make environmental data for human medicinal products more transparent to all stakeholders through the development of a publicly available database.



This project aims to validate approaches to prioritise the risks of human medicinal products. A recent review of prioritisation approaches is described in Burns et al. (2018; [4]) that could form the basis for strategies employed in this project. It is important that the predictive *in silico*, *in vitro* and *in vivo* tools and models:

- are extended to include other targets and endpoints in a wider range of taxa and environmental compartments;
- have their predictive capability maximised at a systems level through the application of innovative machine learning approaches and artificial intelligence innovation;
- are validated to understand their predictive capability and applicability domain;
- are assessed for their feasibility to be integrated earlier into drug development to flag environmental concerns sooner than within the current industry model; and
- are applied to established APIs that lack comprehensive datasets to address and prioritise concerns about the environmental risks associated with legacy medicinal products.

Thus, the focus of this project will be on developing methods and guidance for targeting predictions and screening assays on the various types of compound classes represented in the area of human pharmaceuticals. Whilst this project is primarily focused on environmental exposure pathways and associated risks for human medicinal products, some of the project outputs could have potential use in the prioritisation of veterinary medicines. The tools and models developed could also be used to help screen or set safe discharge targets for API manufacturing sites. To deliver these objectives the following issues or themes fall within the scope of the project:

- to work across a broad group of stakeholders including the pharmaceutical industry to define what constitutes a greener API;
- to weigh the feasibility of designing greener APIs with the priorities of patient efficacy and safety;
- to drive innovative approaches to assess environmental risks. Such innovative approaches should include: (i) improving the predictability and applicability of the fish plasma model, (ii) providing three-dimensional *in vitro* cell culture approaches to assess API uptake, metabolism, elimination and toxicity in fish as a key priority for the pharmaceutical industry given the high level of drug target conservation in fish, and (iii) applying artificial intelligence and machine learning approaches to improve comparative toxicological predictions between preclinical and environmental safety assessments. The tools being developed must have the potential to be applied much earlier within drug development than existing environmental assessments and possibly be aligned with ongoing preclinical drug, safety and metabolism assessments;
- to consider environmental impacts in other environmental taxa and for other environmental compartments beyond surface waters, e.g. groundwater, secondary poisoning etc.;
- to address concerns with off-target effects and the environmental relevance of these effects;
- to assess and determine the validity of the tools and models for underrepresented mechanisms-of-action (MOA) classes of APIs and define the applicability domain for the each of the tools and models according to OECD standards;
- to apply and validate the tools, models and methodologies developed with an ambition to assess at least 25 legacy APIs, including key metabolites, selected in agreement with key external stakeholders. It is expected that any ERA data for priority APIs identified, generated and validated in this project will be made publicly available outside the iPfE-25 programme;
- to maximise the knowledge generation potential of a pharmaceutical ecotoxicology/environmental database including the integration of predictive capabilities and maximisation of data accessibility and transparency to all stakeholders;
- to enable the pharmaceutical ecotoxicology/environmental database to capture spatially refined exposure assessments and measured environmental concentrations for prioritised compounds and the integration of tools and models to provide probabilistic or semi-probabilistic approaches to ERA;

- to develop a database as a central resource for the collation of ERA supporting data with the support of the EMA and national competent authorities, in order to minimise duplicate testing, particularly on vertebrates, and remove any requirement for inefficient monograph type approaches.

APIs that are potential sex steroid receptor agonists and antagonists have a categorical inclusion, and require a tailored ERA, hence these fall outside the remit of this topic call. Also given that antibiotics have a mode of action largely restricted to prokaryotic organisms and only require limited testing to conclude on environmental risk they don't require further consideration within this topic call. Finally, due to complexity of investigating environmentally relevant mixtures of APIs and other chemicals models should be developed and validated based on exposure to single compound exposures. However, it should be recognised that many of the tools and models being developed and validated in this project could be applied to mixture assessments.

## Expected key deliverables

The expected deliverables should be achieved during the 5-year duration of the funded project.

- Establish a clear definition of what constitutes a greener API and how feasible this ambition is relative to the priorities for patient efficacy and safety.
- Agreement on future ERA and risk prioritisation strategy with our key stakeholders (i.e. the EC and EMA) together with an associated socioeconomic impact assessment for the implementation of this strategy.
- Delivery of validated predictive models/tools together with supporting documentation and guidance that can (i) be integrated earlier within drug development and (ii) prioritise established or legacy APIs for a tailored ERA. The validated tools and models should be made publicly available and consider including:
  - clearly defined validity domain for each tool and model developed within the project and consideration of underrepresented classes of APIs within their validation;
  - the scientific basis for false negative and false positive predictions needs to be considered as do the different regulatory and industry tolerances for false predictions against regulatory decision making and its consequences for drug development;
  - tailored and definitive ERA data for approximately 25 APIs, including some key metabolites, that have been used to test, validate and refine the prioritisation framework and supporting guidance.
- An updated knowledge-driven ecotoxicology and ERA database with integrated software to support semi-probabilistic and probabilistic risk assessments. The fully transparent, long-term hosted and sustainable software should integrate mode of action/read across grouping with associated structural alerts, a wider coverage of APIs together with recommendations for an EU-wide Pharmaceutical Ecotoxicology Database supported by industry and the European Commission. These data are expected to be available in the public domain.

## Expected impact

The overall aim of this project is to apply innovative approaches to ensure the environmental safety of human medicinal products such that both (i) environmental concerns do not become a barrier to patient access to medicines, and (ii) the intended use of medicines does not pose an unacceptable risk to the environment.

This project aims to determine the extent to which human medicinal products pose a risk to the environment and to provide innovative tools and models to assess environmental properties earlier within drug development. Current empirical approaches to identify environmental hazard and risk are not suitable for integration earlier within drug development; they are long in duration and require significant test material, hence bespoke models trained and validated on actual pharmaceuticals may offer a genuine alternative.

The current European guidelines for environment risk assessment came into force in 2006 [2]. Therefore, human medicinal products authorised before this date have incomplete environmental datasets and often lack long-term chronic ecotoxicology data. It is estimated that approximately 1500 active pharmaceutical ingredients lack sufficient environmental data to conclude on the risks that they pose to the environment. Within the recommendations made by Deloitte [3] as part of the European Commission strategic review on pharmaceuticals in the environment, an ERA catch-up procedure was advocated for (all) legacy pharmaceuticals that lack data. To conduct a full Phase II Tier A ERA on all medicines authorised before 2006

equates to about EUR 1 billion worth of ERA testing, a significant amount of vertebrate testing, and would saturate the environmental CRO capacity to conduct such studies, in addition to testing for new APIs, for decades. Therefore, an intelligent approach to prioritisation and testing is required. The validation and implementation of such an approach through iPiE-25 could save the pharmaceutical industry more than EUR 500 million without compromising environmental protection. This is serious money and a resource that can be invested in developing innovative medicines for patients, in particular where there is an unmet patient need. This project aims to refine, extend, validate and implement these prioritisation approaches to ensure the environmental safety of established medicinal products.

The transparency and accessibility of environmental data for human medicinal products remains a concern to many stakeholders [3] and the current lack of visibility is resulting in duplicated regulation testing by the pharmaceutical industry within marketing applications. To maximise the transparency of environmental data to all stakeholders this project aims to develop an EU-wide pharmaceutical ecotoxicology database. The availability of environmental data (e.g. ecotoxicological endpoints) in the public domain will (i) help all stakeholders better understand the risks posed to the environment by human medicinal products, (ii) allow environmental chemists to present their monitoring work in the context of risk, and (iii) reduce duplication of environmental testing across the industry. The database will also enable the environmental risks of a human medicinal product to be actively managed across its product life cycle and help facilitate the industry extended environmental risk assessment (eERA) model.

Applicants should also indicate how their proposal will impact the competitiveness and industrial leadership of the European Union by, for example, engaging suitable small and medium-sized enterprises (SMEs).

## Potential synergies with existing consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap and duplication of efforts and funding.

Possible synergies and collaborations could exist with:

- the IMI iPiE Project (<http://i-pie.org/>) and the iPiE-SUM database (<https://ipiesum.eu/>)
- the EcoDrug database (<http://www.ecodrug.org>)
- the IMI eTox project (<http://www.etoxproject.eu/>)
- the United Kingdom Water Industry Research (UKWIR) Chemicals Investigation Programme
- the NERC-Defra Chemicals in the Environment directed research programme
- the NORMAN Network (<https://www.norman-network.net/>)
- ChemPop Project funded in the UK which will consider correlations and possibly causations of historical aquatic and terrestrial faunistic and floristic data with historical micro-/macropollutant presence
- US FDA Environmental Assessments European Medicines Agency and environmental data within European public assessment reports (EPAR)
- regulatory agencies developing the Japanese and Canadian ERA schemes
- Global Chemical Outlook of the UNEP (United Nations Environment Programme): <https://www.unenvironment.org/>
- EU Technology Plattform SusChem Europe: <http://www.suschem.org/>
- Start – Strategien zum Umgang mit Arzneimittelwirkstoffen im Trinkwasser: <https://www.researchgate.net/project/start-Strategien-zum-Umgang-mit-Arzneimittelwirkstoffen-im-Trinkwasser>

## Industry consortium

The industry consortium is composed of the following EFPIA companies:

- AstraZeneca (lead)
- Bayer
- BMS
- Eli Lilly
- GSK
- Novartis
- Roche
- Sanofi
- Servier

The industry consortium will contribute the following:

- expertise and experience in leading and managing large scale public-private partnerships;
- provide physico-chemical, ecotoxicology and environmental fate data that are regulatory compliant (provision of existing data by the industry partners does not count as in-kind support);
- drug discovery and development expertise;
- computational chemistry expertise;
- support for test compound selection and experimental design;
- synthesis of test materials (e.g. 14C API or metabolites) for validation work where existing material is not available;
- design and execution of environmental risk assessments that comply with EMA and FDA regulations;
- identification of appropriate assays to support tailored environmental assessments;
- techniques and statistical methodology development;
- expertise in regulatory sciences and in strategic approaches to collaborate with environmental authorities to introduce innovative environmental methodologies;
- legal expertise related to intellectual properties management and complex partnership co-development structures.

Specific industry contributions are listed under the relevant work packages (WPs) and need to be taken into account by the applicant consortia.

## Indicative duration of the action

The indicative duration of the action is 60 months.

## Indicative budget

The indicative in-kind and financial contribution from EFPIA partners is EUR 4 550 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be non-EU/H2020 Associated Countries in kind contributions.

The financial contribution from IMI2 JU is a maximum of EUR 4 550 000.

## Applicant consortium

The applicant consortium will be selected based on the submitted short proposals.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in partnership with the industry consortium which will join the selected applicant consortium in preparation of the full proposal for stage 2. Applicant consortia could consist of members from academia, SMEs and subject matter experts in environmental fate, toxicity, modelling and risk assessment. SMEs could include contract research organisations (CROs) providing regulatory compliant studies to support the validation work; alternatively, they could provide tools, assays, models or database development to help deliver the topic objectives. Scientists from regulatory agencies are also actively encouraged within the consortium and wider regulatory engagement will be invited via the formation of a scientific advisory board for iPiE-25.

This requires mobilising, as appropriate:

- experience in leading, managing and measuring impact of public-private partnership consortia;
- expertise in programme management and professional provision of project management services, administration, governance and compliance;
- communication expertise, preferably for stakeholder management of large-scale consortia;
- expertise in ecotoxicology, environmental exposure assessment and environmental risk assessment;
- expertise in environmental exposure modelling and approaches for semi-probabilistic and probabilistic environmental risk assessment;
- proven ability to generate regulatory compliant environmental risk assessment studies;
- expertise in mode-of-action-driven ecotoxicology;
- expertise in data management and curation, database development, data visualisation;
- expertise in the development and implementation of evidence-based decision software;
- social science experience to support engagement with stakeholders across the product life cycle;
- expertise in analytical and environmental chemistry to support environmental assessments and environmental monitoring;
- statistics and statistical modelling expertise relevant for the design and analysis of ecotoxicology and environmental monitoring studies;
- expertise in artificial intelligence and machine learning approaches to big data analysis;
- expertise in drug discovery and drug development;
- proven ability to impact environmental policy and regulation;
- expertise in assessing and judging the quality and relevance of ERAs and supporting studies.

## Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the industry contributions and expertise provided below.

In the spirit of the partnership, and to reflect how IMI2 JU Call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

The below architecture for the full proposal is a suggestion. The architecture of the full proposal should be designed to fulfil the objectives and key deliverables within the scope of this proposal.

### **Work package 1 – Determining the feasibility of greener drug design (year 1 and 2)**

One of the options identified within the European Commission strategic review of pharmaceuticals in the environment recommended an EU/industry co-funded initiative to promote the design of APIs that pose lower risks to the environment (Option 3; [3]), so-called ‘green drugs’. The overall aim of this work package is to determine the feasibility of greener drug design.

The goals of this work package may include:

- Consulting with stakeholders across the product life cycle of a human medicinal product to identify what range of properties may constitute a greener drug and its relative importance versus patient efficacy and safety, of which latter must be fundamental for human medicines. This consultation should include medicinal chemists, drug discovery biologists, drug safety and metabolism experts, environmental risk assessors (regulatory and industrial), pharmacists, physicians and patient groups. The focus should be based on risk rather than hazard alone and should consider looking beyond the final active pharmaceutical ingredient to consider environmental impacts across the product life cycle. We anticipate a stakeholder workshop to disseminate, discuss and refine the findings of this review.
- Identifying the specific challenges of integrating environmental considerations earlier within the drug discovery and development cycle. Specific consideration should be given to current innovation and best practice in drug stabilisation and drug delivery strategies, particularly for oral therapy, versus what may constitute a ‘green drug’.
- Reviewing and quantifying the anticipated impact that innovations in personalised medicines, nano-based therapies and biologically-based pharmaceuticals may bring to the environment [5].
- Identifying a series of potential ‘green’ interventions and an associated roadmap for implementation where environmental considerations could be integrated across the product life cycle to proactively manage environmental risks of human medicinal products together with a health and socioeconomic impact assessment. This should be illustrated with potential case studies where possible.

Industry members of the project will bring their knowledge of drug discovery and development, together with relevant strategies to improve drug stability and delivery to help determine the feasibility of greener drug design. Industry will also describe the financial risks, levels of attrition and the criteria for model/ toolbox integration earlier within the development life cycle. Industry will also contribute its environmental knowledge into the activities to define a greener medicinal product and actively participate in stakeholder events and workshops.

### **Work package 2 – Development of an EU-wide Pharmaceutical Ecotoxicology Database (years 1–5)**

To maximise the transparency of environmental data to all stakeholders this work package aims to develop an EU-wide pharmaceutical ecotoxicology and environmental fate database that captures (i) robust and reliable environmentally relevant toxicity thresholds for pharmaceuticals in a standardised format, and (ii) environmental risk assessments at an active substance rather than a product level to provide a view of environmental risk irrespective of product use.

The database should be knowledge-based and curated to ensure that the reliability and relevance of data is sufficient for regulatory decision-making. The database should also include decision-based reasoning and arguments for the inclusion/exclusion of data that can be open to scrutiny.

To help support a ‘reality check’ of predicted environmental concentration-based risk assessments, the database and associated software should support semi-probabilistic and probabilistic risk assessments that also include measured environmental concentrations and predictions from spatially explicit exposure modelling.

The fully transparent, long-term hosted and sustainable software should also integrate (i) mode of action/read across grouping with associated structural alerts, (ii) a wider coverage of pharmaceutical actives and (iii)



recommendations for how it can be migrated to a sustainable EU-wide Pharmaceutical Ecotoxicology Database supported by industry and the European Commission.

Industry members of the project will provide environment data to support the development of the database. They will also contribute to the design of the database and help identify the types of visualisation tools and outputs that can be built into the functionality of the database and associated software. Industry will also work with the European Commission and the European Medicines Agency to ensure the wider sustainability of the EU-wide Pharmaceutical Ecotoxicology Database.

### **Work package 3 – Tool-box development and refinement (years 1–4)**

This work package is focused on driving innovative approaches to (i) assess and identify environmental risk earlier within drug development and (ii) screen and prioritise the risks of established APIs that lack environmental data. It is expected that appropriate tools and models, such as the fish plasma model, will be extended to consider active pharmaceutical ingredients with a wider range of chemical properties and mechanisms of action. Such innovative approaches may include:

- improving the predictability and applicability of the fish plasma model through experimental validation accounting for plasma protein binding and availability [6];
- providing three-dimensional *in vitro* cell culture approaches or 'organs on a chip' to assess API uptake [7][8], metabolism [9], elimination and toxicity in fish as a key priority [10][11], given the high level of drug target conservation in fish [12];
- modelling internal API concentrations in wildlife species other than fish;
- applying artificial intelligence and machine learning approaches to improve comparative toxicological predictions between preclinical and environmental safety assessments [13][14]. Chronic ecotoxicity predictions integrating MOA would be particularly welcome. The tools being developed must have the potential to be applied much earlier within drug development than existing environmental assessment and possibly be aligned with ongoing preclinical drug, safety and metabolism assessments [15][16];
- considering environmental impacts in other MOA relevant environmental taxa and for other environmental compartments beyond surface waters, e.g. terrestrial risk assessment, irrigation and groundwater-related risks [17][18][19], secondary poisoning etc;
- addressing concerns with off-target effects and the environmental relevance of these effects;
- providing guidance how these tools can be integrated within a framework to prioritise established human medicinal products for a tailored environmental risk assessment.

Industry members of the project will partner across all aspects of the work package and provide appropriate expertise and generate test materials and where required new data to support model development. Industry will also help inform how the guidance can be pragmatically included within our existing business models.

### **Work package 4 – Validation of the prioritisation approach (years 1–5)**

This work package should validate the prioritisation approaches advocated by work package 3. It is important that the predictive tools and models are validated such that they can be integrated with confidence earlier within drug development and used to effectively prioritise established or legacy APIs for a definitive or tailored ERA. The validated tools and models should include:

- tailored and definitive ERA data for approximately 25 APIs, including some key metabolites, that have been used to test, validate the toolbox and refine the prioritisation framework and supporting guidance;
- supporting documentation and guidance;
- clearly defined validity domain for each tool and model developed within the project and consideration of underrepresented classes of APIs within their validation;
- integrating the new experimental data into this project database, thereby strengthening its power and coverage;

- a consideration of the scientific basis for false negative and false positive predictions and the different regulatory and industry tolerances for false predictions and the consequences for regulatory decision-making and drug development.

Industry members of the project will contribute across all aspects of this work package. This may also include the generation of new tailored ERA data specifically designed to support the validation approach.

#### **Work package 5 – Toolbox integration and guidance (year 2–5)**

Once the prioritisation approach has been validated the toolbox needs to be integrated where appropriate within the drug discovery and drug development pipeline, and within a formal framework to prioritise established human medicinal products. This work package will engage with relevant stakeholders across the product life cycle to implement this guidance.

Industry members of the project will contribute across all aspects of this work package.

#### **Work package 6 – Dissemination (possibly in conjunction with WP 7, year 1–5)**

Dissemination of the project structure as a whole, of the descriptions of work for all work packages, of intermediate results and of the final tools that will be developed within this project, by means of:

- a regularly updated project website, reporting on progress of the project;
- collation of publications;
- congress posters and presentations by members of the different work packages;
- at least one final conference where the overall results and produced tools from iPiE-25 will be presented to both subject matter experts and the interested public at large.

Industry members of the project will contribute across all aspects of this work package.

#### **Work package 7 – Coordination and management (year 1–5)**

Appropriate coordination and management activities are key components for rounding up the work plan. Scientific coordination will deal with strategic direction by gathering and reacting to new scientific ideas, optimising the use made of the project committees, and supervising work package leaders as they execute their role. It will also comprise the definition of quality policies and continuing assessment of the project's degree of success. Management will put all the contractual, administrative and financial mechanisms in place to ensure a smooth workflow during the project lifetime.

Industry members of the project will be embedded in partnership throughout the coordination and management of the project, its work packages and agreed milestones and deliverables; it is anticipated that an industry partner will co-lead each work package. Industry will also work with key stakeholders in the EC and the wider pharmaceutical industry to ensure the long-term sustainability of the database.



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## Conditions for this Call for proposals

All proposals must conform to the conditions set out in the H2020 Rules for Participation ([https://ec.europa.eu/research/participants/portal/doc/call/h2020/common/1595113-h2020-rules-participation\\_oj\\_en.pdf](https://ec.europa.eu/research/participants/portal/doc/call/h2020/common/1595113-h2020-rules-participation_oj_en.pdf)) and the Commission Delegated Regulation with regard to IMI2 JU <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0622&from=EN>.

The following conditions shall apply to this IMI2 JU Call for Proposals:

Applicants intending to submit a Short proposal in response to the IMI2 Call 17 should read this topics text, the [https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2\\_ManualForSubmission\\_v1.7\\_November2018.pdf](https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2_ManualForSubmission_v1.7_November2018.pdf) and other relevant documents (e.g. [IMI2 JU Model Grant Agreement](#)).

<b>Call Identifier</b>	<b>H2020-JTI-IMI2-2019-17-two-stage</b>
<b>Type of actions</b>	<b>Research and Innovation Action (RIA)</b>
<b>Publication Date</b>	<b>22 January 2019</b>
<b>Stage 1 Submission start date</b>	<b>22 January 2019</b>
<b>Stage 1 Submission deadline</b>	<b>25 April 2019 (17:00:00 Brussels time)</b>
<b>Stage 2 Submission deadline</b>	<b>07 November 2019 (17:00:00 Brussels time)</b>
<b>Indicative Budget</b>	
From EFPIA companies and IMI2 JU Associated Partners	EUR 43 108 139
From the IMI2 JU	EUR 40 786 000

## Call Topics

<p><b>IMI2-2019-17-01</b> <b>Optimising future obesity treatment</b></p>	<p>The indicative contribution from EFPIA companies is EUR 7 100 000</p> <p>The indicative IMI2 JU Associated Partners contribution is EUR 1 201 139</p> <p>The financial contribution from IMI2 JU is a maximum of EUR 8 301 000</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>IMI2-2019-17-02</b> <b>Open access chemogenomics library and chemical probes for the druggable genome</b></p>	<p>The indicative contribution from EFPIA companies is EUR 23 800 000</p> <p>The indicative IMI2 JU Associated Partners contribution is EUR 6 457 000</p> <p>The financial contribution from IMI2 JU is a maximum of EUR 27 935 000</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>IMI2-2019-17-03</b> <b>Intelligent prediction and identification of environmental risks posed by human medicinal products</b></p>	<p>The indicative contribution from EFPIA companies is EUR 4 550 000</p> <p>The financial contribution from IMI2 JU is a maximum of EUR 4 550 000</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>

## LIST OF ACRONYMS

Acronym	Meaning
ABAC	Accrual Based Accounting System
AD	Alzheimer's disease
AD (HR)	Administrator
AER	Average error rate
AMR	Antimicrobial Resistance
API	active pharmaceutical ingredient
AST	Assistant
AWP2018	Annual Work Plan 2018
CA (Budget)	Commitment Appropriation
CA (HR)	Contractual Agent
CDISC	Clinical Data Interchange Standards Consortium
CEOi	Global CEO Initiative
CFAST	Coalition for Accelerating Standards and Therapies
CFS	Certificates on Financial Statements
C-Path	Critical Path Institute
CPD	Continuing professional development
CRO	Contract research organisation
CSC	Common Support Centre
CV	Cardiovascular
DG AGRI	Directorate-General Agriculture and Rural Development (European Commission)
DG HR	Directorate-General Human Resources and Security (European Commission)
DG GROW	Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (European Commission)
DG RTD	Directorate-General for Research and Innovation (European Commission)
DG SANTE	Directorate-General for Health and Food Safety (European Commission)
DPO	Data protection officer
E&T	Education & Training
EBiSC	European induced pluripotent stem cell
EC	European Commission
ECA	European Court of Auditors
EDPS	European Data Protection Supervisor
EEG	Electroencephalograph
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHR	Electronic Health Record
EMA	European Medicines Agency
ERA	environmental risk assessment
ESFRI	European Strategy Forum on Research Infrastructures
EU	European Union
FDA	Food and Drug Administration
FG	Function Group
FTE	Full-Time Equivalent
fNIH	Foundation for the National Institute of Health
FP	Full Proposal
FP7	Seventh Framework Programme
FWC	Framework Contract
GA	Grant Agreement
GAP	Global Alzheimer's Platform
GB	Governing Board
GPCRs	G-protein-coupled receptors

Acronym	Meaning
<b>H2020</b>	Horizon 2020 is the financial instrument implementing the Innovation Union, a Europe 2020 flagship initiative aimed at securing Europe's global competitiveness. For more information, click here: <a href="http://ec.europa.eu/programmes/horizon2020/en/what-horizon-2020">http://ec.europa.eu/programmes/horizon2020/en/what-horizon-2020</a>
<b>HCT</b>	Human challenge trials
<b>Helmsley Charitable Trust</b>	Leona M. and Harry B. Helmsley Charitable Trust
<b>HR</b>	Human resources
<b>HTA</b>	Health Technology Assessment
<b>HTS</b>	High-throughput screening
<b>IAC</b>	Internal Audit Capability
<b>IAPO</b>	International Alliance of Patients' Organisations
<b>IAS</b>	Internal Audit Service of the European Commission
<b>ICC</b>	Internal Control Coordinator
<b>ICS</b>	Internal Control Standards
<b>ICT</b>	Information Communications Technology
<b>ILG</b>	Industry Liaison Group
<b>IMI1 JU</b>	Innovative Medicines Initiative 1 Joint Undertaking
<b>IMI2 JU</b>	Innovative Medicines Initiative 2 Joint Undertaking
<b>IMI JU</b>	Innovative Medicines Initiative Joint Undertaking
<b>iPS cells</b>	Induced pluripotent stem cells
<b>ISA</b>	Information System for Absences
<b>ITF</b>	EMA Innovation Task Force
<b>ITI-PF&amp;S</b>	Innovative therapeutic interventions against physical frailty and sarcopenia
<b>JDRF</b>	Juvenile Diabetes Research Foundation
<b>JUs</b>	Joint Undertakings
<b>KM</b>	Knowledge Management
<b>KPI</b>	Key performance indicator
<b>MAPPs</b>	Medicines adaptive pathways to patients
<b>MEP</b>	Member of the European Parliament
<b>MOA</b>	mechanisms-of-action
<b>MRI</b>	Magnetic resonance imaging
<b>MS</b>	Multiple sclerosis
<b>MTA</b>	Material transfer agreement
<b>ND4BB</b>	New Drugs for Bad Bugs
<b>NIMH</b>	National Institute of Mental Health
<b>OAC</b>	Obesity Action Coalition
<b>OECD</b>	Organisation for Economic Co-operation and Development
<b>OLAF</b>	European Anti-Fraud Office
<b>PA</b>	Payment Appropriation
<b>PEC</b>	Predicted Environmental Concentration
<b>PET</b>	Positron emission tomography
<b>PBT</b>	persistent, bioaccumulative and toxic
<b>PiE</b>	pharmaceuticals in the environment
<b>PM</b>	Person/month
<b>PMDA</b>	Pharmaceuticals and Medical Devices Agency
<b>PPP</b>	Public-private partnership
<b>PRO</b>	Patient reported outcomes
<b>QST</b>	Quantitative sensory testing
<b>R&amp;D</b>	Research and development
<b>RA</b>	Rheumatoid arthritis
<b>RAE</b>	Risk assessment exercise
<b>RCSA</b>	Risk and control self-assessment
<b>RepER</b>	Representative error rate
<b>ResER</b>	Residual error rate

Acronym	Meaning
RP	Reporting Period
SC	Scientific Committee
SAICM	Strategic Approach to International Chemicals Management
SEND	CDISC SEND Controlled Terminology
SGGs	Strategic Governing Groups
SMEs	Small and medium-sized enterprises
SLC	Solute carriers
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short Proposal
SRA	Strategic Research Agenda
SRG	States Representatives Group
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TA	Temporary Agent
TTG	Time to Grant
TTP	Time to Pay
US	United States
WHO	World Health Organisation
WP(s)	Work Package(s)



