



The Interim Evaluation of the Innovative Medicines Initiative 2 Joint Undertaking (2014-2016) operating under Horizon 2020

Experts Group Report

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*Research and
Innovation*

**The Final Evaluation of the Innovative Medicines Initiative Joint Undertaking (2008-2016)
operating under the 7th Framework Programme**

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Expert Group Report

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LIST OF ACRONYMS

BBI JU	Bio-based Industries Joint Undertaking
C-Path	Critical Path Institute
EC	European Commission
ECG	Electrocardiogram
EFPIA	European Federation of Pharmaceutical Industries and Associations
ELF	European Lead Factory
EMA	European Medicines Agency
EP	European Parliament
EU	European Union
FDA	Food and Drug Administration
FP7	Seventh Framework Programme
FTE	Fulltime equivalent
GB	Governing Board
GDP	Gross Domestic Product
GHIT	Global Health Innovation Technology Fund
H2020	Horizon 2020 financial instrument
ICT	Information and Communications Technology
IMI	Innovative Medicines Initiative
IP	Intellectual Property
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
JPIs	Joint Programming Initiatives
JPND	EU Joint Programme - Neurodegenerative Disease Research
JTI	Joint Technology Initiative
JU	Joint Undertaking
KPIs	Key Performance Indicators
NGO	Non-Governmental Organisation
PPP	Public Private Partnership
R&D	Research and Development
SC	Scientific Committee
SC1	Societal Challenge 1 (H2020)
SGGs	Strategic Governing Groups
SMART	Specific, Measurable, Achievable, Relevant, Time-phased
SMEs	Small and Medium sized Enterprises
SPH	Scientific Panel for Health
SRA	Strategic Research Agenda
SRG	States Representatives Group
SWOT	Strengths, Weaknesses, Opportunities and Threats analysis
TFEU	Treaty of the Functioning of the European Union
ToR	Terms of Reference
VC	Venture Capital
WHO	World Health Organisation

Abstract

This report summarises the interim evaluation of the public private partnership Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU), that started in 2014 as a follow up to the first IMI JU. The evaluation period covers activities until 31 December 2016. In general, IMI2 JU was meant to support the competitiveness and leadership of the European (pharmaceutical) industry and to improve European citizens' health. In addition to these general objectives the Council Regulation stated more specific objectives.

An expert group was formed and asked to assess the effectiveness, efficiency, relevance, coherence and added value of IMI2 JU. For this purpose numerous documents and data were consulted, including results from a survey of beneficiaries and from a public consultation. Interviews with representatives of the different stakeholder groups provided deeper insight. The findings were evaluated against the specific objectives outlined in the Council Regulation.

It was concluded that the IMI2 JU programme remains both relevant and justified. Positive contributions on the drug development process are expected, but results are yet to be realised as the first projects under IMI2 JU only started in 2014. The added value, especially with respect to socio-economic outcomes needs more time to become evident. To realise the ambitious and important goals set by IMI2 JU, the expert group suggested that the existing IMI framework may benefit from some improvements with a particular focus on how to encourage the involvement of other industrial sectors beyond pharmaceutical and existing healthcare industry.

Résumé

Le présent rapport résume l'évaluation intermédiaire du partenariat public-privé "Initiative en matière de Médicaments Innovants 2" (IMI2), qui a débuté en 2014, dans le prolongement de la première entreprise commune IMI. L'évaluation couvre les activités jusqu'au 31 décembre 2016. En règle générale, l'entreprise commune IMI2 est destinée à soutenir la compétitivité et le leadership de l'industrie européenne (produits pharmaceutiques), ainsi qu'à améliorer la santé des citoyens européens. En plus de ces objectifs généraux, le règlement du Conseil a indiqué plusieurs objectifs plus spécifiques.

Un groupe d'experts a été constitué et invité à évaluer l'efficacité, l'efficience, la pertinence, la cohérence et la valeur ajoutée de l'entreprise commune IMI2. À cette fin, de nombreux documents et données ont été consultés, y compris les résultats d'une enquête réalisée auprès des bénéficiaires et d'une consultation publique. Des entretiens avec des représentants des différents groupes de parties prenantes ont fourni des renseignements plus approfondis. Les conclusions ont été formulées par rapport aux objectifs spécifiques énoncés dans le règlement du Conseil établissant IMI2.

Il a été conclu que le programme de l'entreprise commune IMI2 reste à la fois pertinent et justifié. Des contributions positives au processus de développement des médicaments sont escomptés, mais les résultats effectifs sont encore à venir étant donné que les premiers projets au titre de l'entreprise commune IMI2 n'ont débuté qu'en 2014. La valeur ajoutée, notamment en ce qui concerne les résultats socio-économiques, a besoin de plus de temps pour devenir évidente. Pour réaliser les objectifs ambitieux et importants fixés par le règlement établissant l'entreprise commune IMI2, le groupe d'experts a suggéré que le cadre existant devrait bénéficier de certaines améliorations, notamment pour encourager l'implication de secteurs industriels autres que l'industrie pharmaceutique et des soins de santé.

Zusammenfassung

Dieser Bericht gibt einen Überblick über die Zwischenbewertung der öffentlich-privaten Partnerschaft für das Gemeinsame Unternehmen „Initiative Innovative Arzneimittel 2“ (IMI2 JU), die im Jahr 2014 begann, als Folgemaßnahme zu dem ersten IMI JU. Die Bewertung erstreckt sich auf die Zeit bis zum 31. Dezember 2016. Im Allgemeinen sollte das Gemeinsame Unternehmen IMI2 die Wettbewerbsfähigkeit und Führungsposition der

europäischen (pharmazeutischen) Industrie unterstützen und die Gesundheit der europäischen Bürger verbessern. Zusätzlich zu diesen allgemeinen Zielen hat die Verordnung des Rates spezifischere Ziele festgelegt.

Es wurde eine Expertengruppe gebildet um die Wirksamkeit, Effizienz, Relevanz, Kohärenz und den Mehrwert des Gemeinsamen Unternehmens IMI2 zu beurteilen. Zu diesem Zweck wurden zahlreiche Dokumente und Daten konsultiert, darunter auch die Ergebnisse aus einer Befragung der Begünstigten sowie einer öffentlichen Konsultation. Interviews mit Vertretern der verschiedenen Interessengruppen lieferten vertiefte Einblicke. Die Ergebnisse wurden anhand der spezifischen Ziele der Ratsverordnung bewertet.

Es wurde der Schluss gezogen, dass das Programm für das Gemeinsame Unternehmen IMI2 weiterhin sowohl relevant als auch gerechtfertigt ist. Positive Beiträge zur Arzneimittelentwicklung werden erwartet, aber Ergebnisse müssen erst noch erreicht werden, da die ersten Projekte unter IMI2 JU erst im Jahr 2014 begonnen haben. Der Mehrwert, insbesondere in Bezug auf sozioökonomische Ergebnisse, braucht mehr Zeit, um klar zu werden. Zur Verwirklichung der ehrgeizigen und wichtigen Ziele des Gemeinsamen Unternehmens IMI2 schlug die Expertengruppe vor, dass der bestehende Rahmen von einigen Verbesserungen profitieren kann, mit einem besonderen Schwerpunkt auf der Förderung der Beteiligung anderer Sektoren über die pharmazeutische und medizinische Industrie hinaus.

1. EXECUTIVE SUMMARY

This report presents the results of the interim evaluation of Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) performed by a group of independent experts in line with the Council Regulation. This report will be used to inform the European Parliament and Council, national authorities, the research community and other stakeholders about the outcomes of IMI2 JU generated up to 31 December 2016. The report contains recommendations to improve the implementation of the IMI2 JU under Horizon 2020. In addition, the report could serve as a basis for the *ex-ante* impact assessment of the next generation of joint undertakings.

The overall objective of this interim evaluation was to assess the progress and mid-term achievements of the IMI2 JU operation during the period 2014 to 2016.

The IMI2 JU is the follow-up of the Innovative Medicines Initiative Joint Undertaking (IMI JU further referred to as IMI1) that was established as a **Public Private Partnership (PPP)** between the European Union, represented by the European Commission (EC, public partner), and the European Federation of Pharmaceutical Industries and Associations (EFPIA, private partner). IMI1 was a Union Body, which became autonomous on 16 November 2009. IMI2 JU started in 2014 with its objectives modified based on the experience drawn from IMI1. The legal framework for IMI2 JU is consistent with the framework for Horizon 2020, with some exceptions related to the PPP nature of the joint undertaking.

The specific **objectives** of IMI2 JU were to support the development of pre-competitive research and innovation activities with the aim to strengthen Europe's competitiveness and industrial leadership and to address specific societal challenges, in particular those to improve European citizens' health and well-being.

The Council Regulation additionally specified that IMI2 JU should focus on **priority medicines identified by the World Health Organisation (WHO)** and increase the success rates of clinical trials. Actions under the IMI2 JU should lead to reduction of time to reach clinical proof of concept in medicine development, such as for cancer, respiratory, neurological and neurodegenerative diseases. The IMI2 JU is also expected to develop new therapies for diseases with high unmet need, such as Alzheimer's disease or with limited market incentives, such as antimicrobial resistance. Furthermore, IMI2 JU should develop diagnostic and treatment biomarkers linked to clinical relevance in various diseases and seek their approval by regulators. New biomarkers for initial efficacy and safety checks should be developed to reduce the failure rate of vaccine candidates in phase III clinical trials. The IMI2 JU should also improve the medicine development process by providing tools, standards and approaches to assess efficacy, safety and quality of regulated health products. Achieving the above objectives should **translate into socio-economic benefits for European citizens, improve the health of European citizens, increase the competitiveness of Europe and help establish Europe as the most attractive place for biopharmaceutical research and development.**

To realise the IMI2 JU objectives the European Union allocated a **budget** of EUR 1.638 billion, to be matched by EUR 1.425 billion contributions of EFPIA and EUR 213 million contributions from Associated Partners such as other industries that are not EFPIA members. Inclusion of non-pharmaceutical industries in IMI2 JU was introduced to respond to the transition of pharmaceutical research into digital, imaging and other supporting technologies.

The roles of the different **governing bodies** in IMI2 JU are clear and well defined. The **Governing Board (GB)** is the main decision making body for IMI2 JU and includes representatives of EFPIA and the European Commission. Different goals and modes of operations of industry and the public partner appeared to interfere with the efficiency of the decision making process. The GB members from the European Commission must report on socio-economic benefits of IMI2 JU to the European Parliament (EP), while the GB members from EFPIA represent interests of global pharmaceutical companies, which are focused on growth, net profit and bringing benefits to their shareholders.

The **IMI Executive Director** and his staff, referred to jointly as the IMI2 JU Programme Office are responsible for the operational management of the IMI2 JU. The GB and the Executive Director are supported by advisory bodies: the **Scientific Committee (SC)**, which gives input on the Strategic Research Agenda and call topics selection, and the **States Representatives Group (SRG)**, which serves as an interface between relevant national bodies and IMI2 JU. The SRG gives feedback in line with national priorities and compares

IMI2 JU activities with other programmes to avoid duplication. **The Stakeholder Forum** is an annual meeting of a broader community of IMI2 JU stakeholders that serves as a forum to exchange information and opinions, receive feedback from various stakeholder groups and promote the achievements of IMI2 JU. More recently thematic **Strategic Governing Groups (SGGs)** have been established as extra advisory groups to provide orientations for the translation of the SRA, and make the development of new topics more transparent and effective and to ensure a better uptake of projects results and strive to sustainability of project outcomes.

The **communication between governing and various advisory bodies** involved in IMI2 JU operations is critical for the implementation of the Strategic Research Agenda (SRA) and the realisation of the goals of IMI2 JU. The expert group identified improvements that could lead to more efficient and effective communication. In particular, a stronger interaction with the SRG could ensure better alignment between national and regional developments and priorities. Also better feedback from the GB on the relevance and impact of contributions from the SC is desirable, similar to the efficient communication of the GB with the SGGs.

The **Strategic Research Agenda (SRA)** for the period 2014-2024, focusses strongly on the development of new medicines, but also places an emphasis on the tools and methods needed to bring new medicines faster to patients. The health priorities to be addressed were aligned with the 2013 update of the World Health Organisation's 'Priority Medicines for Europe and the World', as specified in the objectives of the Council Regulation. By the end of 2016 IMI2 JU launched ten calls covering seven scientific areas from the SRA in 46 topics.

The **process of developing the SRA and call topics was considered by many stakeholders to lack transparency and to be dominated by EFPIA partners.** Most stakeholders reported that it was **unclear how to contribute to the development of the SRA or the development of the annual work programme.** Moreover, the top-down process of call topic design combined with the fact that there can only be one winning consortium, raised questions about the usefulness of the competition process.

Several sources reported that there have been **contacts prior to the evaluation between the leading industrial partners and the applicant consortium** and that some consortia may have been pre-formed. This situation had created a more advantageous position because the same starting information may not have been available to all. Some of the best European research groups indicated they were, for this reason, hesitant to reply to an IMI call for proposals. If certain partners are preferred, this should be transparent and indicated in the call.

There is a solid financial monitoring system of the projects, but there is no system in place to guarantee that the industrial commitments in the project will be maintained. A major risk to successful project execution was the premature withdrawal of EFPIA partners. Premature withdrawal of an EFPIA member from a project would have implications for both its content and on the budget commitments. Moreover, the calculation of the in-kind contributions was considered by a number of stakeholders to lack transparency. It was reported that often EFPIA companies are not willing to make time sheets available for auditing the in-kind contributions, claiming that it violated their confidentiality on engagement in other non-IMI projects which could lead to disclosure of unauthorised information. This issue was present for IMI1 and remains unresolved.

The calculation of the in-kind contributions from activities from outside Europe was also an important issue. The efficiency of the joint undertaking to support the competitiveness of the European pharmaceutical sector is questionable when the investments from outside Europe were taken into account, even though these are global companies that are making the investments.

The main achievement of IMI2 JU on which there was general consensus, was that since the joint undertaking started, collaborations between different competing global companies, SME's and academia became possible. These collaborations created trust and new partnerships, including partners from a number of expertise areas, such as patient representative groups or regulatory bodies, which are essential stakeholders for medicines to enter the market with quality, safety and efficacy guarantees and in the shortest possible time. Together with the available budget and long term strategy, these collaborations were considered an important asset for European pharmaceutical research. The IMI2 JU actions have also contributed to **access to research infrastructure.**

The large scale and ambition of the IMI2 JU projects, their long-term vision and strategy were also viewed positively. Although, at the same time, the scale and ambition of projects posed challenges for management and coordination, especially for **SMEs**. The involvement of SMEs (from the health sector or from elsewhere) to strengthen the EU's competitiveness has proven to be a challenge that was harder to solve than originally anticipated. The SME participation in IMI2 JU decreased by approximately 30% when compared with IMI1 and was 15 to 25% lower than in Horizon 2020 initiatives (without SME-specific instrument and IMI2 JU) in terms of participation and funding, respectively. It was, in general, difficult for biotech SMEs that are developing new products to get public funding in IMI2 JU, as these types of companies have limited activities in the pre-competitive space. It is questionable whether the focus on precompetitive space for funding is, therefore, the best way to proceed, if SME participation is desired. The creation of the right innovation ecosystem that covers the whole value chain may prove more effective than targeting only precompetitive research.

An additional barrier for SMEs in large consortia was that SMEs often lack human and financial resources and expertise to invest in consortium negotiations, especially on Intellectual Property (IP) issues. In contrast, assets created by IMI2 JU projects may still be beneficial for SMEs. IMI2 JU has made some efforts to facilitate the participation of SMEs. In contrast to IMI1, in IMI2 JU, the **IP regulation has been more fully aligned with the one of Horizon 2020** with only a few derogations. This alignment may have simplified the understanding of the IP policy, but still some limitations remain, because exclusive rights to project results, which are a prime requirement to attract venture capital, were not negotiable. This was a major disincentive to some of the best European actors against participation in IMI2 JU projects. The expert group advocates that the IP policies should include more flexibility to create more opportunities to agree exclusive rights to project results under specified conditions.

Another change from IMI1 was that IMI2 JU was now accessible to **mid-cap companies** to participate as a partner in the in-kind contributing consortium and also as an EU-funded beneficiary in the consortium. The benefit of being part of the industry consortium and contribution to the projects in kind is that this allows input into the design of the call topic and what is required to achieve specific goals. The accessibility to IMI2 JU projects for mid-cap companies was certainly considered an improvement, but the expert group noticed that some of the main players in Europe were still missing from the formed consortia. In addition, companies outside the biopharmaceutical sector were also still missing.

When the first IMI JU programme was launched it was clear that the **development of new medicines in the future will depend on the involvement of other sectors**, such as imaging, diagnostics, medical devices developers, and technology providers using electronics, IT, data management. Therefore, from the outset, IMI2 JU was given an additional mission to **broaden its action spectrum** and to try and include companies from beyond the biopharmaceutical sector. IMI2 JU actively promoted and communicated opportunities to involve sectors other than the pharmaceutical sector. However, it is questionable whether this effort was really in alignment with the accelerated development of innovation in medicine and with the arrival of new industries in the health market such as Google, Facebook, Samsung or Huawei.

The importance of big data in biomedical innovation is growing fast and induces a transformative shift in biomedical developments. A number of large companies, as well as SMEs and mid-cap companies working in these domains, are now present in Europe and aware of the tremendous potential of the health care market. Some of the projects and calls launched in 2016 reflected that digital technologies can play an increasingly important role in research and healthcare. Such IT companies have participated in other joint undertakings and H2020 programmes but currently seem reluctant to participate to IMI2 JU. Among the reasons mentioned for this reluctance was that the companies may prefer not to be represented by EFPIA as the sole overarching private partner in the joint undertaking. In addition, the companies would prefer to be eligible for funding as in some other programmes, rather than having to make in-kind contributions.

EFPIA's '**Partners in Research**' membership category **offered companies outside the pharmaceutical sector an opportunity to contribute to IMI2 JU as EFPIA members**. The IMI office claimed that IMI2 JU "has already been successful in attracting non-pharmaceutical companies". This assessment should be viewed with caution, as some of the main European leaders in medical imaging are still not involved in IMI2 JU projects. **The European pharmaceutical industry risks losing a substantial opportunity if it cannot meaningfully engage other industry sectors**. Non-European leaders in IT, internet or

electronics are already gearing up to dominate the health industry, which will be potentially detrimental to the objective of making companies in Europe market leaders.

One suggested approach to overcome some of these barriers could be to collaborate with the initiatives that have a tradition of funding technology providers, such as ECSEL JU, the Electronic Components and Systems for European Leadership Joint Undertaking. However, global companies are already very active in the health area and European pharmaceutical industries may need to react rapidly to embrace these technologies and move towards new biomedical developments.

A strong engagement with patients in IMI2 JU was evident. The **patient organisations appreciated the opportunity to participate in the design of projects**, which was not possible in other Horizon 2020 programmes. **IMI2 JU was successful in welcoming new Associated Partners**, not only patients organisations but also **private foundations**. Many of these organisations were based in the United States. Their involvement in IMI2 JU illustrated its role and achievements in making Europe an attractive place for medical research and the development of medicines.

The **regulatory bodies** were seen as major stakeholders to align with, or to include, in the IMI2 JU projects. Close collaboration with the regulatory bodies should bring added value to the alignment of project outputs with medical and patient needs and there was consensus that researchers, academics, small and medium-sized enterprises, the pharmaceutical industry and regulatory agencies should work together to ensure that medicines are authorised in a shorter timeframe whilst maintaining safety. Specific actions and consideration are therefore **needed to increase the participation of regulators in IMI2 JU projects**, especially in the early phases of medicine developments. The participation of regulatory agencies slightly increased from 16.9% of IMI1 projects to 20% of IMI2 JU projects, which was reflected in the budget allocation that increased from 0.8% under IMI1 to 1.0% of the total EU contribution in IMI2 JU. In IMI2 JU, in addition to EMA, seven national regulatory agencies from six countries participated in five projects, in areas covering vaccines, 'big data' to improve the care of patients with blood cancers, or haematologic cancers and access to beneficial treatments for the right patient groups at the earliest appropriate time in a sustainable fashion.

The major group of stakeholders driving the research projects in IMI2 JU came from **academia**, based in either universities or research organisations. Together, academia made up 68% of the EU-funded participants.

Analyses of the **geographical distribution** of EU-funded partners in the first 25 IMI2 JU projects indicated that only 24% of the projects had an EU-funded partner from a EU-13 country. More efforts will be needed to improve participation from all parts of Europe.

Unlike under IMI1, **projects under IMI2 JU did take sustainability of project outcomes under consideration** and this element was discussed from the start of the project. However, the idea of the need for sustainability of generated data, biobanks, patient material and various infrastructures beyond the funding period was not supported by all stakeholders, as some saw IMI2 JU more as an instrument to catalyse large-scale research, but not to maintain databases once the projects were terminated.

Many of the reported outcomes of IMI, however, were not measurable as a monitoring system based on **SMART** (Specific, Measurable, Achievable, Relevant, Time-phased) **Key Performance Indicators** (KPIs) remained absent from the process that assesses the outputs of IMI2 JU. Information on the outputs and results from IMI interventions therefore seemed primarily based on examples and success stories, and were qualitative rather than being supported by quantitative data. Importantly however, it should be taken into account that in this interim evaluation period, only 25 IMI2 JU projects have started and none of these have been finalised yet.

To date, since the establishment of IMI, the fast response to the Ebola outbreak in the IMI2 JU projects and progress made towards the development of an Ebola vaccine is the only example of bringing new, safer and more effective therapies or products to patients, and of reducing the time to develop such new products. However, specific achievement such as faster validation and approval of biomarkers because of early involvement of regulatory agencies or realising a reduction of time to reach clinical proof of concept as one of the objectives that would contribute to improving the European pharmaceutical competitiveness

cannot yet have been achieved because of the early stage of IMI2 JU. In this respect the **added value** for patients or society in general was currently **hard to demonstrate**.

IMI Programme Office and EFPIA representatives found it difficult to identify socio-economic outcomes and claimed that more time was needed before health indicators would suggest improvements. Nevertheless, the same sources argued that since its origin in 2008, **IMI may have contributed to resilience of the European pharmaceutical industry at the time of the crisis**, as the number of clinical trials and research remained stable across Europe following the crisis in 2008.

The lack of an accountable performance measurement system meant it was still not clear whether IMI2 JU was 'refuelling' the pharmaceutical industry in Europe, despite the fact that the actors in the IMI2 JU projects were mostly European based companies and European universities or research organisations, but there are no guarantees that the funded projects will lead to the development of new therapies in Europe.

It was stressed by the IMI Executive Director and his staff, EFPIA and GB representatives that **a long-term strategy was required before the joint undertaking will have a demonstrable positive effect on the European competitiveness of the pharmaceutical industry**.

In terms of **effectiveness**, an obvious question was whether the objectives of IMI2 JU could have been achieved using a smaller public budget or using the regular calls and instruments of the framework programme. A main argument in favour of IMI2 JU was that it produced a considerable **leverage of private funds**, albeit mainly in the form of in-kind funding, which could not be achieved under the regular framework instruments. It was firmly believed by IMI representatives, also from non-EU organisations, that IMI2 JU was envied elsewhere in the world and that, if the joint undertaking did not exist, there would be other joint ventures securing in cash financing for companies. However, the expert group suggested that it may be that another joint venture model could provide a simpler solution than the IMI2 JU framework.

The expert group concluded that **the reasons to create a PPP to strengthen the European pharma industry were valid and the goals were justified. Thanks to the joint undertaking, for the first time competing companies were collaborating in precompetitive research** and deciding together, which call topics should be launched to address challenges that a single company could not tackle. IMI2 JU was considered to be a unique initiative that has no counterpart elsewhere. However, the expert group was not totally convinced that the right framework conditions have been established to achieve those goals developed after IMI1 and that the more specific objectives of IMI2 JU are yet fully addressed. The expert group could **not identify quantitative data to support that sufficient efforts had been taken to maintain the European pharmaceutical industry at the front edge of innovation**, and whether the current organisation of IMI2 JU, with EFPIA as the leader and coordinator of projects for the industry, was able to adequately tackle new challenges. The potential benefits of the IMI2 JU programme with other instruments that could exist and be modified or could be created in the 9th Framework Programme should now be compared, to allow the European industry (including from non-pharmaceutical sectors) to adapt and meet the new challenges to develop medicines for the future benefit of patient populations in Europe.

2. INTRODUCTION

2.1 Purpose of the evaluation

Council Regulation 557/2014¹ establishing the Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) stipulated the Interim Evaluation of the IMI2 JU.

The results of this evaluation will be used to inform the European Parliament and Council, national authorities, the research community and other stakeholders on the outputs realised by the IMI2 JU operating under Horizon 2020 up until 31st December 2016.

¹ <http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32014R0557&from=EN>

The results of this evaluation will be used to:

- improve the implementation of the IMI2 JU under Horizon 2020,
- contribute to the formulation of the 2018-2019 IMI2 JU Annual Work Plans, and
- serve as a basis for the ex-ante impact assessment of the next generation JUs.

2.2 Scope of the evaluation

The underlying objective of this interim evaluation was to assess progress and mid-term achievements of the IMI2 JU operation during the period 2014 to 2016. It was a challenging objective considering that only a very limited number of projects were completed by the end of 2016. As stipulated in Article 32(3) of the Council Regulation 1291/2013, the interim evaluation of IMI2 JU should focus on the following main aspects:

- **Openness:** the extent to which the JUs enable world-class research that helps Europe drive in to a leadership position globally, and how they engage with a wider constituency to open the research to the broader society.
- **Transparency:** the extent to which the JUs keep an open non-discriminatory attitude towards a wide community of stakeholders and provide them with easy and effective access to information.
- **Effectiveness:** The progress towards achieving the objectives set, including how all parties in the public-private partnerships live up to their financial and managerial responsibilities.
- **Efficiency** (a requirement set in Article 25(3) of the Council Regulation 1291/2013): will consider the relationship between the resources used by an intervention and the changes generated by the intervention.

The evaluation panel also evaluated the progress of the joint undertaking towards the objectives set and the level of implementation of recommendations from the previous interim evaluations of the first IMI JU.

This report however does not cover the evaluation of the predecessor initiative IMI JU (also referred as "IMI1") as it is the subject of a specific and separate evaluation report.

3. BACKGROUND TO THE INITIATIVE

3.1 Description of the initiative and its objectives

3.1.1 IMI2 JU Legal Basis

The IMI2 JU is a Public Private Partnership between the European Union, represented by the European Commission (public partner), and the European Federation of Pharmaceutical Industries and Associations (EFPIA - private partner). The first IMI JU was set up by the *Council Regulation for the implementation of the Joint Technology Initiative (JTI) on Innovative Medicines*² on the basis of Article 187 of the TFEU.³ The first IMI JU was established under European Law until 31 December 2017. It is a Union Body, which became autonomous on 16 November 2009, meaning that it has the operational capacity to implement its own budget. Before the autonomy, the Commission was responsible for the management of the IMI JU.⁴

The joint undertaking was given a follow-up initiative to last until 31 December 2024 under Horizon 2020. This initiative was set up by the Council regulation No 557/2014 of 6 May 2014 on the establishing the Innovative Medicines Initiative 2 Joint Undertaking (hereafter called IMI2 JU, subject of the present evaluation)⁵.

² Council Regulation No 73/2008 (OJ L30 of 04.02.2008, p.38-51)

³ TFEU: Treaty on the Functioning of the European Union; Article 187 (ex-Article 171 of the EC Treaty): The Union may set up joint undertakings or any other structure necessary for the efficient execution of Union research, technological development and demonstration programmes.

⁴ Article 16 of the Council Regulation setting up the IMI JU

⁵ Council Regulation No 557/2014 (OJ L169 of 6 May 2014, p.54-76)

3.1.2 IMI2 JU Objectives

The objectives of IMI2 JU, when compared to IMI1, have been redefined to be more explicit (Box 1). The objectives of IMI1 were summarised in the Second Interim Evaluation Report of IMI1 as:

"The IMI JU objective is to remove bottlenecks and significantly improve the efficiency, effectiveness and quality of the drug development process, with the long-term aim that the European pharmaceutical sector produces safe, effective, innovative medicines more rapidly. It also aims at stimulating investment in the biopharmaceutical sector in Europe in order to leverage research capabilities in a sector where the EU traditionally enjoys a comparatively strong position. For the past two centuries pharmaceuticals have been a stronghold of the European industry and they still provide by far the largest contribution to the European trade balance in high-technology, R&D intensive sectors".⁶

The objectives of IMI2 JU are consistent with the first IMI1 to support the development of pre-competitive research and innovation activities with the aim of strengthening competitiveness and industrial leadership. In addition, the objectives were to address societal challenges, and in particular to help improve health and well-being in Europe. The Council Regulation, however, now further specified that the objectives of IMI2 JU were to focus on priority medicines identified by the World Health Organisation for which success rates of clinical trials should increase. In addition, activities of the JU should lead to reduction of time to reach clinical proof of concept in medicine development for diseases in the areas of cancer, respiratory, neurological and neurodegenerative conditions. The IMI2 JU was also expected to develop new therapies for diseases with high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance. Furthermore, it was specified that IMI2 JU should develop diagnostic and treatment biomarkers for diseases linked to clinical relevance and approved by regulators. New biomarkers for initial efficacy and safety checks should be developed to reduce the failure rate of vaccine candidates in phase III clinical trials. The IMI2 JU should also further improve the drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.

To realise the objectives, the European Union financial contribution to IMI2 JU was set to EUR 1.638 billion, of which EUR 1.425 billion was to match the contribution of EFPIA and EUR 213 million to match additional contributions from other Members, or from Associated Partners that could be industries other than pharmaceutical industries. This budget was set to respond to the transition of pharmaceutical research to include other companies, such as technology providers, diagnostics companies, or data handlers.

According to the Council Regulation, the joint undertaking will run until 31 December 2024, but to take into account the duration of Horizon 2020, all calls for proposals by the IMI2 JU will be launched before the end of 2020. Exceptions to this deadline may be possible, but only in duly justified cases may calls for proposals be launched until 31 December 2021.

⁶ Gambardella, A., Orsenigo, L. and F. Pammolli (2000): *Global Competitiveness in Pharmaceuticals: A European Perspective*. Published in: DG Enterprise, European Commission (2001)

Box 1 Objectives of IMI2 JU according to Article 2 Council Regulation (EU) No 557/2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking:

The IMI2 Joint Undertaking shall have the following objectives:

- (a) to support, in accordance with Article 25 of Regulation (EU) No 1291/2013, the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership or to address specific societal challenges in particular as described in parts II and III of Annex I to Decision 2013/743/EU, and in particular the challenge to improve European citizens' health and well-being;
- (b) to contribute to the objectives of the Joint Technology Initiative on Innovative Medicines, in particular to:
 - (i) increase the success rate in clinical trials of priority medicines identified by the World Health Organisation;
 - (ii) where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases;
 - (iii) develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance;
 - (iv) develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators;
 - (v) reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks;
 - (vi) improve the current drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.

3.1.3 IMI2 JU Governance

Current members of the IMI2 JU are the European Union and EFPIA. Any legal entity that supports research and development in a Member State or Associated country was eligible to become member, provided it contributes to the funding to achieve the objectives and accepted the Statutes of the joint undertaking.

As stipulated in the Council Regulation IMI2 JU had five bodies: the Governing Board, the Executive Director, the Scientific Committee, the States Representatives Group, and the Stakeholder Forum. The latter three are advisory bodies for the IMI2 JU. A schematic representation is given in figure 1 and table 1.

The Governing Board

The Governing Board (GB) comprises five representatives per member, while the Union holds 50% of the voting rights.

The Executive Director

The Executive Director is appointed by the GB and is a member of staff, appointed for three years, which may be extended on one occasion, for a period not longer than four years after an assessment.

The Executive Director is supported by the Programme Office (replacing the former Executive Office) for the execution of all tasks described in the new Council Regulation. The Programme Office comprises the staff of the IMI2 JU and has to carry out the following specific tasks (see Art. 9(5) of IMI2 JU Statutes):

- (a) provide support in establishing and managing an appropriate accounting system in accordance with the financial rules of the IMI2 JU;
- (b) manage the calls for proposals as provided for in the annual work plan and administer the grant agreements and decisions, including their coordination;
- (c) provide to the Members and to the other bodies of the IMI2 JU all relevant information and support necessary for them to perform their duties as well as responding to their specific requests;
- (d) act as the secretariat of the bodies of the IMI2 JU and provide support to advisory groups set up by the GB.

The Scientific Committee

The Scientific Committee (SC) should have a maximum of eleven members appointed for a renewable period of two years. The SC is expected to give advice, while taking activities under H2020 into account, on the content of the Strategic Research Agenda (SRA), on the annual work plans and on the annual activity reports.

The States Representatives Group

The States Representatives Group (SRG) should consist of one representative of each Member State or associated country and may invite observers to its meetings, such as representatives from regional authorities or SME associations. The SRG is meant to review information and provide opinions or recommendations on (Articles 11(3) and 11(5) of IMI2 JU Statutes):

- (i) programme progress of the IMI2 JU and achievement of its targets, including the information on calls and proposals evaluation process;
- (ii) updating of strategic orientation;
- (iii) links to Horizon 2020;
- (iv) annual work plans;
- (v) involvement of SMEs;
- (vi) technical, managerial and financial matters;
- (vii) annual plans, in particular when those matters affect national or regional interests.

This group should provide information and function as an interface with IMI2 JU on (Article 11(4) of IMI2 JU Statutes):

- (a) the status of relevant national or regional research and innovation programmes and identification of potential areas of cooperation, including deployment, to allow synergies and avoid overlaps;
- (b) specific measures taken at national level or regional level with regard to dissemination events, dedicated technical workshops and communication activities.

The GB should report to the SRG any follow up it has given to recommendations or proposals and give reasons if relevant, why these were not followed up.

The Stakeholders Forum

The Stakeholders Forum is open to all public and private stakeholders, and international interest groups. The Stakeholders Forum receives information about the activities of the IMI2 JU and is invited to provide comments.

The Strategic Governing Groups

In line with the Statutes of IMI2 JU (Art. 7(3)(p)), the GB of IMI2 JU introduced the Strategic Governing Groups (SGGs) as other advisory groups in 2014.⁷ The SGGs are established in order to ensure the coordination of the JU's work in certain strategic areas and to ensure that the development of new topics was more transparent and effective. As such, the SGGs are made up of representatives of companies active or interested in the area covered by the scope of the SGG as well as of representatives from the European Commission, the IMI2 JU Programme Office and the SC.

In 2016, the seven established SGGs were focused on the following areas:

- Neurodegeneration (ND)
- Immunology (Imm)
- Data and knowledge management (Data)
- Infections control (Infect)
- Diabetes / metabolic disorders (Metabo)
- Translational safety (Transla)
- Oncology (Onco)

The Scientific Panel for Health

In addition to the governance bodies described above the Council Regulation also specified that IMI2 JU should consult, where appropriate, the Scientific Panel for Health (SPH), although the panel was not formally part of the governance structure.

The Council Decision formulates it as (recital (25) of IMI2 JU Regulation):

'The Scientific Panel for Health was set up by Horizon 2020 as a science-led stakeholder platform in order to elaborate scientific input, to provide a coherent scientific focused analyses of research and innovation bottlenecks and opportunities related to the Horizon 2020 societal challenge on health, demographic change and well-being, to contribute to the definition of its research and innovation priorities and to encourage Union-wide scientific participation. Through active cooperation with stakeholders, it helps to build capabilities and to foster knowledge-sharing and stronger collaboration across the Union in that field. The IMI2 JU should, therefore, collaborate and exchange information with the Scientific Panel for Health, where appropriate.'

The IMI2 JU Programme Office continues to be housed in Brussels on the same premises as most of the JUs (Clean Sky2 (CS2), Fuel Cells and Hydrogen 2 (FCH2), Bio-Based Industries (BBI), Electronic Components and Systems for European Leadership (ECSEL), and Shift2Rail).

⁷www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_GB_DEC_2016_21_Decision_on_new_SGGs_Charter_SIGNED_30SEP2016.pdf

Figure 1: IMI2 Joint Undertaking Governance Structure

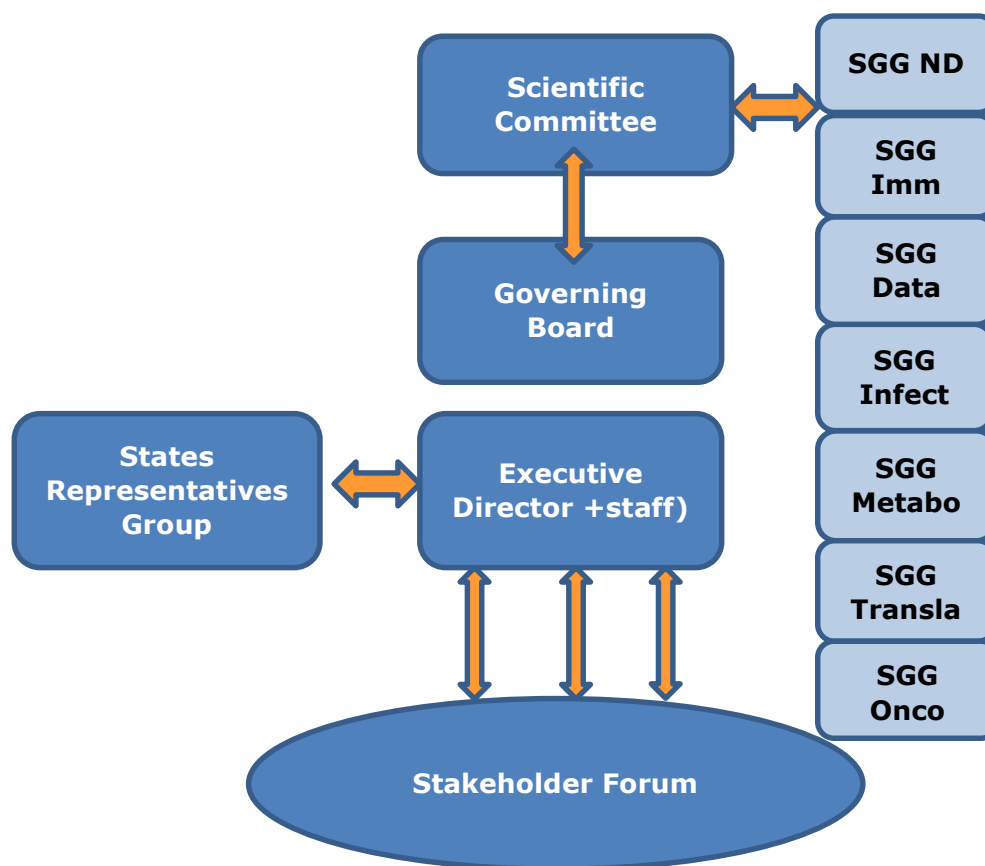


Table 1: IMI2 JU bodies and functions

Body	Function
IMI2 JU Governing Board (GB)	Represents the European Commission and EFPIA. Overall responsibility for strategy and operations of the IMI2 JU.
IMI2 JU Executive Director (and IMI2 JU Programme Office)	Legal representative and Chief Executive responsible for day-to-day management and activities. Total of 41 IMI2 JU staff on 31 December 2016.
IMI2 JU Scientific Committee (SC)	Advisory body to IMI2 JU (e.g. research agenda and scientific priorities).
IMI2 JU States Representative Group (SRG)	Represents Member States and Associated Countries. Advisory body (e.g. research agenda and scientific priorities) and interface between stakeholders and IMI2 JU.
IMI2 JU Stakeholders' Forum	Meeting open to all stakeholders.
IMI2 JU Strategic Governance Groups (SGG)	Ensure the coordination of IMI's work in certain strategic areas and work to make the development of new topics more transparent and effective. The SGGs are made up of representatives of companies, from the European Commission, the IMI2 JU Programme Office and the IMI2 JU Scientific Committee. The SGGs were created on the basis of Article 7(3)(p) of IMI2 JU Statutes, which article allows the Governing Board to set up advisory groups where appropriate.

3.2 Baseline

As stated in the impact assessment accompanying the Proposal for a Council Regulation on the Innovative Medicines Initiative 2 Joint Undertaking,⁸ 'Europe has no choice but to innovate and provide earlier, more accurate diagnostics and effective new drugs to be able to maintain its citizens' health and well-being'.⁹ 'Only a bold, focused and well-coordinated

⁸ <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013SC0245&from=sv>
⁹ <http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:52013SC0245>

intervention at EU level will enable Europe to reverse a trend of declining R&D productivity of new drug development, patent expiry and a loss of opportunities to create jobs in highly dynamic economic sectors'. Box 2 summarises the arguments for such an EU intervention as was developed in the impact assessment.

Box 2 Rationale for EU intervention (published in 2013)¹⁰

- The pharmaceutical industry is important for Europe's growth and competitiveness – currently generating an annual turnover of €157 billion and employing 660,000 people of whom 110,000 are researchers - but its future competitiveness will depend on its innovation performance.
- The development of new treatments for diseases that affect public health faces important challenges: declining R&D productivity of new drug development despite large investment, patent expiry and lack of return on investment.
- A mismatch still remains between public health needs (e.g. treatments for Alzheimer's) and where industry chooses to invest (many 'me-too drugs').
- The rapid introduction of new and more effective diagnostics and treatments is needed to improve the health and well-being of Europe's (ageing) citizens, to contain rising healthcare costs, and to ensure the future competitiveness of the European pharmaceutical industry.
- However, the development of such diagnostics and treatments is complex, expensive and risky.
- Industry is not willing to invest alone in public goods such as shared databases and networks that could speed up development, or in disease areas that require complex and costly R&D with uncertain financial returns [market failures].
- Biopharmaceutical capabilities and data are dispersed across Europe, therefore assembling the required databases and building networking tools are virtually impossible through only public intervention at individual Member State level. Mobilising the necessary critical mass of knowledge and financial resources can only be undertaken at the EU level [EU added value].
- To develop an effective supra-structure (networks, databases, etc.), consensus and collaboration must take place across the entire sector. This cannot be done through traditional EU collaborative research. A Joint Technology Initiative is needed.

The rationale outlined in the impact assessment report has not changed substantially since the establishment of the first IMI JU in 2008. It remains unclear whether the first IMI JU did contribute to meet the goals of improving the pharmaceutical industry's competitiveness and removing bottlenecks in the drug development process to deliver safe, effective and innovative medicines faster. Europe was still lagging behind the US in terms of its investment in pharmaceutical R&D at the time of preparing for the possible follow-up initiative of the first IMI1. The analysis also focussed on the increasing healthcare costs associated with chronic diseases and ageing of the population. Although these are significant challenges they are similar in the US and therefore cannot explain the discrepancy between Europe and the US in terms of R&D investment in this sector.

The impact assessment report concluded that the European market has become less attractive and its share of the world market was shrinking, due to government restrictions on market access and reimbursement combined with an expensive pharmacovigilance system. In addition, it was reported how European companies tended to develop mostly less innovative chemical drugs and invest less in the development of breakthrough biotechnology medicines as compared with their US counterparts.

¹⁰ Commission staff working document impact assessment. Accompanying the document: Proposal for a Council Regulation on the Innovative Medicines Initiative 2 Joint Undertaking (2013). <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013SC0245&from=en>

Public funding in R&D partnerships can contribute to de-risking of the drug development process and was therefore believed to be necessary to bring the required incentives for cross sectoral collaborations and the sharing of resources data and expertise. However, public intervention at national level cannot support the risky collaborative research needed, while the industry itself was not willing to invest sufficiently.

The impact assessment report put forward ambitious and clear objectives for the development of better treatments:

1. To increase by 2020, the success rate in clinical trials by 30% in diseases identified from the 'Priority Medicines for Europe and the World Report' that has been prepared by the WHO in 2004 and was updated in 2013.¹¹The objective of improving the success rate in clinical trials was expected to be achieved by:
 - validating 12 novel drug targets (i.e. clinical proof of concept demonstrated in a phase 2b clinical trial);
 - improving from 70 to 80% the predictive capacity of early stage (non-human) safety testing models;
 - establishing two new clinical trial networks in areas of high unmet need.
2. To reduce the time to reach clinical proof of concept in immunological, respiratory, neurological (including neurodegenerative) diseases to 5 years (from the current 7) by:
 - reclassifying these four major disease groups, thereby allowing a significantly better diagnosis and simplifying the conduct of clinical trials.
3. To develop at least two new therapies for diseases for which there is a high unmet need, such as for Alzheimer's disease (only two treatments of limited efficacy have been developed until now), or limited market incentives such as in the case of antimicrobial resistance (two new classes in the past 30 years).

The report further set specific objectives for diagnostics, vaccines and the drug developing process as a whole:

1. For diagnostics the specific objective is to develop diagnostic and treatment biomarkers for four diseases (from diseases mentioned above) clearly linked to clinical relevance, approved by regulators; the current rate of development of such markers is lower than that of validating targets.
2. In the area of vaccines the specific objectives are to:
 - develop a transparent and comprehensive infrastructure model to gather data on disease incidence and medico- and socio-economic burden of major infectious diseases;
 - develop tested novel biomarkers to predict vaccine efficacy and safety (two markers each) early in the process to improve multiple candidates screening leading to a 50% reduction in the failure rate in phase III clinical trials;
 - develop two novel adjuvants for human use, which will allow increasing the body's immune response to the vaccine, boosting in particular reaction in specific target groups, such as the elderly and non-responders;
 - identify for two major infectious diseases and for two types of cancer or chronic disorders (e.g. autoimmune diseases) at least: two novel predictive models for efficacy; two novel predictive models for safety. Also contribute to strengthening the link between human and veterinary vaccine research.

and

3. The specific objectives are interlinked with the overarching goal to convert science into effective prevention and treatment, so that the right prevention, diagnosis or therapy is delivered to the right patient at the right time.

¹¹Kaplan, W., Laing, R.,. Priority Medicines for Europe and the World. WHO, Department of Essential Drugs and Medicines Policy. 2004 http://whqlibdoc.who.int/hq/2004/WHO_EDM_PAR_2004.7.pdf

The report suggested that additional specific objectives may be added when other industries would join the JU. A number of operational objectives were put forward:

- provide structures that facilitate partnerships along the entire life science research and innovation cycle, such as from early discovery to product development, to pharmacovigilance research and surveillance, in an effective innovation-driven collaborative setting that is focused on optimising life sciences research and innovation for diagnostics, prevention and therapeutic agents and approaches, and support for the development of evidence-based regulation;
- establish networks for open innovation along the whole innovation cycle of novel medical research and technologies, bringing public research institutions, academia, life science industries, SMEs, patient organisations, regulators, payers, public health authorities and the animal health sector;
- reduce the fragmentation of research and innovation and increase the level of private-sector spending in Europe;
- develop and implement strategic agenda setting in a pan-European structure with the necessary critical mass and budget, ensuring continuity and allowing life science industries to make long term investment plans;
- facilitate research that provides evidence earlier in the drug and vaccine development process through risk-sharing mechanisms.

The impact assessment report further analysed the budget needs and concluded that a total EU contribution of EUR 1.5 billion to match the EFPIA contribution would be sufficient to achieve the specific objectives described. Increasing the EU part with another EUR 225 million would allow achieving additional objectives should other industries participate.

4. EVALUATION QUESTIONS

The focus of the evaluation questions were to assess whether the goals put forward when setting up IMI JU have been met and also to analyse whether the expectations on effectiveness, efficiency, research quality and openness and transparency, as outlined in section 2.2 of this report, were realised.

The following evaluation questions were specified in the Terms of Reference for the expert group:

1. Background of initiative, objectives and relevance
2. Effectiveness of the Innovative Medicines Initiative
 - a. *State of play of implementation*
 - b. *Main achievements*
 - c. *Extent to which the objectives of the Joint Undertaking have been met*
3. Efficiency of the Innovative Medicines Initiative
 - a. *Joint Undertaking mission and governance*
 - b. *Modalities of operation*
 - c. *Operational efficiency*
4. European added value
5. Coherence
6. Synthesis, conclusions and recommendations

The expert group was also asked to assess:

- **Openness:** The extent to which the JUs enable world-class research that helps Europe drive in to a leadership position globally, and how they engage with a wider constituency to open the research to the broader society.
- **Transparency:** The extent to which the JUs keep an open non-discriminatory attitude towards a wide community of stakeholders and provide them with easy and effective access to information.

The objectives of the interim evaluation were to assess progress and mid-term achievements of the IMI2 JU operation during the period 2014 to 2016.

The expert group was asked to address in its evaluation operational aspects of the IMI2 JU and the outputs generated by the funded projects, in relation to the budget, the methodology and the mechanisms to realise the objectives.

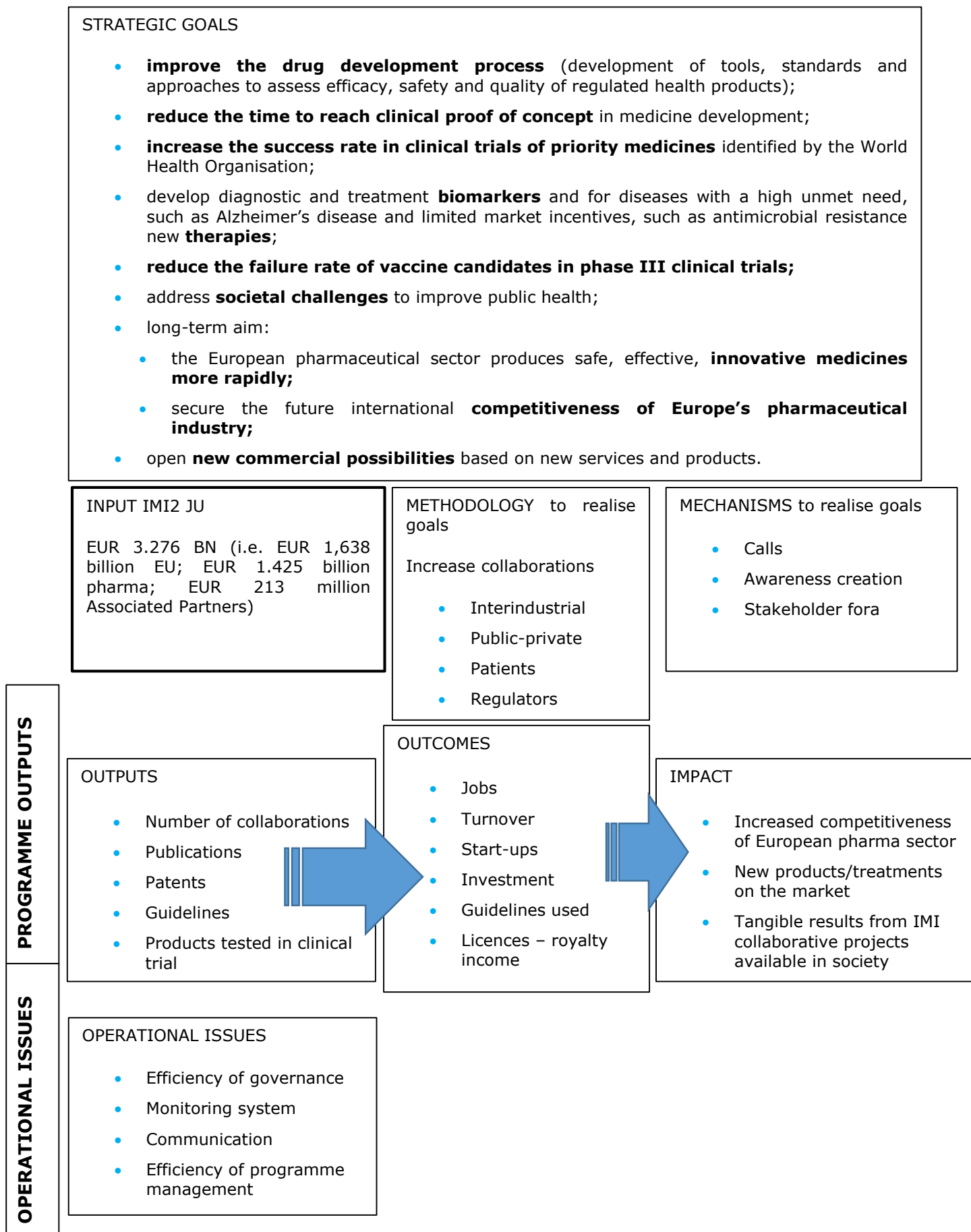
Using the input, methodology and mechanisms provided, the expert group wanted to analyse the short-term performance reflected by outputs, mid-term performance reflected by outcomes and the longer term impact that the IMI2 JU has realised or was expected to deliver. An intervention logic diagram for the evaluation is presented in figure 2.

In line with the Impact Assessment Report that formed the basis of the IMI2 JU, primary outputs of the IMI2 JU activities, the number of collaborations, publications and patent applications can be used. Secondary outputs from IMI2 JU funded projects could include guidelines for best practices, biomarkers approved for use in clinical trials, products tested in clinical trials, licenses given or royalties generated from IMI research projects. By the end of the joint undertaking, the number of jobs created, start-ups, turnover generated, investments made in IMI projects or investments attracted due to IMI2 JU activities should be analysed. Next to the economic indicators it would be interesting to analyse whether guidelines developed under IMI2 JU or biomarkers were used outside of the IMI2 JU projects.

The operational performance will be addressed by analysing the efficiency of the governance and the programme management, of the monitoring system, and of the communications strategy.

The IMI2 JU would be deemed to have succeeded if a true impact had been realised, i.e. whether the European pharmaceutical industry attracted new research activities and investments, and became more competitive. New products originating from IMI2 JU research projects that were now available on the market are another important indicator.

Figure 2: Intervention logic diagram



5. METHOD/PROCESS FOLLOWED

5.1 Process/Methodology

In line with the Council regulation an independent expert group was appointed to assist the European Commission in carrying out the interim evaluation of IMI2 JU.

The expert group comprised five individuals whose areas of expertise encompass various aspects of the pharmaceutical drug discovery and development process, research funding, technology transfer and commercialisation, IP and marketing, finance as well as policy assessment and evaluation issues. Short biographical sketches of the experts are presented in Annex 1.

The terms of reference provided a set of general questions, which had to be addressed by the expert group. These general questions were translated into more specific questions that were addressed during interviews with stakeholders (the list of questions is available in Annex 2).

The evaluation started in October 2016 and ended with the delivery of the evaluation report by 30 June 2017. The work consisted of a combination of remote work, conference calls and seven expert group meetings in Brussels. The expert group built its assessment on:

- (i) documents and other published information, and on extensive data compilations prepared by IMI Office and Commission services (see Annex 3 for the list of documents, most of them available on the IMI website);
- (ii) interviews with a wide range of IMI stakeholders, including representatives of both founding members, IMI2 JU bodies, participants of on-going IMI-supported research projects, representatives of regulatory bodies, patients organisations, research and SME associations (see the list in Annex 4); and on
- (iii) a survey of project coordinators and a public consultation.

After evaluation of the IMI2 JU performance to-date, a SWOT analysis (strengths, weaknesses, opportunities and threats) was carried out to place the assessment in the broader strategic framework, to review findings, and to develop robust recommendations.

5.2 Limitations – robustness of findings

The expert group was entrusted with two challenging tasks involving the final evaluation of IMI JU, and the interim evaluation of IMI2 JU. The fact that both programmes had (slightly) different objectives and that the legal framework and issues such as the IP policy have changed, did not facilitate the task. Moreover, at the time of preparing this report, most of the first IMI JU projects were still running, some of which will continue as long as 2021, and the first projects of IMI2 JU only started two years ago in December 2014.

The guidance and help of EC representatives has been instrumental, especially in providing information and directing the expert group where to find the information, to produce this report. The numerous data sets have been delivered to the expert group at various times during the evaluation. All the data sets were defined with a cut-off date of 31 December 2016.

A substantial volume of information was available, but a performance analysis framework using SMART (Specific, Measurable, Achievable, Relevant and Time phased) KPIs was missing, which complicated the task of analysing the information. The experts had to rely on their individual background expertise and common sense to try to make a considered analysis. This particular limitation will be inherent to all evaluations that use an expert group.

The public consultation was provided as an additional source of information. However, the statistical relevance of the information from this survey may be questioned as for this EUR 3 billion programme with 296 participants (and 488 participations), open to the entire EU and beyond only 93 parties responded and not all EU countries were represented by respondents. Over half, 59% (n=55), of the respondents indicated they are very familiar with IMI2 JU and 62% indicated to be directly involved with IMI2 JU, but only 43% reported to have applied for funding and only 30% reported to be a beneficiary of IMI2 JU. One fifth of the

respondents were an EFPIA member, while roughly one-third (36%) of the respondents did not indicate how they were really involved in IMI2 JU. The low response rate combined with the fact that it is not clear whether the responses are relevant made it difficult to rely on.

The beneficiary satisfaction survey is even less statistically relevant. Only 34 responded of which 62% (21 out of 34) were part of the industry consortium. As the industry consortium and the applicant consortium are formed separately in the design of a project, the appreciation for the application and evaluation processes will be different.

Other information was gathered from the interviews with stakeholders, and was therefore often a mixture of appreciations for IMI1 and for IMI2 JU, sometimes also linked with the affiliation the interviewee was representing. The expert group did not find it easy to extract the messages that specifically related to IMI2 JU.

Most of the interviewees identified by the expert group, readily agreed to participate, which was also an indication of the potential impact of the joint undertaking. It was harder though to get feedback from Members of the European Parliament, although the final evaluation report will be shared with the EP. We were grateful that Mrs. Grosstete agreed to answer the experts group's questions in writing.

The expert group found it difficult to evaluate IMI2 JU because some pieces of information were missing or came to them very late in the evaluation process. **There were no quantitative data available that indicated whether the big pharmaceutical companies were increasing their research investments in Europe, that would indicate that Europe had become a more attractive location for biopharmaceutical research.**

As this is only an interim evaluation of the IMI2 JU which launched its first calls only in 2014, projects were less evolved, which make it hard to make an assessment on the value and impact of the outputs.

6. IMPLEMENTATION STATE OF PLAY

This section describes how the IMI2 JU, set up by the Council Regulation 557/2014, was implemented and provides information about the patterns in the participation of European research actors and about the distribution of funds among beneficiaries. This information is the basis for the analysis on whether IMI2 JU has attracted the main research actors in Europe and how it has achieved this. The information also highlights the main research and structural trends.

6.1 Overview of calls launched during the period 2014-2016

A total of ten calls for proposals were launched under IMI2 JU between July 2014 and the end of December 2016: four calls were launched in 2014; four calls in 2015; and two calls in 2016. Calls 8 (IMI2-2015-08) and 9 (IMI2-2016-09) were still ongoing at the end of 2016 while call 10 (IMI2-2016-10) had just been published.

These ten calls for proposals represented a total of 46 topics. Each of the ten calls had a different number of topics with just one topic each for call 4 (IMI2-2016-04) and call 8 (IMI2-2015-08), up to seven topics for call 7 (IMI2-2015-07) and eight topics for the ongoing call 10 (IMI2-2016-10). Two of the calls were single stage calls and the ongoing IMI2-2015-08 is an open call with five cut-off dates planned until mid-2018. The number of proposals submitted per call ranged between 3 (for call 4 - IMI2-2015-04) and 38 (for call 3 - IMI2-2015-03).

A total of 25 IMI2 JU grant agreements had been signed by the end of December 2016, in addition to the 38 projects still running from the first phase of IMI JU. This meant that a total of 63 IMI funded projects were 'active' by the end of December 2016.

The 25 IMI2 JU projects had been selected to address the 24 topics published in the six first calls of IMI2 JU. Annex 5 gives an overview of the funded projects and the total projects costs. The **total project cost** was EUR 552.7 million.

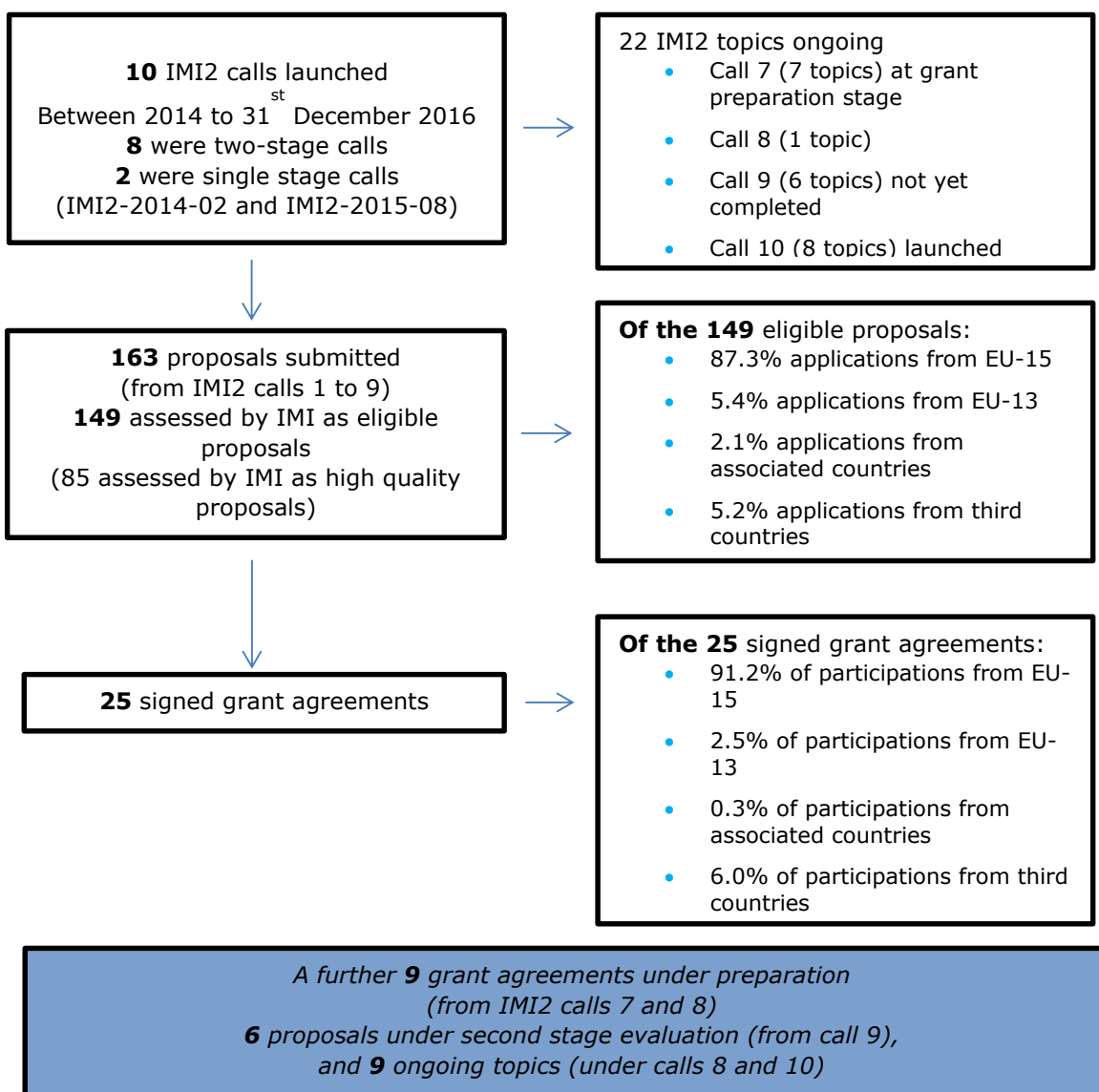
The budget committed to fund these total project costs with these 25 grant agreements represented:

- EUR 275.88 million of EU contribution;
- EUR 249.15 million of EFPIA contribution (including EUR 0.2 million of financial contribution to IMI2 JU); and
- EUR 14.43 million of Associated Partners contribution (including EUR 7.0 million of financial contribution to IMI2 JU).

A further nine proposals had been selected from calls 7 (IMI2-2015-07) and 8 (IMI2-2015-08), and were still under grant preparation as of 31 December 2016. These nine proposals represented a further estimated EUR 61.54 million of EU contribution and EUR 62.89 million of EFPIA contribution. Altogether, the 25 signed grant agreements and nine additional grant agreements under preparation represented a total contribution (from EU, EFPIA and Associated Partners) of EUR 663.9 million.

Figure 3 summarises the number of proposals submitted, deemed eligible under the relevant IMI2 call, signed grant agreements and currently under grant preparation.

Figure 3: Summary of number of proposals for IMI2 JU



6.3 Participation patterns broken down by country and region

All 28 of the EU-28 Member States were represented in the 149 eligible submitted proposals under calls 1 to 9. Participants in the 25 first signed grant agreements from calls 1 to 6 came from 17 of the 28 EU-member states. At the end of December 2016, a further 9 grant agreements were in preparation from calls 7 and 8 and the Full project proposals still to be evaluated from call 9. When compared with IMI1, IMI2 JU had a broader depth of countries involved in the proposals across the Member States as only 23 of the EU-28 countries were represented in IMI1. In terms of the number of applications in 'eligible' proposals, the United Kingdom was the EU Member State that took part in the largest share (17.5%) of applications, followed by Germany (14.7%), and Italy (11.7%). Surprisingly, the pattern of success rates of applications between proposals and retained proposals, differed from the pattern of the number of applications in eligible proposals. The highest rate of successful applications was represented by The Netherlands (52.9%) followed by the UK (42.8%) and Luxembourg (41.7%).

Substantial discrepancies were seen when comparing the types of countries from across the EU that submitted proposals assessed to be eligible for IMI2 funding. The types of countries taking part in IMI2 JU were grouped under four headings: EU-15; EU-13; associated countries and third countries (Annex 6 defines these headings). EU-15 countries contributed to 87.3% of the applications in eligible proposals, while EU-13 countries contributed to only 5.4% of these. The share of applications from associated countries was only 2.1% and 5.2% for third countries, which is appropriate given that this funding stream aims to encourage participation in the EU.

These trends were confirmed when looking at the number of retained proposals. Of the retained proposals, **91.5% of applications were from a EU-15 country but only 1.8% from a EU-13 country**, 0.5% from associated countries and 6.2% from third countries. This shows the majority of applications in the retained proposals were represented by the EU-15 states, which was also mirrored in the success rates of applications between eligible proposals and retained proposals: 34.9% for EU-15 countries; 11.2% for EU-13 countries; 7.9% for associated countries. Third countries were again performing better with a success rate of applications between eligible and retained proposals of 39.8%.

The co-ordinators for the 25 projects with signed grant agreements were based in: UK (n=7); Germany (n=4); Spain (n=3); Sweden (n=3); The Netherlands (n=4); Switzerland (n=1); Belgium (n=1); France (n=1); Italy (n=1).

When comparing IMI1 and IMI2 JU, it appears that the EU contribution to countries in the EU-15 group maintained around 95% of the total EU contribution (93.9% in IMI1 vs 95.0% in IMI2 JU). The EU contribution to countries in the EU-13 group decreased in the period of the interim evaluation from 1.3% in IMI1 to 0.5% in IMI2 JU.

Also for associated countries the funding level under IMI2 JU dropped in this period from 4.7% under IMI1 to 0.1%. The participation of third countries has in contrast been increased in terms of the share of public funding in the IMI2 JU projects to 4.4% whereas this was only 0.1% in IMI1, mainly due to the Ebola projects.

6.4 Participation patterns by type of beneficiary organisations

For the purpose of summarising the types of participants, seven categories were grouped under the headings: academia, secondary and higher education establishment; EFPIA; non-profit research organisation; patient organisation; regulatory/community bodies; SME; other.

In IMI2 up until the end of December 2016, there were 488 participations in total (of which 365 were EU-funded participants), within the 25 signed grants:

- 35.7% (n=174) of the participations came from academia;
- 19.7% (n=96) of participations represented non-profit research organisations;
- 8.8% (n=43) represented SMEs;
- 24.6% (n=120) represented EFPIA;
- 6.8% (n=33) categorised as other;

- 2.5% (n=12) represented patient organisations;
- 1.4% (n=7) represented regulatory/community bodies;
- 0.6% (n=3) represented associated partners.

Under IMI2 JU, **SMEs represented 8.8% of all participations, and 11.8% of all EU funded participations**. This decreased from respectively 11.22% of all participations and 15.96% of the EU funded participations under IMI1. The participations of EFPIA companies decreased from 29.6% of all participations under IMI1 to 24.6% under IMI2 JU. The associated partners are a new addition to IMI2 JU. The Associated Partner category was created with the goal of opening up IMI's activities to a wider range of stakeholders. As such, examples of organisations that could become IMI Associated Partners include philanthropic organisations and charities that run their own health research programmes, as well as organisations working in sectors related to healthcare such as ICT, imaging, diagnostics, and animal health. Like EFPIA partners in IMI projects, Associated Partners do not receive any funding from IMI, but contribute to the projects, mainly through in-kind contributions (such as their experts' time, access to resources / equipment) and financial contributions.

6.4 Characterisation of the academic players

Two ranking systems were used by the European Commission to assess the status of the universities taking part in IMI2 JU projects: (1) the European Multirank and (2) the Shanghai ranking system. Both ranking systems showed that more than 50% of all participations and the EU contribution were for organisations ranked amongst the 150 first universities. Four fifths (80%) of the Universities participating in IMI2 JU were in the overall World top 500 and one quarter of the Universities were in the overall World top 100, using European Multirank, which was an improvement compared with IMI1 (72% and 12%, respectively).

A substantial number (n=96) and variety of key non-university research organisations already participated in IMI2 JU projects. These represented a **mixture of academic and non-academic institutions**, such as research active hospitals and national research organisations. Most of these entities represented the Member-15 states.

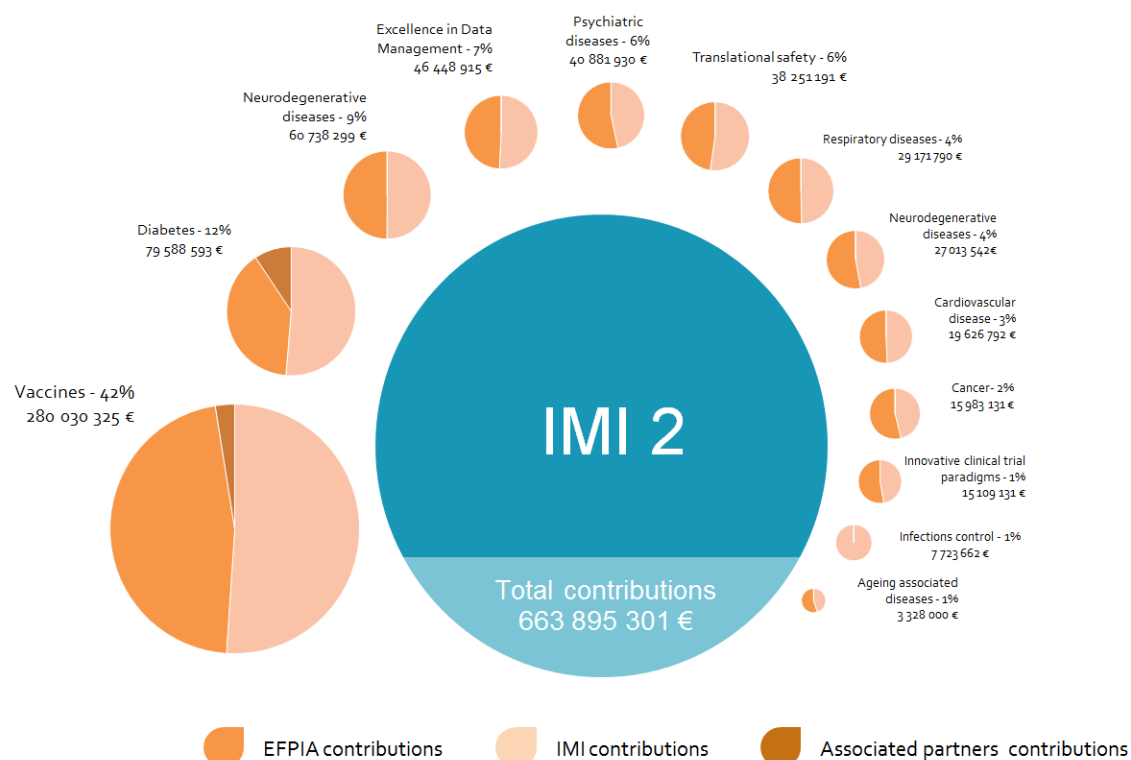
6.5 Characterisation of the industrial players

The total EFPIA contribution for the 25 first projects was EUR 249.15 million out of which EUR 82.8 million is in-kind contribution from outside the EU and Associated Countries. Thirty four EFPIA companies participate in the first IMI2 JU projects, of which 20 companies with headquarters outside of the EU, which was a higher proportion (20/34 = 59%) than under IMI1 [19/40 = 47.5%]. Overall, of the 34 companies, 29 ranked in the top 100 of the Pharmaceutical and Biotechnology section of the scoreboard World 2500 ranking, only five of the companies did not appear in this ranking. Of the 14 companies with headquarters in the EU, 12 were in the top 30 ranking of the Pharmaceutical and Biotechnology section of the Scoreboard EU 1000, two others cannot be found in this ranking. Although fewer European companies participated so far in IMI2 JU, they ranked higher.

6.6 Participation patterns per specific thematic topic broken down by type of beneficiary organisations

Figure 4 illustrates the distribution of funding for each of the 12 defined scientific areas. The data summarised in Figure 4 also show the contribution to the total funding awarded from IMI2 JU, EPFIA, and Associated Partners respectively.

Figure 4: Distribution of funding for each of the 12 defined scientific areas



6.7 Success rates in terms of successful proposals, activity types of applicants and budget share

Using the data, for the six completed IMI2 JU calls, the **average (mean) success rate**, representing the proportion of the number of signed grant agreements signed per number of eligible proposals (n=96), **was 26%**. The average success rate, however, ranged from 14.3% for IMI2-2015-03 to 57% for IMI2-2014-02. Half of the calls (n= 3 calls) had a success rate above the average value of 26%. The call IMI2-2015-03 comprised six topics with a range of focus including the vaccine-related research and increasing the role of patients in medicine development. The call IMI2-2014-02 comprised five topics of which four focussed on vaccines and one looking at developing rapid diagnostic tests. There was no clear pattern across the calls and associated topics in terms of the observed success rate. In IMI2 JU, for the two-stage calls, only one proposal per topic was funded, and overall more than 52% of the proposals ranked as high quality were not funded (28 high quality proposals not funded out of 53 high quality proposals from the six calls).

6.8 EU contribution: distribution of funds, broken down by country and region where possible, activity type of beneficiaries, and thematic area

Table 2 shows the project costs awarded per call for the 25 signed grants in IMI2. Of the 25 funded projects with signed grant agreements by the end of December 2016 within IMI2 JU, the total project cost was EUR 52.74 million awarded to a total of 296 participants (representing 488 participations), of which 246 participants (representing 365 participations) were awarded EU funding.

The average (mean) project cost was EUR 22.1 million.

Table 2: Awarded costs for the 25 projects with signed grants in IMI2

Call	Number of Signed Grants	Project Total Costs * (€ m)	EFPIA Cont. (€ m)	Associated Partners Cont. (€ m)	EU Cont. (€ m)
Call 1, two stages (H2020-JTI-IMI2-2014-01-two-stage)	1	36.58	12.75	5.58	17.63
Call 2, single-stage (H2020-JTI-IMI2-2014-02-single-stage)	8	218.91	100.68	0	114.09
Call 3, two stages (H2020-JTI-IMI2-2015-03-two-stage)	5	103.44	43.94	7.0	49.06
Call 4, two stages (H2020-JTI-IMI2-2015-04-two-stage)	1	3.83	1.98	0	1.13
Call 5, two stages (H2020-JTI-IMI2-2015-05-two-stage)	6	97.49	44.27	1.85	47.48
Call 6, two stages (H2020-JTI-IMI2-2015-06-two-stage)	4	92.49	45.54	0	46.5
Total	25	552.74	249.15	14.43	275.88

*note due to rounding errors may not sum exactly

The **total EU contribution** for the 25 funded IMI2 JU projects was EUR 275.88 million. The average (mean) EU contribution was EUR 11.04 million per project.

The EU contribution per topic ranged from EUR 1,023,325 for the topic 2 of call 2 (IMI2-2014-02) on the topic 'manufacturing capability', to EUR 85,014,965 for the topic 1 'Vaccine development phase I, II and III' of call 2 (IMI2-2014-02) with 3 projects funded under this topic.

The **JU contribution** (€283.1 million consisting of €275.88 million of EU contribution, €0.2 million of financial contribution from EFPIA industries and €7.0 million of financial contribution from Associated Partners) was distributed **over the different classes of participating countries** as follows:

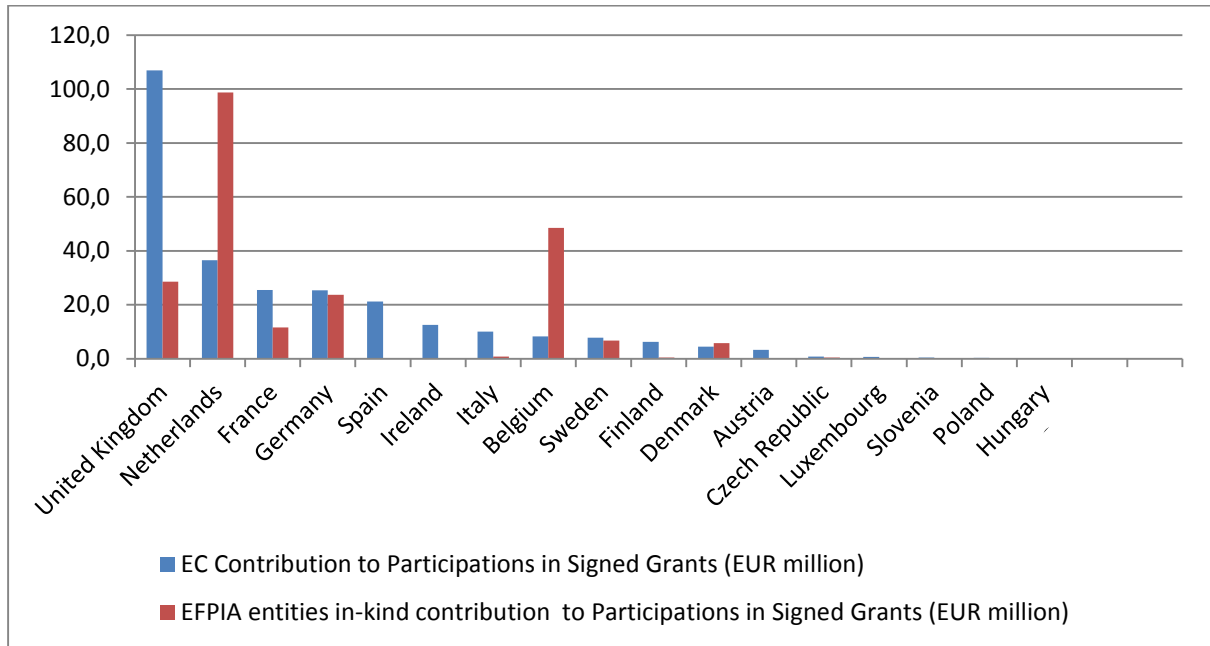
- for Member-15 EUR 268.8 million, representing a share of 95.0% of the total EU contribution;
- for Member-13, EUR 1.5 million (0.5%);
- for associated countries EUR 0.4 million (0.1%); and
- for third countries EUR 12.4 million (4.4%).

This spread across the different classes of countries showed a different pattern to the one observed in IMI1, which was:

- 93.9% for Member-15;
- 4.7 % for associated countries;
- 1.3% for Member-13; and
- 0.1% for third countries.

Figure 5 shows the total JU contribution awarded to each country for the 25 signed grants agreements. The largest EU contribution under IMI2 JU was awarded to the UK (EUR 106.9 million), followed by the Netherlands (EUR 36.5 million) and France with (EUR 25.4 million).

Figure 5: Total contribution (EUR million) for each participating country



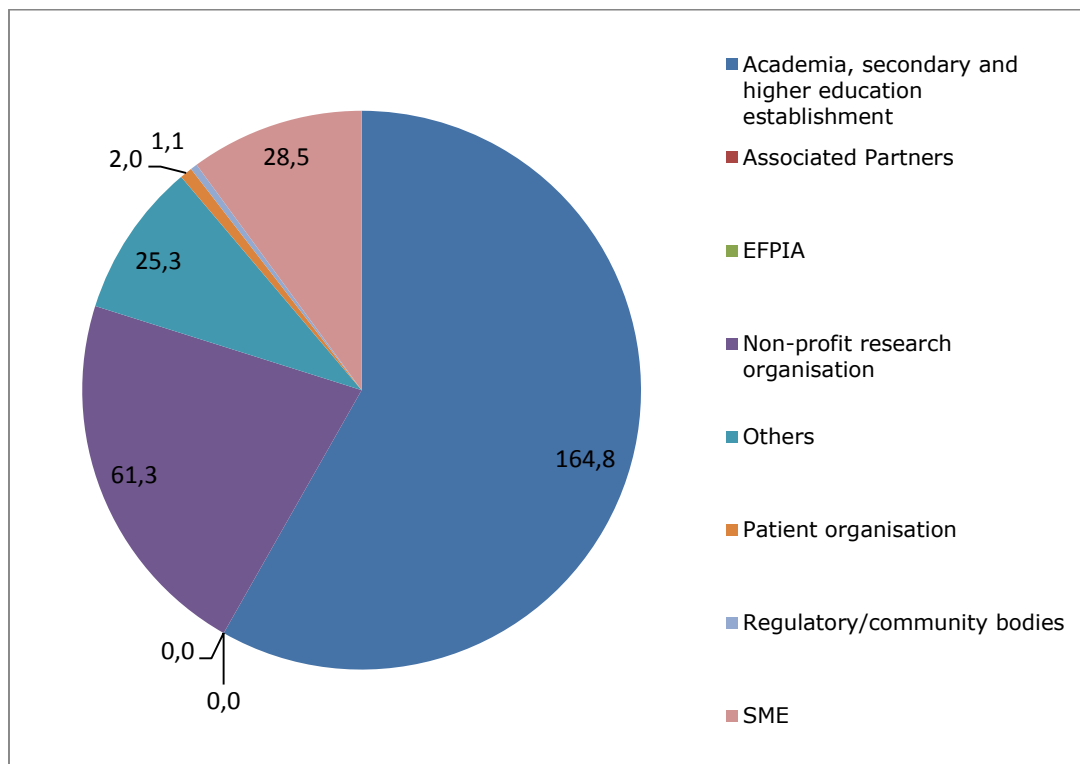
The **total JU contribution** (EUR 283.1 million consisting of EUR 275.88 million of EU contribution, EUR 0.2 million of financial contribution from EFPIA industries and EUR 7.0 million of financial contribution from Associated Partners) going to the different types of participants is shown in Figure 6. The share of the total EU contribution for each type of participant was:

- 58.2% for academia, secondary and higher education establishments;
- 21.6% for non-profit research organisations;
- 9.0% for other types of organisations;
- 0.7% for patient organisations;
- 0.4% for regulatory/community bodies; and
- 10.1% for SMEs.

The **average (mean) JU contribution** for each type of organisation was:

- EUR 0.9 million for Academia, secondary and higher education establishment;
- EUR 0.6 million for non-profit research organisations;
- EUR 0.8 million for other types of organisations;
- EUR 0.2 million for patient organisations;
- EUR 0.2 million for regulatory/community bodies; and
- EUR 0.7 million for SMEs.

Figure 6: Total JU contribution (EUR million) for each type of organisation



6.9 Average grant size in terms of budget and number of participants

The average (mean) project total costs from the first six calls (25 projects) for IMI2 JU was EUR 22.1 million. In IMI2 JU up until the end of December 2016, there were 296 participants in total (representing 488 participations), of which 246 were EU-funded (representing 365 participations, and a total of EUR 275.88 million). EU contribution). The average EU funding was EUR 1.12 million per EU-funded participant and EUR 0.76 million per EU-funded participation. The number of participants in a consortium varied from 52 (Harmony) (of these 45 were beneficiaries of EU funding) to only three (EBOMAN) (of these two were beneficiaries of EU funding). The median number of EU funded beneficiaries per project was 13, with a mean of 14.6 EU funded beneficiaries per project.

Annex 5 gives an overview of the funded projects and the total projects costs.

7. ANSWERS TO THE EVALUATION QUESTIONS

7.1 Effectiveness

7.1.1 Main Achievements

As specified in the Impact Assessment Report that informed the proposal for a Council Regulation on the IMI2 JU, the interim evaluation should address whether the number of milestones have been achieved. A set of nine milestones were identified (Box 3). Annex 7 summarises IMI2 JU progress against these milestones.

Box 3: Milestones to measure IMI2 JU achievements at the interim evaluation

1. two clinical trial networks to be established by 2016;
2. all projects for arriving at taxonomy of disease started by 2017;
3. six projects for validating novel targets started by 2016, further 3 projects started by 2017;
4. trials for developing novel treatments started by 2017;
5. projects for developing diagnostic markers started by 2017;
6. infrastructure to gather data on disease incidence and medico- and socio-economic burden of major infectious diseases established by 2016;
7. projects for developing novel biomarkers to predict vaccine efficacy and safety started by 2016, results on one markers by 2017;
8. projects for developing of adjuvants started by 2016;
9. projects for developing efficacy and safety models for vaccine research started by 2016, results for one model by 2017.

Milestone 1 specified that two clinical networks should be established by 2016. The list of projects provided to the expert group indicated some projects that 'envision' the establishment of networks, but it was not possible to conclude whether the milestone was reached with the information provided.

As for milestone 2 on the taxonomy of diseases, the impact assessment report specified that the focus of IMI2 JU has to be on immunological, respiratory, and neurological diseases (including neurodegenerative diseases). The information provided to the expert group indicated that most projects had addressed diseases other than those specified. Furthermore, it was not clear what the actual outputs of the projects were, except that they focus on the identification of new biomarkers and stratification of patient groups. No conclusions could be drawn on whether or not the taxonomy of the diseases addressed was changed or will be changed from the results of the projects. At the same time, the projects are in progress so final results are not yet available.

Milestone 3, like milestone 1 is quantitative and specified that by 2016 six projects for validating novel targets should have been started by 2016. It was shown that by 2016 four of the six projects expected had started.

All other milestones only asked to list projects, trials and infrastructures without quantitative goals. For milestones 4 and 8 there were no projects identified.

In Annex 7 it is noted furthermore that the milestones proposed were not aligned with the actual focus and activities of the IMI2 JU, because **many projects focused on infectious diseases, or were designed to engage with patients and patient advocacy groups or involved the use of big data**. It was furthermore clear that no targets were identified to cover these activities and focal areas and also seven of the nine proposed milestones did not set targets, but merely asked for listings.

It seemed therefore appropriate to conclude that the milestones were not fully serving the purpose of informing the interim evaluation of the IMI2 JU. The expert group regretted that the indicators and milestones that were outlined in the impact assessment report were not translated into an accountable performance measuring system based on performance indicators. This is further outlined in section 7.2.1.5 on the robustness of the monitoring and control systems.

Quantitative data summarising the overall achievements, at the programme level, from the IMI2 JU were limited. It was possible to summarise outputs from individual projects. The interviews provided information on the views of stakeholders about key outputs from individual projects but could not provide explicit information on the outputs of the IMI2 JU

programme as a whole. The expert group, however, realised that at the time of the interim evaluation, IMI2 JU had been running for just two years and no projects have been completed. Therefore, success stories could only be attributed to specific examples of projects.

One of the first calls concerned the Ebola virus outbreak in Africa and the role of IMI2 JU was very effective. A clinical trial of an investigational Ebola vaccine regimen took place in Sierra Leone, Kenya, Uganda, Tanzania, Burkina Faso and Ivory Coast (from projects EBOVAC1, EBODAC and EBOMAN). A diagnostic device designed to test for the Ebola virus and other related filoviruses has been successfully tested in three European reference labs and has also passed initial field studies in Sierra Leone (from project MOFINA).

In diabetes, INNODIA has been establishing a Clinical Trial Network for type 1 diabetes (a network of well characterised and accredited clinical centres), and a European network for pancreatic organ donors with diabetes.

As IMI2 JU is building on the activities of IMI1, some of the general achievements from IMI1 were also achieved for IMI2 JU. One of the main achievements, on which there was a shared general consensus, was that both IMI1 and IMI2 JU enabled active collaboration between competing global companies, SME's and academia. These data are summarised in section 6 of this report. Together with the budget and long-term strategy, this achievement was considered to be an important asset for European research developing new medicines that may be expected to support its future development.

These new types of collaborations created an environment of **trust** to develop **new partnerships**, including partners from **other areas of expertise, such as regulatory bodies, essential stakeholders for medicines to enter the market and/or patient representative groups**. These new partnerships enabled the IMI2 JU funded consortia to cover the entire value chain and bring new products or treatments faster to market for the benefit of patient populations. These new collaboration models could potentially have sustained effects beyond the timeframe of the funding from IMI2 JU, as the importance of cross disciplinary working is realised.

Representatives from EFPIA, IMI and the SGG reported that IMI1 and IMI2 JU had stimulated a **mind change in academia**, encouraging participants to move away from 'blue skies' research, while at the same time participants from industry became less sceptical about working with academia. The fact that IMI is generating a unique opportunity for SMEs, academia and industry to collaborate has created a broad platform that make technologies and patient material accessible to all relevant stakeholders. It also enabled academia to work directly in a clinical setting. This approach was seen by a number of stakeholders as a necessary prerequisite to address complex diseases such as cancer and has created opportunities to understand the potential effectiveness of treatments in clinical practice as well as the clinical trial setting.

Another shared achievement for both IMI JU and IMI2 JU was that they have **enabled access to key elements of infrastructure for successful research**. Some examples include: facilitating SMEs to have direct contact with clinicians to inform the appropriate design of clinical trials; development of databases of patients cohorts. Both IMI1 and IMI2 JU have also contributed to: clearer understanding of the working mechanism of molecules and identification of mechanisms to inform the stratification of patients to better target medicines to enable (i) increased effectiveness and hence, for example, extending the periods between disease episodes and/or (ii) reduced healthcare costs by minimising the number of stays in hospital.

IMI2 JU had an additional mission to IMI1 to broaden its action spectrum to include companies beyond the biopharmaceutical sector, such as technology providers. In contrast to IMI1, **mid-cap companies were eligible to receive funding** as a partner in the applicant consortium. Like in IMI1 mid-cap companies could also choose to participate as a partner by joining the industry consortium and contribute in kind, which then allows to participate in the design of the topic.

Specific achievement such as faster validation and approval of biomarkers, because of early involvement of regulatory agencies was reported by interviewees, although this was not evident yet from quantitative data on IMI2 JU. In the case of IMI1, EMA provided the panel

of experts with several examples of projects they have seen for approval or scientific advice about the approval process of innovative methods of drug development and tools.

Another objective formulated for the IMI2 JU was to reduce time to reach clinical proof of concept. This was hard to assess, because of the lack of quantitative data from completed projects.

Nevertheless, there were examples of project results from IMI1 that were expected to be sustained and potentially become more important as the IMI2 JU was continuing some of the activities from the first joint undertaking. The establishment of the SGGs, in particular, was expected to contribute to the sustainability of project outputs. Building on the close-out meetings initiated with IMI1 projects will further support sustainability of important project outcomes. **Sustainability of project results was expected to be more likely achieved under the IMI2 JU**, as projects have to include maintenance plans for important achievements in their initial business plan.

One of the projects which started under IMI1 and that was exploring options to find a sustainable follow up initiative under the IMI2 JU was the European Lead Factory (ELF). This project brought together a collection of compounds from industry and newly synthesised molecules from academia. The collection of compounds was then made accessible to allow academics and SMEs and not only members of the consortium to screen for potentially interesting drug targets. This operational mode may prove a good example of how it is possible to reach added value by joining forces and a strong argument to use a European platform for follow up studies. However, the IMI2 JU rules do not allow this IMI1 specific approach to value compounds, but EFPIA companies could design other methods (in line with the legal framework) to identify costs corresponding to in-kind contributions brought as compounds. A topic for a successor to ELF is foreseen to be published in one of the upcoming IMI2 JU calls.

Interestingly, the need for sustainability of project results beyond the funding period was not supported by all parties and in particular not supported by some representatives of the European Commission and the pharmaceutical industry. For these representatives, the PPP activities were viewed more as instrumental to catalyse concepts, but not to maintain databases once the projects were terminated. It seems that **clear criteria are needed to inform which project outcomes should be offered funding for sustainability**. It was noted that when there was no budget found to maintain outcomes such as databases, it was an indication that industry was not sufficiently interested. To keep databases sustainable, the business plan should have foreseen this from the start, as is now in place for IMI2 JU. As the importance of some of the outcomes of IMI2 JU projects is acknowledged, the IMI2 JU Governing Board however agreed on a call topic to be published in July 2017 addressing the issue of maintaining important resources beyond the original projects timeframes.

The ultimate goal of establishing a joint undertaking on innovative medicines development, was to support and increase the competitiveness of the European pharmaceutical industry. The socio-economic impact of IMI2 JU in Europe should therefore be addressed during the interim evaluation. Both the IMI Programme Office and EFPIA representatives found it difficult to identify **socio-economic benefits** and indicated that **more time was needed before specific economic indicators would be able to indicate a change**. It was also mentioned that it remained rather unclear what, and how, to monitor the socio-economic benefits from IMI. The published report on the potential socio-economic impact of nine completed IMI1 projects suggested some possible metrics to begin recording to allow the benefits to be quantified.¹² The findings from this report still have to be put into practice.

According to one of the interviewees, IMI1 may have contributed to resilience of the European pharmaceutical industry at the time of the crisis in 2008, as the number of clinical trials and research remained stable across Europe. This effect could be expected to be further supported by the IMI2 JU. In addition, the same source also stated that pre-IMI disinvestment has been switched to new investments in European biomedical research in pharmaceutical companies, including in difficult research areas such as dementia diseases,

¹² www.imi.europa.eu/sites/default/files/uploads/documents/Publications/SocioeconomicImpactAssessment_FINALMay2016.pdf

although quantitative data supporting these statements were not available for the expert group.

As outlined in the final evaluation report on IMI1 the number of clinical trials decreased after 2010 to the number of just before the economic crisis of 2008 and remained relatively stable around that level until the end of 2016. However, no numbers were available to directly compare with other economic areas, such as in the US. Therefore, it is difficult to attribute a direct effect of IMI1 or IMI2 JU on the stability of number of clinical trials in Europe as an indicator for economic resilience.

Specific and measurable outputs from projects were in general difficult to find, although information on the achievements, in addition to publications, from IMI funded projects are listed on the IMI-website.

In summary, it was deemed **too early to report on specific achievements of IMI2 JU**. It was stressed by all IMI, EFPIA and GB representatives **that a long-term strategy was required before the joint undertaking on innovative medicines and follow-up initiatives could have a demonstrable effect to build and maintain the competitiveness of the European pharmaceutical industry.**

7.1.2 Extent to which the objectives of the Joint Undertaking have been met

This section addresses the progress towards meeting the IMI2 JU objectives and how all parties in the PPP live up to their financial and managerial responsibilities. The objectives spelled out in the council regulation are summarised in Box1.

7.1.2.1 Implications for the joint undertaking moving from FP7 to Horizon 2020

The overall regulation under the IMI2 JU, including the financial rules and IP policy were consistent with the Horizon 2020 rules, with some specific exceptions, linked to the public-private nature of the initiative. The main differences in the IP rules after IMI1 are outlined in section 3.1.6.

The overlap in project implementation between IMI1 and IMI2 JU combined with a significant difference in the main objectives as well as the changes in the legal framework (from FP7 to Horizon 2020) raised concerns among several of the interviewed IMI JU office representatives. As most of the IMI1 projects were still ongoing, the IMI office staff faced challenges in navigating through two different strategical and operational frameworks.

The differences between IMI1 and IMI2 JU introduced a certain discontinuity in monitoring progress towards meeting the goals and objectives of both phases of the public-private partnership. The fact that no satisfying monitoring system was available to demonstrate the progress to achieve the goals and objectives as well as the socio-economic impacts of both phases of the joint undertaking was perceived by the expert group to be a major weakness of both IMI1 and IMI2 JU.

7.1.2.2 Extent to which the IMI2 JU achieved the objectives set in Article 2 of the Council Regulation establishing IMI2 JU

IMI2 JU mission and Strategic Agenda setting

The objectives of the IMI2 JU have been introduced in Section 3. The objectives were translated into a mission statement that was discussed during a Governing Board meeting in 2016 and at the time of drafting of this report is awaiting validation by the Governing Board. It is presented in the draft intervention logic model as:

"IMI facilitates open collaboration in research to advance the development of, and accelerate patient access to personalised medicines for the health and wellbeing of all, especially in areas of unmet medical need."

The website outlines the IMI2 JU specific goals as: "to develop next generation vaccines, medicines and treatments, such as new antibiotics".¹³ The IMI2 JU in addition has defined six specific objectives (Box 1) that it intended to achieve en route to reaching these ambitious goals. These objectives were quite different from IMI1, as those of IMI1 were defined in more general terms and focused in contrast to IMI2 JU almost exclusively on precompetitive research.

To address these objectives the Strategic Research Agenda (SRA) was designed. The SRA serves as the basis for the annual work plan. The first Strategic Research Agenda (SRA) was published in 2008, updated in 2011, and ended in 2013 coinciding with the end of the governance period of the first IMI JU. With the start of IMI2 JU, a new SRA, for the period 2014-2024, focussed strongly on the development of new medicines, but also emphasised on the need for tools and methods to bring new medicines faster to patients.

In 2004, WHO was commissioned to produce a report on Priority Medicines for Europe and the World by the Netherlands Ministry of Health. In 2013 the European Commission requested that the report be updated as a resource to be used in planning the Horizon 2020 combined research program for the European Union. According to the Council Regulation establishing IMI2 JU, one of the objectives of IMI2 JU was to increase the success rate in clinical trials of the priority medicines identified by the WHO.

Formulation and implementation of IMI2 JU Research Activities

Every year, IMI draws on its legislation and the SRA to set out annual research priorities. These form part of the Annual Work Plan, which is approved by the Governing Board and published online. These annual priorities are based on the need for collaboration in complex areas of biomedical research and innovation. The health priorities that were addressed were aligned with the 2013 update of the World Health Organisation's 'Priority Medicines for Europe and the World', as specified in the objectives of the Council Regulation.¹⁴ The influence of WHO's priorities and its relationship with IMI2 JU is reflected in figure 4.

The first IMI2 projects concerned mainly Ebola and related diseases. It should be noted that IMI2 JU was able to set up a rapid and efficient launch of several calls when it was clear that Ebola virus represented a real threat for Europe, at a time where there were no means to detect and appreciate the gravity of the outbreak.

It was appreciated that IMI2 JU, in spite of what could appear as a huge, rigid administrative structure, had been successful in implementing in a very short period of time of just a few months several Ebola projects involving European and African teams. Four IMI2 clinical trials, up to now, have been realized in Sierra Leone, Kenya, Uganda, Tanzania, Burkina Faso and Ivory Coast. Two projects concern the implementation of a phase 1 or phase 2 prime-boost Ebola vaccine.

Some of the Ebola projects included training and social and human science aspects, which are essential components to develop and sustain projects in Africa even if the threat of Ebola had (at least temporarily) disappeared.

Diabetes, another major WHO concern, has been to date addressed in two IMI2 JU projects (Innodia and Rhapsody).

Annex 8 lists the areas addressed under the IMI2 JU during the interim evaluation period. It can be concluded that these topics may be expected to contribute to achieving the objectives according to Article 2 of the Council Regulation.

7.1.2.3 Extent to which the IMI2 JU achieved the objectives set in Article 2 of the Council Regulation establishing IMI2 JU - Networking and pooling of stakeholders

The section below summarises how IMI2 JU projects have brought many types of stakeholders to work together towards common goals.

¹³ <http://www.imi.europa.eu/content/imi-2>

¹⁴ www.who.int/medicines/areas/priority_medicines/en/

The major group of stakeholders driving the research projects in IMI2 JU came from **academia** either universities or research organisations as outlined in section 6. Together they made up more than 55 % of the participations (including the in-kind contributors) and close to 75% of the EU funded participations. In terms of EU-funded participations in grant agreements, UK was the first recipient (69 participations), Netherlands (54), Germany (51), Italy (32), France (31). Countries from Eastern Europe were poorly represented as in IMI1, e.g. Poland (2).

In terms of EU funding the UK received EUR 107 million, The Netherlands EUR 36.5 million, Germany and France EUR 25 million, and Spain EUR 21 million. It should be noted that these amounts are mainly related to the first IMI2 calls on Ebola virus.

The participation of **SMEs** in IMI2 JU projects was viewed to be of major importance as it was a key element for the success of this multidisciplinary approach of innovation in medicine in the future. SMEs are seen as essential cog-wheels that drive competitiveness of the European health industry. However, when comparing the involvement in IMI1, **the SMEs participation decreased under IMI2 JU.**

The barriers for SME participation were addressed by IMI2 JU in a workshop that was organised in May 2016. The conclusions of this workshop were summarised in a report and were confirmed by several interviewees.¹⁵ One of these barriers was that Venture Capital (VC) funded SMEs were more adverse to risk-taking strategies than owner-capital SME in an environment that strongly competes for funding. VC-funded SMEs were strategically more narrowly focussed and if the funding call was not aligned with the SME strategy, then these types of SMEs were less likely to participate. Owner-capital SMEs were more flexible in this respect.

The timeline projections before a return on investments can be expected also should be taken into account. As noted by EFPIA it can take 13 years from the scientific investigation into a disease that may identify potential treatments for that disease through to the availability of a medicine to patients. Some estimates indicate that an average biotech project takes 15 to 20 years before a return on investment can be expected. An IMI project timeline is clearly too short to realise a return on investment in its running period.

It is important to note further that **SMEs often indicated they were bad equipped when taking part in consortium negotiations, especially when discussing Intellectual Property (IP) issues.** SMEs often come in late to join the (large) consortium. At this stage, SMEs cannot always fully weigh on the negotiations and contribute to the design of the projects. Testimonials from SMEs in the interviews with the expert group indicated that some SMEs had the perception that IP rules were customised for big pharmaceutical companies, although these are the same for H2020 with few derogations. It is more likely however, that the size of the consortia, which include large companies with professionals to address the IP issues, combined with a lack in the required human and financial resources to invest in time consuming and hard negotiations, created, to both SMEs and academic partners, this threatening perception of the current approach to IP.

The focus on precompetitive research was for most SMEs in fact their core business, which may pose a certain threat as this implies that taking part in IMI projects interfered with exclusivity rights for exploitation. According to the interviewed IMI representatives, the observed shift in IMI2 JU when compared to IMI1, from merely precompetitive research projects towards addressing the whole cycle of innovation, was appreciated by the SMEs.

Similar sentiments to those on IP issues were expressed about the IMI2 topic descriptions, which were defined top down by the pharmaceutical companies and perceived to be too narrow. In this way, SMEs were obliged to follow the lead of big pharma, while SMEs on the contrary often need more flexibility.

One SME representative reported how they found the IMI projects, in general interesting, especially when the topic formed part of the core business of the SME's goals. This representative also saw the benefit of SME's, large pharmaceutical companies and academic groups being brought together. For this SME the available funding was the main reason for

¹⁵ www.imi.europa.eu/sites/default/files/uploads/documents/Events/SMEworkshop_notes.pdf

participation in an IMI project, but when compared with Horizon 2020, the latter was appreciated as better supporting innovation.

IMI has made efforts to facilitate the participation of SMEs. In addition to the direct involvement of SMEs as IMI beneficiaries, some projects like the European Lead Factory or ENABLE that started under IMI1 led support to the activities of SMEs. These were encouraging signals but in this evaluation period participation of SMEs in IMI2 JU decreased from 15.96% of all EU funded participations under IMI1 to 11.78% in IMI2 JU. There were 192 SMEs participations and a EUR 128 million IMI2 JU contribution. The share of the total EU contribution to SMEs in IMI2 JU has also decreased so far from 13.25% to 10.33% of the total EU funding. Under IMI2 JU, the 43 SME participations as of end 2016 corresponded to 36 different SMEs, of which 28 did not previously participate in IMI1 and seemed to cover other fields than pharmaceuticals. One reason given by an SME participant was that IMI was interesting when the company was small, and the IMI1 budget was used to consolidate the activities, but that interest became less valuable as the company grew, for several reasons including sharing IP and opportunities provided by other EU instruments.

The participation of SMEs in IMI2 JU may be hampered further, because it was also competing with programmes at national level which may have facilitating factors such as proximity and language. In addition, there was sometimes less competition for funding at national level and the chance of success may be increased through the EU structural funds or other national funding programmes. Furthermore the SME instrument and Eurostars have become strong competitors as a source for collaborative projects.

Unlike in IMI1, mid-cap companies were eligible for participation in IMI2 JU, not only in the biopharma designing consortium with in-kind contributions to the project, but also as the responding consortium receiving EU funding for the activities. A major advantage to be a partner in the designing consortium was that specific goals can be introduced that may be of specific relevance to the partner. Still many important mid-cap players remained absent in IMI2 JU. Many of the barriers for SMEs were also likely to apply for the mid-cap companies, such as IP issues or the relevance of the topic description. It was unclear to the expert group how IMI2 JU can improve participation of these mid-cap companies.

Another major goal introduced by IMI2 JU was the inclusion of stakeholders representing **sectors other than the biopharma sector**. A budget of EUR 213 million from the EU was allocated to achieve this and its importance is illustrated in Box 4. Given the current development towards a connected society, the innovative technologies in bio-imaging, and the progress made towards personalised medicine, it was clear that technology providers, companies addressing data storage and handling or developing communication aids are essential partners for biomedical innovation.

Box 4 Transforming healthcare

The technological evolution is of paramount importance as illustrated from the title of a recent article (Jan 2015) published in the Wall Street Journal: "The Future of Medicine Is in Your Smartphone". The author adds: "with innovative digital technologies, cloud computing and machine learning, the medicalized smartphone is going to upend every aspect of health care. And the end result will be that the patients are about to take center stage for the first time".

Smartphone real-time data collection and the use of embedded sensors is the key to a better health. The possibility to trace ECG, measure pulse rate and rhythm, oxygen saturation, systolic blood pressure, physical activity and sleep, will completely transform the follow-up of a patients. The smartphone is of course only one of the numerous technologies that is revolutionising the medicine in the future. The "conventional" medicine as it is provided today by the pharmaceutical industry will probably reach an end sooner rather than later. The developments open huge opportunities for innovative applications.

Examples of the new developments are numerous and range from the digital contact lens which aims to change the course of diabetes management by measuring blood glucose levels from tears, to tiny digestible sensors that can be placed in pills and transmit pill digestion data to physicians and family members. These technologies will improve adherence and compliance which are crucial issues in improving patients' health and hence will contribute to keeping healthcare costs under control. Also radiology is one of the fastest growing and developing areas of medicine. A single multi-functional machine will be able to detect simultaneously biomarkers and symptoms at once, while *in silico* clinical trials and Organs-on-Chips technology allow unlimited testing of drugs or components. This will significantly reduce clinical trials costs as studies will be faster, more safe and more accurate.

Central to the development of the future healthcare are the Big Data resulting from genome, microbiome and metabolome analysis which is also crucial for the pharmaceutical industry. Artificial intelligence, use of high performance computing is expected to further reduce the cost of drug development by predicting in advance which potential medicines will be effective and safe in patients. Data management and handling, and computing capacity are essential parts of tomorrows' healthcare. However, there is a risk that monopolies are being created in a limited number of global companies, controlling essential data.

www.wsj.com/articles/the-future-of-medicine-is-in-your-smartphone-1420828632

As Big Data acquisition, data transmission, storage and safety are increasingly becoming important in medicines development, the need for standardisation becomes more relevant than ever to provide a mechanism to assimilate data from heterogeneous sources.

A number of large companies, as well as of SMEs, active in these domains are present in Europe. There is an ongoing awareness of the tremendous growth (potential) of the health care market although most of the IT companies did not participate in IMI2 JU as seen from the list of non-pharma industries in IMI2 JU grant agreements and call topics. They seemed to prefer not to be associated with and represented by EFPIA.

IMI2 JU tried to involve a wide range of stakeholders from around Europe and beyond in its projects. Some stakeholders took part into IMI2 JU as Associated Partners or by becoming members of EFPIA. Others, such as patients' organisations and SMEs, were more likely to join projects as funding beneficiaries.

EFPIA's 'Partners in Research' membership category offered companies outside the pharmaceutical sector to contribute to IMI2 JU as EFPIA members. In 2016, EFPIA Partners in Research with expertise in fields such as diagnostics, medical technology, imaging and data analysis were committed to new IMI2 JU Call topics. IMI actively promoted and communicated opportunities to involve other sectors than the pharmaceuticals sector.

Actions taken to achieve the objective of IMI2 "to reach out to new stakeholders towards broadening the network of collaboration in the healthcare family" may need to be strengthened to keep pace with the accelerated development of innovation in medicine and with the arrival of new industries in the health market.

A numbers of **calls launched and projects started in 2016 reflected that digital technologies play an increasingly important role in research and healthcare and the awareness of IMI2 JU of the importance of attracting other industries.**

- The RADAR-CNS project aims to develop new ways of measuring major depressive disorder, epilepsy and multiple sclerosis using wearable devices and smartphone technology.
- Big Data for Better Outcomes (BD4BO) programme was launched in 2016. It aims to facilitate the use of diverse data sources to deliver results that reflect health outcomes of treatments that are meaningful for patients, clinicians, regulators, researchers, healthcare decision-makers, and others.
- HARMONY will capture, integrate, analyse and harmonise anonymous patient data from numerous high-quality sources to unlock valuable knowledge on haematological malignancies.

By December 2016, the IMI office showed that **IMI2 "has already been successful in attracting companies in sectors** such as: Imaging (e.g. GE Healthcare, Zeiss, Piramal Imaging, or Bruker), animal health (Zoetis), diagnostics (e.g. Biomérieux), advanced IT technologies (e.g. Intersystems, Health IQ, or SAS), and medical technologies and devices (e.g. Medtronic or Dexcom)".

However, the involvement of other industries brings **more complexity to the open innovation model handled by IMI2 JU as the business models of the non-pharmaceutical companies are not the same as those of EFPIA members** and need to be taken into account. In addition, **IP is handled differently.** Some of the non-pharmaceutical companies were reluctant to share their IP in IMI2 JU (type of) projects. As a result a number of important imaging companies were absent from the IMI2 programme and the number of diagnostic companies and medical devices companies was low. Participation of non-pharmaceutical companies in general should be increased to take up a leading role in the development of the medicines of tomorrow.

In summary, three barriers were identified that made it difficult to encourage the involvement of companies other than pharmaceutical companies:

- Global technology providers in projects other than supported by IMI2 JU, tend to be funded, instead of contributing with in-kind contributions.
- The cycle, and business models, used by technology providers were completely different when compared with those of pharmaceutical companies; there is virtually no pre-competitive space and the way intellectual property is handled is entirely different.
- There was no organisation comparable to EFPIA representing technology providers. The category created by EFPIA for Associated Partners may not result in the intended goal as non-pharmaceutical companies may feel not truly represented by EFPIA.

One approach to overcome some of these barriers could be to collaborate with the initiatives that have a tradition of funding technology providers, such as the Electronic Components and Systems for European Leadership Joint Undertaking, ECSEL JU. The expert group was, however, sceptical that this suggested approach would be successful, because global companies, such as Google, Samsung, Huawei, were already very active in medtech, indicating the sense of urgency for Europe. The expert group strongly suggested that discussions with ECSEL JU should be accelerated and open programmes for new collaborations should be developed.

Another approach would be to ensure that the non-pharmaceutical companies were represented in the IMI2 JU governance structures by an organisation which could match the role of EFPIA.

IMI2 JU also aimed to **increase the participation of patient organisations.** Although in principle, integration of patient organisations in an IMI2 JU project seems straightforward, as these organisations do not bring IP nor research infrastructure, it has not been easy to

achieve increased participation. The participation level of patient organisations increased (from 2.2% of the EU-funded participations in IMI1 to 3.3% in IMI2 JU), while the corresponding budget allocated (0.6% of the total EU contribution) remained at a similar level when compared to IMI1.

In one IMI2 JU project a patient organisation (JDRF International) provided an in-kind contribution of EUR 4.7 million, but according to an interviewee, how to value the assets they were bringing in the form of the network and the participation for the calculation of their in-kind contributions, had been difficult. In all other cases the patient organisations were EU beneficiaries or participated through advisory bodies to the projects. The participation of patient organisations as beneficiary of EU funding was EUR 1.6 million for the first phase of IMI2 JU whereas it was EUR 5.7 million for the overall duration of IMI1. The patient organisations appreciated **the opportunity to participate in the design of projects which was not possible in other Horizon 2020 programmes**. A strong engagement with patients was evident, and was probably linked to the fact that they regularly actively participated in workshops and during the annual Stakeholder Forum. However, there is ongoing discussion within IMI2 JU about how, and which, patient groups can be further engaged and what criteria should be handled for their input without creating a bias or conflict of interest.

Efforts to increase patients' involvement further need to continue and the IMI representatives realised that this is an ongoing learning process. Under IMI2 JU the opportunities for patient organisations to participate have been improved and feedback or contributions from patient organisations in call topics were made easier.

At the of end of 2016, IMI2 JU had been successful in attracting three associated partners, being **non-governmental organisations**, to projects among the first 25 signed grant agreements:

- The Bill and Melinda Gates Foundation (BMGF) (PERISCOPE project);
- The diabetes charity JDRF (INNODIA and BEAt-DKD projects);
- and the Leona M. and Harry B. Helmsley Charitable Trust (INNODIA project).

Some further Associated Partners are expected to join new projects that will be selected from the calls still ongoing at the end of 2016:

- Autism Speaks;
- Simons Foundation Autism Research Initiative (SFARI);
- and T1DExchange on diabetes.

Many of the above mentioned organisations are based in the United States. Their involvement in IMI2 JU illustrates IMI's role and achievement in making Europe an attractive place for medical research and drug development. From IMI's side, their participation in projects helped to **build and strengthen links between projects and complementary initiatives on the other side of the Atlantic**. In the longer term, these links will contribute to IMI's strategy to promote the internationalisation of its projects and create a global community with Europe at its heart.

The **regulatory bodies** were also seen as major stakeholders to align with, or to be included, in the IMI2 JU projects. Involvement with the regulatory bodies brings added value and there was consensus that researchers, academics, small and medium-sized enterprises, the pharmaceutical industry, patients organisations and regulatory agencies need to work together to ensure that medicines are authorised in a shorter timeframe and are safer. Regulators will provide the regulatory tools needed to achieve greater efficiency and effectiveness in drug development. However, it was important to avoid possible conflicts of interest with industry. Participation of the regulators in IMI2 JU projects was further complicated because a negative public perception may undermine a close participation with industry. Also for regulators IMI2 JU projects were often considered too top down and too complex.

The participation of regulators in IMI2 JU projects remained limited, although it slightly increased from 16.9% of all IMI1 projects to 20% of all IMI2 JU projects, which was reflected in the budget allocation that increased from 0.8% under IMI1 to 1.0% of the total EU contribution in IMI2 JU.

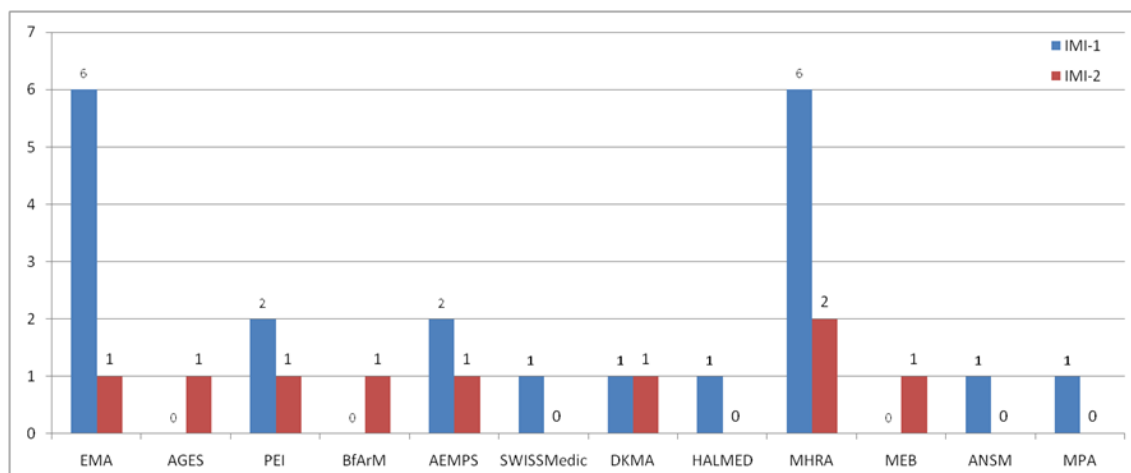
EMA as well as seven national regulatory agencies from six countries participated in five of the 25 IMI2 JU projects (20% of the projects), in areas covering vaccines, 'big data' to improve the care of patients with blood cancers, or haematological cancers and access to beneficial treatments for the right patient groups at the earliest appropriate time in a sustainable fashion (Figure 7).

At this point of evaluation, the participation figures can only indicate a trend and cannot be compared directly with the IMI JU. However, two important agencies, AGES and BfArM, participated for the first time. In contrast, it was striking that the UK MHRA, which used to be the largest regulatory agency participating in IMI1 after the EMA, has not yet been a participant in IMI2 JU projects.

EMA was participating to IMI2 JU at several levels. It was represented in the SC of IMI2 JU, in stakeholders meetings or at the Regulatory Summit. EMA has been a partner in some of the IMI1 projects, and so far also in one IMI2 JU projects. To reach a broader audience, EMA encouraged companies to approach them early on in the development of the projects and recommended that any advice given in such consultations should become publically available so the advice which was often generic, could serve as a model for different projects. Briefing meetings, run by regulatory bodies, at the start of a project may be helpful. The organisation also promoted the idea that projects created an advisory board on which EMA can participate. **IMI2 JU was considered useful to improve the dialogue between industry and regulators** and to raise awareness of academic partners about the importance of taking the regulatory needs into account when developing a project to improve the process of bringing new products to society. In addition, EMA recommended that payers and patients should be involved early in the IMI2 JU projects to improve access to medicines.

Of the total of the European medicines agencies network, only a very small fraction (Figure 7) have participated in IMI2 JU projects, which means that specific actions need to be developed for regulators to increase their participation. Alternatively, a different type of collaboration could be envisaged. These actions should aim primarily to disseminate concrete examples of positive results from the collaboration between industry and regulators among the European regulatory system for medicines, and to enable regulatory agencies to participate in the definition of priorities and topics from the perspective of health systems and public health priorities.

Figure 7: Overview of the participating regulatory agencies



EMA	European Medicines Agency, United Kingdom
PEI	Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel, Germany
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios, Spain
SwissMedic	Swissmedic, Berne, Switzerland
DKMA	Danish Medicines Agency, Denmark
HALMED	Croatian Agency for Medicinal Products and Medical Devices, Zagreb, Croatia
MHRA	Medicines and Healthcare Products Regulatory Agency, (including the NIBSC centre), London, United Kingdom
MEB	College Ter Beoordeling van Geneesmiddelen, GBG-MEB, The Netherlands
ANSM	Agence Française de Sécurité Sanitaire des Produits de Santé, Saint-Denis Cedex, France
MPA	Medical Products Agency, Uppsala, Sweden
AGES	Agentur für Ernährungssicherheit, Austria
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte, Germany

7.1.2.4 Enhanced trust, exchange of knowledge between stakeholders, disciplines and projects

One of the major achievements since IMI1 that cannot be denied was that IMI collaborations have enhanced trust between academic and industry partners. There has been a mind shift that led to better understanding of each other's needs and values. Some projects resulted in the validation of new targets and the development of diagnostic markers to predict new vaccine efficacy and safety, particularly in the field of diabetes and Ebola virus. Furthermore, the project closeout meetings should provide a powerful mechanism to develop into knowledge warehouses, that analyse and summarise the outcomes of IMI2 JU projects to maximise and exploit the outputs and make progress in the respective thematic areas. The Strategic Governing Groups (SGGs) could be instrumental to further develop more of the opportunities generated by IMI projects.

7.1.2.5 Effectiveness of the implementation

7.1.2.5.1 Formulation and implementation of IMI JU Research Activities

As outlined in section 7.1.2.1 the IMI2 JU SRA was developed to fulfil the mission and to address the objectives of the IMI2 JU. The SRA is the basis to specify the annual research priorities defined in the Annual Work Plan. These annual priorities are based on the need for collaboration in complex areas of biomedical research and innovation and are a result of consultations between EFPIA companies and the other stakeholders, including the European Commission. Drawing on the **annual priorities**, a consortium of **EFPIA companies** and, in some cases, **other large companies or organisations** active in health research, agree on the **need to work together** and with **other stakeholders** on a **specific issue**. A **topic text** is drafted and, following **consultation** with various groups (including the SC and the SRG), the call text is sent to the GB for approval. When granted, the IMI2 JU Programme Office launches a Call for proposals on its website and the European Commission's **Participant Portal**.

The general sentiment among a significant proportion of stakeholders interviewed by the expert group was that the process of translating the objectives and mission of IMI2 JU into an SRA and how this is used to set the annual works programme and call topics was not transparent and **too much top-down industry driven and dominated by EFPIA partners with insufficient inclusion of other significant stakeholders in the European biopharma ecosystem**, including the academic, research and clinical centres, SMEs, regulators and patient groups. Despite the fact that feedback on the SRA, work programmes and call topics were obtained from the SC, the SGG and the SRG, it was not clear to most stakeholders how such feedback was taken into account or why certain decisions were made.

The fact that the development of call topics were predominantly defined by EFPIA partners has been a continuous source of criticism. In interviews, the topics were often described as too narrow and too prescriptive and not allowing sufficient flexibility and creativity to design the best projects. Several times various interviewed stakeholders indicated a lack of transparency in how the call topics were defined and the top-down approach has been frequently challenged as a barrier to innovation. Also the size of the consortia was criticised as potentially slowing down the progress of the projects. These visions were shared by several academic researchers as well as by SME participants.

These concerns were in line with the results of the public consultation: 50% of the stakeholders agreed or strongly agreed (33% and 17% respectively) that the current way of defining topics for the calls of proposals is open and inclusive; 37% disagreed or strongly disagreed (28% and 9% respectively) with the above statement. This issue, similar to the IP rules, was not addressed in the beneficiary survey. In contrast 90% of the responders agreed or strongly agreed that the EU should cooperate with industry in the context of a public-private partnership so that the life science research brings better results to the patients and the market in Europe – albeit perhaps in a different, improved and more transparent and open manner.

The IMI representatives indicated that the first step in the process was to agree to collaborate on projects and to commit sufficient budgets. As the pharma companies allocated half of the budgets to the proposed projects the industry (EFPIA members) consider it was justified they proposed the content of the call topics. Moreover, it was reasoned that the call topics were open for feedback from the SC and from the SRG.

Research activities are realised through projects that were selected from open and competitive calls for proposals, and after peer review by independent experts. For most calls a two-stage procedure was used. In the first stage, applicant consortia composed of the potential EU funded beneficiaries (academia, SMEs, etc.) were invited to submit a short proposal responding to the call topics. In the second stage, for each topic, one successful applicant consortium was invited to submit a full proposal integrating the EFPIA or IMI2 Associated Partners.

The selection criteria of experts for the evaluations included gender balance and geographic distribution and followed the same rules to be eligible as expert as to those of experts functioning in H2020. A minimum of three, but mostly five to seven experts per project evaluation were consulted. EFPIA can give input on the competences required, but was not involved in the selection of experts. Also the SC was solicited to review the experts, but were also not involved in the selection of projects.

Among those interviewed, the quality of the evaluation process itself was not questioned, but several sources reported that there had been contacts between the leading industrial partners and the applicant consortium at stage 1 of 2-stage calls, prior to the evaluation. Prior contacts between the applicant consortium with the leading companies and pre-formed consortia may create a more advantageous position for this applicant consortium as it may have had access to more detailed starting information than the competitors. Some of the leading European research groups interviewed indicated that for this reason they were hesitant to apply for IMI2 JU calls. If certain partners were to be preferred, this should be transparent and indicated in the call. Although actual evidence of such interactions could not be found, it was clear that a substantial group of stakeholders expressed serious reservations about transparency and openness to ensure fair competitive process in the winning proposal selection.

The issue of the pre-evaluation contacts between the lead company in a call topic and an applicant consortium has also been suggested as perhaps the reason (or part of) why the participation of eastern European countries was an order of magnitude lower than that of countries which have a long-standing tradition of collaborating with big pharma companies. Although participation of EU-13 countries was low both in IMI2 JU projects (2.5%) and the rest of the Societal Challenge for Health, demographic change and wellbeing, under Horizon 2020 projects (6.8% of all participating countries) the share of EU-13 participations in IMI2 projects corresponds to only about one third of the share of EU-13 participations in the rest of the Societal Challenge for Health, demographic change and wellbeing, under Horizon 2020.

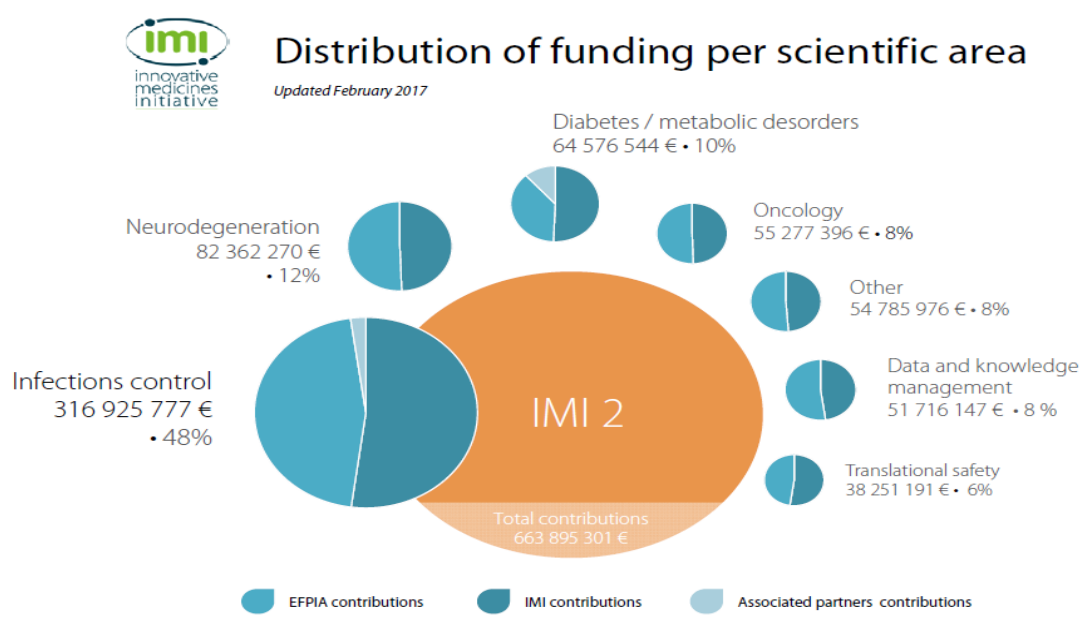
The public consultation survey results generally seemed to suggest that the broader stakeholder community is not familiar with the proposals evaluation process as two thirds of the respondents chose not to reply or had no opinion on the issue whether “IMI2 JU organises a sound and fair proposal evaluation system based on both scientific and technological excellence and industrial relevance” and 28% of the respondents agreed (20.4%) or strongly agreed (7.5%) while about 5% disagreed or strongly disagreed.

The beneficiary satisfaction survey also addressed the evaluation process. However, as the number of respondents is low and for 62 % coming from the industry consortia the results are questionable as already outlined in section 5.2.

The main concern of the expert group was that the current way of drafting the call topics did not sufficiently involve key components of Europe’s biomedical ecosystem, such as SMEs and some of the best and most competitive research groups or leading institutions with documented track records and of verifiable economic impact as indicated by SMART KPIs and solid metrics.

An overview of the financial contribution per scientific area is given in figure 8.

Figure 8: Distribution of funding per scientific area - update January 2017 (IMI office)



A major achievement of IMI2 JU was the effects of close collaboration between academia and industry and also large pharma companies working together. Such collaborations would have been more difficult, if not impossible, to achieve if the PPP had not been established. Nevertheless, the SME involvement in IMI2 JU, which was around 10% of EU contribution received (more than 30% decrease from IMI1 and 25% lower compared to participations in the rest of the Societal Challenge for health, demographic change and wellbeing, under Horizon 2020, even when the SME instrument is excluded). The SME engagement certainly needs improvement as the participation and received contribution are both significantly below the 20% participation target for Horizon 2020. Some of the interviewees, from academia and SMEs suggested that public funding may be better invested to support the competitiveness of European SMEs with calls and funding directed towards more SME oriented topics.

7.1.2.5.2. IMI2 JU Knowledge Management and IP Policy

The current IMI2 JU Knowledge Management and IP Policy and provisions were based on the following documents:

- Articles 23 to 31 of the IMI 2 Model Grant Agreement¹⁶;
- A presentation summarising the IMI2 IP provisions, including details of what is new under IMI 2 compared to IMI 1¹⁷;
- A video of a presentation of the IMI 2 IP Policy given by IMI Legal Manager Magali Pointot at the IMI 2 Open Info Day in Brussels, Belgium, in September 2014¹⁸.

All of these documents were available for downloading at the IMI JU website at: http://www.imi.europa.eu/content/documents#ip_policy; or at:

<http://www.imi.europa.eu/content/intellectual-property-policy>.

The main differences between IMI1 and IMI2 JU IP policy were the following:

- The IP and access rules under IMI1 were modified and more flexible than the general IP provisions of FP7, while in general IMI2 JU all IP and access rules are consistent with the general Horizon 2020 horizontal rules with very limited derogations;
- The concept of non-exclusivity that is common to the general framework of Horizon 2020 is also implemented under IMI2 JU;
- The protection of research results for beneficiaries receiving funding and open access to publications are mandatory;
- Under IMI2 JU it is no longer possible to derogate from the principle of ownership (with consent of generator) as was the case under IMI1: IP ownership belongs to the entity that created it;
- The access rights to background and research results are mandatory as detailed in Table 2.

The use of Horizon 2020 general IP principles may be simpler from the legal consistency point of view; however, this approach has introduced a lack of flexibility and adjustments, making it sometimes difficult to protect original owners of the IP, which undergoes modifications or improvements in IMI2 projects.

The access rights (Table 3) were sometimes perceived to be risky and/or unclear for asset-driven SMEs that feel their background IP, as well as the related IP generated from the projects were not sufficiently protected. According to the IMI2 JU office, effectiveness and impact of the IMI2 JU initiative would benefit from a more flexible and case-specific approach of IP and access regulations.

¹⁶ www.imi.europa.eu/sites/default/files/uploads/documents/Rev_Grant_Agreement_2011/IMI2_JU_Mode|_Grant_Agreement.pdf

¹⁷ www.imi.europa.eu/sites/default/files/uploads/documents/Intellectual%20Property/IMI2_IPrules_April2015.pdf

¹⁸ [/www.youtube.com/watch?v=Ws458QimRDU](http://www.youtube.com/watch?v=Ws458QimRDU)

Table 3: Access Rights Conditions in IMI2 JU Projects

Access rights granted by a beneficiary to/on	Background (necessary and identified)	Results	Sidelight
Beneficiaries for completion of the action	Royalty-free	Royalty-free	N.A.
Beneficiaries and affiliates for Research Use	Fair & reasonable terms for background needed for using the results	Fair & reasonable terms	N.A.
Third Parties for Research Use after the action	Fair & reasonable terms for background needed for using the results	Fair & reasonable terms	N.A.
Beneficiaries and affiliates or Third Parties for Direct Exploitation	To be negotiated	To be negotiated	N.A.

According to some of the leading research organisations and SMEs that were interviewed, the non-exclusive nature of the access rights under the IP policies form a significant barrier to participation in IMI projects and creation of economic activity in the EU-based biopharma ecosystem. The inability to effectively protect the IP (due to access rights provisions) in general prevents IP owners/ inventors to raise private investments for further development and commercialisation. It should be noted, however, that this issue was not specific to IMI2 JU, but was generally the case for Horizon 2020. The issue of IP and access rights has not been addressed in the public consultation survey nor in the survey of beneficiaries. In the opinion of the interviewed IMI Programme Office staff who deal with IP issues, applying Horizon 2020 rules the non-exclusivity provisions create a difficulty to protect original owners, when improvements are introduced by a consortium (i.e. in the Ebola project). The IP policy should allow sufficient flexibility to negotiate exclusivity rights under certain conditions. One common and rigid legal framework with no flexibility (“one size fits all” approach) appeared to discourage SMEs from broader participation and limits innovation under Horizon 2020 in general and IMI2 JU specifically.

7.1.2.5.3. Communication and dissemination strategies

An improved communication and dissemination strategy has been developed for IMI2 JU, which more effectively and efficiently addressed the needs in this domain than under IMI JU. The approach to communication and dissemination as part of the IMI2 JU was based on the IMI Communication Strategy document that was created and approved in 2015 (Figure 9). The strategy was updated annually and the last update was in January 2017. However, the document was not publically available at the time of preparation of this report. The IMI Communication Strategy defined general and specific objectives and set a comprehensive framework for IMI communication and dissemination. The IMI Communication Strategy aimed to increase the level of awareness of IMI amongst all target groups, while also identifying critical success factors. The need for effective communication is an important area that is also referred to in later sections of this report.

The IMI2 JU communication objectives were to:

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

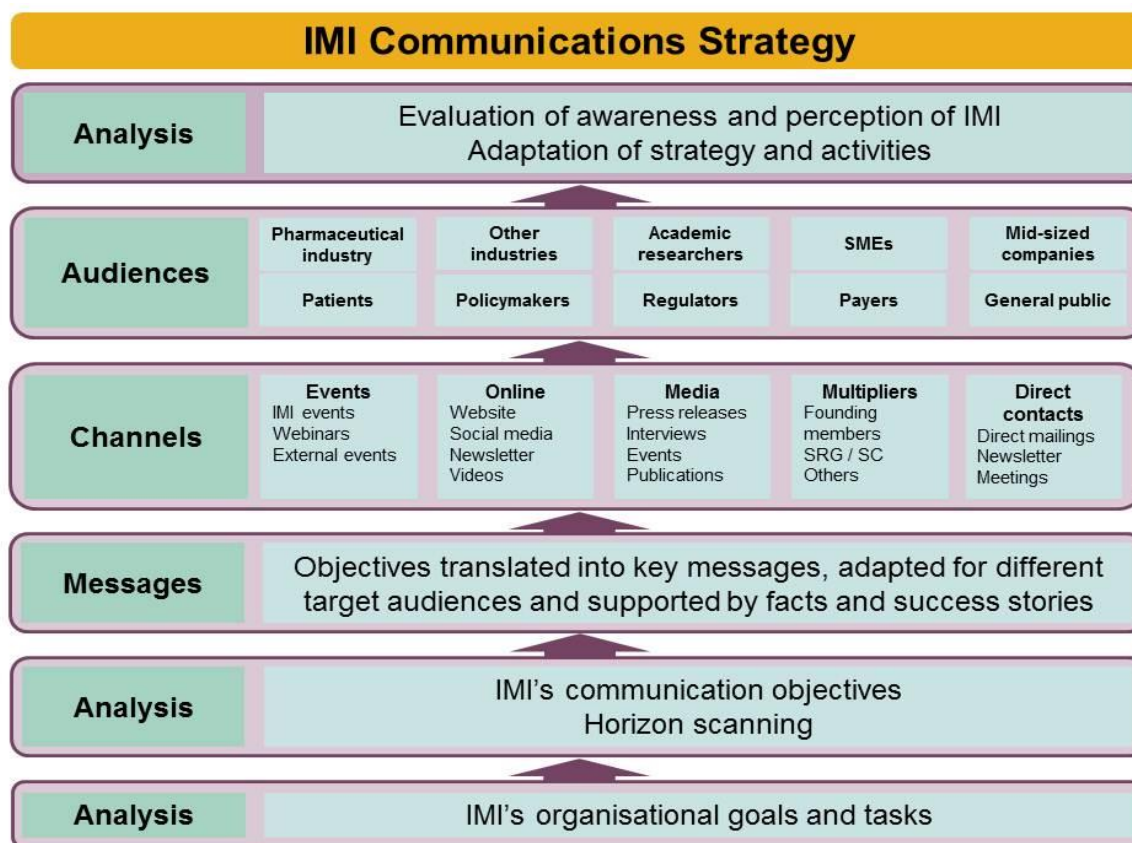
The IMI Communication Strategy identified two points of particular importance for action:

- continuing to reiterate the basic facts about IMI to counter misinformation;
- gathering both quantitative and qualitative proof of the positive impacts of IMI and turning these into formats that are appropriate for different target audiences.

The tasks of IMI2 JU set out in the legislation creating the initiative that relate to communication included to:

- publish information on the projects, including participating entities and the amount of the financial contribution of the IMI2 Joint Undertaking per participant;
- engage in information, communication, exploitation and dissemination activities by applying mutatis mutandis Article 28 of the Regulation (EU) No 1291/2013, including making the detailed information on results from calls for proposals available and accessible in a common Horizon 2020 e-database;
- liaise with a broad range of stakeholders including research organisations and universities; and to
- organise regular communication, including at least one annual meeting with interest groups and with its stakeholders via the Stakeholder Forum to ensure openness and transparency of the research activities of the IMI2 Joint Undertaking.

Figure 9: IMI Communication Strategy as outlined in the January 2017 update



IMI2 JU also provided a Communication guide for IMI projects, which sets out the rules that all IMI2 JU projects should follow when preparing communication products. It also set out ways in which the IMI2 JU Programme Office can help to promote projects' achievements, activities, events, etc.¹⁹

¹⁹http://www.imi.europa.eu/sites/default/files/uploads/documents/ProjectDocs/CommunicationGuide_IMIprojects_v2016.pdf

The suggested communication elements in the guide included:

- Project results (especially if published in a peer reviewed journal / presented at a conference, etc.);
- Creation of new tools/ data bases for drug discovery;
- Public project events (including symposia held during scientific and other conferences, exhibition booths at conferences, etc.);
- Major press coverage of the project;
- The launch of a new activity in the project (e.g. a new clinical study); and
- Any aspect of the project where input from the wider drug development community is needed (e.g. a survey).

Based on the 2016 Annual Activity report of IMI2 JU, the communication activities have been realised through several communication channels and have targeted a wide range of stakeholder groups. Various channels are used to address internal (inside the IMI2 consortia) and external (stakeholders from research organisations, SMEs, patient organisations, regulators as well as the general public, politicians, member state representatives) target groups. These channels include:

- events, such as international conferences, like BIO or BioEurope, stakeholder fora, webinars, meetings, info sessions, workshops, roundtables, debates;
- publications, such as scientific peer reviewed publications, electronic newsletters, other on-line materials, printed articles and information brochures;
- the IMI2 JU website: <http://www.imi.europa.eu/content/home>;
- social media, such as Facebook, Twitter and LinkedIn;
- Newsletters and internal bulletins; and
- traditional media channels including news, newspaper and periodical articles, movie clips.

According to the results of the IMI Beneficiary Survey (relevant to both IMI1 and IMI2 JU), the following communication channels of IMI2 JU were generally considered useful: e-mail contact (91% of responders), face-to-face contact (meetings, events – 88%), telephone contact (73%). The majority found information on the IMI JU Website slightly useful (67%), with only 11% finding it very useful), while other on-line communication channels such as live web briefings & chat and recorded messages (videos) were found less useful (respectively: 44% and 26% of responders finding these very useful or slightly useful). However, given the low response rate to the survey, these findings should be viewed with caution.

In terms of communication and dissemination efficiency to the general public, the perception evident from the public consultation on IMI2 JU was also indicative that there is some room for improvement. Only 42 to 43% of the responders agreed (and only 7% strongly agreed) that the JU website provides the general public and potential new members and participants with easy access to information. In particular only 6% strongly agreed and 35% agreed at all that the IMI JU website provided easy and effective access to knowledge generated by the projects funded under both IMI1 and IMI2 JU.

Several interviewees indicated there was room for improvement with respect to communication and knowledge dissemination, which may also improve the sustainability of outcomes of IMI projects. Access to IMI1 project outcomes for entities outside of the relevant consortia was reported to be difficult. It was too early to assess this aspect for IMI2 JU, as none of the projects have been completed and only a few past their mid-stage. Nonetheless, a built-in system should ensure platform accessibility to the entire community of academic centres and industry. The GB and IMI Programme Office have a role here, but also project coordinators should be more involved. Ideally a communication and dissemination plan should be part of the project from the start. In addition an **access policy to project outcomes for entities outside of the relevant consortia should be clear at the project level as well as at the IMI2 JU level**. This does not necessarily mean free access, but open access on fair and reasonable terms. Such access policy should be part of the communication and knowledge dissemination strategy.

The communication strategy includes the monitoring of the effects of the communication activities. Special emphasis is made to increase patient involvement. Initial milestones were defined, which will then allow to set a baseline and the identification of SMART targets to assess the success of the communications strategy to increase patients' involvement in IMI2 JU programmes.

Initial milestones are:

- implementation of more patient-friendly procedures;
- publication of certain initial materials;
- identification of and successful outreach to key organisations and opinion leaders.

Once these are in place, IMI2 JU can monitor levels of patient interest in IMI, as measured by involvement in committees and panels, visits to patient pages of the website, interest on social media and attendance at events.

The IMI2 Programme Office monitored the impact of the communication activities in different ways. The number of sessions and users were analysed with Google Analytics. In line with the IMI2 JU performance indicators, the IMI website should attract an average of 10,000 visitors per month. This target has been reached since 2013. Furthermore, the number of followers in social media such as Twitter, LinkedIn is being followed and shown to be gradually increasing every year.

The effectiveness of the communications actions is further visible through the press coverage both in popular, but mostly in specialist press, which indicated that IMI2 JU is covered in the 28 EU member states and the US. The UK, Germany and Italy reporting most frequently on IMI2 JU.

The communication strategy, tools and channels to raise awareness of IMI2 JU, appeared to be logical and well thought through, reasonable and extensive. However, based on decreasing participation rates of SMEs, insufficient participation of other industry sectors and some of the results of beneficiary and public surveys identified above, the monitoring of the **effectiveness and impact of communication and dissemination actions could be improved.** In addition, broader communication and access to results and outcomes of IMI2 JU projects was still needed and expected to broaden the participation of different stakeholders in IMI2 JU.

7.1.2.5.4. Openness and transparency

Despite the comprehensive communication strategy and the extensive efforts the IMI2 JU office has not been able to eliminate some of the stakeholders and general public concerns regarding the following issues:

- Lack of evidence of achieving a measurable socio-economic impact;
- Concerns with the truly open competitiveness of the calls for proposals;
- Concerns with the transparency of the in-kind contribution by the industry;
- Concerns with the flexibility and openness of EFPIA companies to other industry sectors; and
- Limited awareness of and access to project results outside of the consortia that generated the results.

The main objective of the communication strategy should not only be to increase awareness, but should also demonstrate the attractiveness and European added value of the initiative. A solid performance assessment methodology that measures not only scientific output in the form of publications, but also gives insights in socio-economic impacts realised would help to take away the continuing concerns about the lack of transparency of IMI2 activities.

Several interviewed stakeholders and expert group members reported that access to IMI project outcomes for entities outside of the consortia that generated the results proved to be difficult. This is a serious weakness of the IM2 JU, and is partly reflected by the public consultation survey results. Less than 42% of responders strongly agree or agree that the IMI2 JU website provided easy and effective access to knowledge generated by the projects funded under this joint undertaking and a similar share (41%) strongly disagreed or

disagreed. 17% had no opinion or gave no answer on this issue. However, project results could also be made available via other ways such as data repositories, or projects websites. Lack of easy access to information on project outcomes may nevertheless significantly reduce the impact of IMI2 JU.

Improved awareness of results and access to those results would help to build further on important project outcomes.

7.1.2.6 Inclusiveness of the best European players

IMI2 JU projects bring together all types of stakeholders. In IMI1 mid-cap companies could not receive EU funding and in many cases these companies still depended substantially on external funding. As it was realised that this was excluding important expertise, it was changed under IMI2 JU, which allow mid-cap companies to participate either as part of the biopharma consortium contributing to the project with in-kind contributions or as part of the public consortium receiving EU financial contributions. A major incentive to be part of the biopharma consortium is that this allows an active role in the planning and preparation of the call topics.

To ensure that the best academic groups or best SMEs contribute to innovation in certain fields, input from these types of stakeholders in the design of call topics is important. In IMI2 JU the opportunities to contribute to topic development or even topic suggestion has significantly improved when compared with IMI1. The IMI-website created an open call for closer involvement in IMI projects in project advisory boards or in the design of projects, bringing ideas to IMI2 JU.²⁰ Although a website is not a guarantee to get feedback of the best players, it is the input from the most appropriate players that can be expected to contribute to the design of new call topics. Likewise, it may be expected that only the experts with more relevant knowledge will be taken up in projects advisory boards.

A matter of debate since the very beginning of IMI JU, the IP rules are preventing some of the major European institutes from broad participation in IMI2 JU projects. Although, in contrast to IMI1, in IMI2 JU the IP regulation had few IMI2 specific derogations when compared with Horizon 2020. Nevertheless, and although some of the best players did not think it was appropriate for them to participate in IMI2 JU projects, according to the data presented in section 6 the participating universities were among the best in Europe and a quarter of them ranked in the world top 100.

Similarly, also the EFPIA companies that participated belonged to the highest ranking companies in terms of R&D spending, with almost all of the European companies that participated so far in IMI2 belonging to the top 30 in the Pharmaceutical and Biotechnology section of the Scoreboard EU 1000.

7.2 Efficiency

This section deals with how efficiently the IMI2 JU mission and strategy have been implemented to achieve the IMI2 JU main objectives. It first analyses the clarity of and the efficiency of communication and shared vision within the governance structure. It also attempts to assess whether the SRA and its research areas were aligned with the mission and objectives of the IMI2 JU as outlined in the Council regulation and the effect of the change from different programming periods FP7 and Horizon 2020. It takes account of the transparency of call topic selection, proposal selection as well as the openness and clarity of the processes. It then takes note of the robustness of the monitoring and control systems within IMI2 JU as a whole and in individual projects & project participants. Under modalities of IMI2 JU operations account has been taken of programme management efficiency, service quality to all stakeholders as well as satisfaction of beneficiaries. Finally, overall metrics of financial and operational efficiency have been analysed.

²⁰ www.imi.europa.eu/content/get-involved

7.2.1 IMI2 JU mission and Governance

7.2.1.1 Roles of the different governing and advisory bodies

The governance structure of IMI2 JU is presented in Figure 1 of this report. In general, the roles of the different bodies in IMI2 JU appeared to be clear and well defined.

Role of the Governing Board

The Governing Board (GB) was the IMI2 JU main decision making body, having overall responsibility for the strategic orientation and the operations of the Joint Undertaking. The GB comprised two members with different goals and modes of operations (EFPIA and the EC), which may interfere with quality of the decision making process. The EC GB members may be expected to demonstrate evidence of bringing benefits to society and patients as well as of bringing economic value added, while EFPIA represented the interests of global pharmaceutical companies, which are focused on growth, net profit and bringing benefits to their shareholders. These different goals may complicate negotiations while aligning interests.

The GB is informed by the Strategic Governing Groups (SGGs), which were strictly advisory bodies that focus on specific disease areas and were active to develop specific call topics, in line with the relevant parts of the Strategic Research Agenda. Another advisory body to the GB is the Scientific Committee (SC), whose advisory role focuses on the strategic research agenda and scientific priorities. Representatives from the SC participate (if feasible) in relevant SGGs and GB meetings. Two additional advisory bodies are the States Representatives Group (SRG) and the Stakeholders' Forum, which is an annual meeting that brings together all stakeholders to create awareness and inform on IMI2 JU.

Role of the IMI2 JU Executive Director and his staff

The day-to-day management of the JU lies with the Executive Director supported by his staff. The role of the IMI2 JU Programme Office did not change from IMI1 and it was still strictly an executive body with little to no decision making power. All important elements of the IMI2 JU operations had to be approved by the GB. More details on the IMI2 JU operational efficiency appear in later sections of the report.

The IMI scientific officers were involved in the logistics and follow up of the projects. They guided the evaluation processes, but in line with their mandate did not contribute themselves to the selection of proposals. Projects were assigned as much as possible in alignment with the expertise and background of the officers. It was the IMI scientific officers that selected expert evaluators from the "EMI" experts' database.

Role of the Strategic Governing Groups (SGGs)

IMI2 JU SGGs functioned as advisory groups to the Governing Board. So far seven of such thematic groups were created to address defined areas in the IMI2 JU Strategic Research Agenda.

The SGGs were made up of representatives of companies active or interested in the area covered by the scope of the SGG, which was not only EFPIA but also potentially the companies from other sectors, such as medtech companies focusing on diagnostics, imaging, or medical devices. It also included representatives from the European Commission, the IMI2 JU Programme Office and the IMI2 JU Scientific Committee, and potentially ad-hoc members.

The objectives of the SGGs and their respective missions were outlined in the charter establishing the SGGs.²¹ To summarise, the work of the SGGs was focused on facilitating an efficient translation of the IMI2 JU SRA and developing a coordinated strategy for selected diseases leading to the identification of annual strategic priorities. They should also provide

²¹www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_GB_DEC_2016_21_Decision_on_new_SGGs_Charter_SIGNED_30SEP2016.pdf

recommendations for high quality and clear call topics, taking into account proposals from industry, Associated Partners and third parties.

It appeared **that the SGGs were very active and had a very significant impact on the decisions of the GB, the call topic selection and determining the research priorities in various disease areas.** The remaining advisory bodies had no significant influence on the activities of the IMI2 JU and its operations. Their roles, as outlined in relevant legal documents and materials on the IMI website have been commented by several representatives of those bodies who were interviewed by the expert group, confirming lower level of engagement and only periodic interactions with the GB and SGGs.

Role of the SC

The main role of the SC was to give strategic science-based recommendations to the GB of IMI2 JU and the Executive Director's office and to comment on the continued relevance of the [Strategic Research Agenda](#) and the scientific priorities that form the basis for the specific IMI2 JU Call Topics. Call topics originate from the EFPIA members and were adopted by the GB with SGGs, SC and SRG recommendations. Typically several EFPIA companies must declare in-kind contributions to initiate a call on a given topic. The call topic proposals were made available to the SC and SRG for comments and advice. According to the chair of the SC, feedback from the SC was generally taken under consideration by the GB and there was communication from the GB back to the SC, whether its recommendations were adopted or not. Other interviewed members of the SC commented that there was insufficient communication and not enough interactions between the SC and the GB. The difference in perception perhaps results from the fact that the SC chair currently was also a member of one of the SGGs and sits as an observer on the GB meetings.

Role of the SRG

The SRG disseminated information from the IMI2 JU to its national and regional stakeholders, and advocated on important national or regional trends with respect to the IMI2 JU goals and work programmes. The SRG was consulted by the IMI2 JU on the work programme and specific call topics to avoid duplication of efforts when similar projects were ongoing in other programmes. There seemed to have been little to no changes in SRG responsibilities from IMI1.

One GB member advocated the enlargement of the SRG with regional representatives to align better with regional policies and trends. Simple agreements with bio-clusters, specific laboratories or infrastructures for participation in the SRG could be considered to broaden the participation. A combination with structural funds could help the development of personalised medicine and align national and regional strategies and initiatives with IMI2 JU objectives. Such recommendations, however, did not appear to be of interest in the context of IMI2 JU to EFPIA and the GB in general.

Role of the Stakeholder Forum

The IMI Stakeholder Forum is an annual event where all stakeholders of a broader community are welcome to learn about IMI's latest activities and plans and provide feedback. The Stakeholder Forum serves both as a place for interactions and discussions between different interest groups and governing bodies, the IMI Programme Office and IMI current and potential beneficiaries. It was also an important promotional event demonstrating the main achievements and promoting the ongoing activities under IMI2 JU.

Role of the Scientific Panel for Health SPH

The Scientific Panel for Health is not a specific advisory body of IMI2 JU. Nevertheless, according to the recitals of Council Decision 557/2014, IMI2 JU should also collaborate and exchange information, where appropriate, with the Scientific Panel for Health. The effective role of this panel for IMI2 JU however, was totally unclear to the expert group. No information could be found on the role or demonstrate possible interactions with IMI2 JU.

7.2.1.2 Communication between the different governing and advisory bodies

The communication between various governing and advisory bodies involved in IMI2 JU operations was critical for the implementation of the SRA and the realisation of the IMI2 JU

objectives. The SRG and SC are represented in the GB as observers and report back to respective advisory bodies on the discussions within the GB. In addition, the IMI Programme Office has a pivotal role to inform the SRG and SC about the GB and IMI2 JU activities.

However, feedback gathered through the interviews indicated that communications between the different governing and advisory bodies could still be significantly improved as there was little or no interaction between the SRG, SC and SGGs, although some SC members also participate in the SGGs. As a result the different advisory bodies were not very familiar with each other nor with the scope of activities carried out by each of them.

Feedback from the different groups goes to the IMI2 JU Programme Office and further to the GB, but it was unclear to the different groups what was done with the feedback provided. A stronger interaction of the GB, SC and SRG may help to include national and regional developments and priorities, while more structured feedback from the SC covering different technological sectors may prove very valuable for future developments and innovation in healthcare.

However, **some improvement from IMI1 to IMI2 JU was observed and the SGGs appeared to be a needed and helpful solution** that improved the governance structure. Also communication with and involvement of patient groups in projects and as a discussion partner was improved under IMI2 JU as became evident during the interviews with the expert group.

7.2.1.3 Robustness of monitoring and control systems

The Impact Assessment Report that accompanied the Commission proposal for a Council Regulation on IMI2 JU proposed a set of indicators to monitor scientific and technological progress and JU operations (Table 4) for the interim and final evaluations of IMI2 JU that were to address the quality and efficiency of the IMI2 JU and progress towards its objectives.

Table 4: List of the proposed indicators.

Scientific and technological progress		
	Indicator	Target
Monitoring achievement of objectives of the JU	Monitoring the achievement of specific objectives	30% increase of the success rate in clinical trials in the relevant disease areas by validating 12 novel drug targets; improving from 70 to 80% the predictive capacity of early stage (non-human) safety testing models; etc.
	Number of open innovation networks established	By 2 years, 1 open innovation network between different industry sectors established, by 4 years 2 further networks established; 2 clinical trial networks established by 2 years
	Number of strategic agenda setting beyond JU	By 2 years strategic agenda setting in 3 research areas defined by the specific objectives; by 4 years 5 more research areas
	Number of partnerships established	By 2 years partnerships in 6 research areas defined by the specific objectives; by 4 years 10 more research areas
Monitoring implementation of the strategic research agenda	Number of data points analysed for reaching at unbiased molecular taxonomy of disease	By 2 years, 1 million, by 4 years 4 million data points analysed
	Number of diseases classified	By 5 years 1 disease area, by 7 years 1 further disease area, by 9 years 2 further disease areas
	Number of trials analysed for learning from negative results	By 2 years 25 trials, by 4 years a further 100 trials
	Level of taking account of health and demographic change and wellbeing policy goals	Strategic research agenda needs to address points 1.1.2, 1.2.2, parts of 1.2.3 and parts of 1.3.1 of partial general approach of Horizon 2020
Monitoring JU operations		
Selection of projects and allocation of funding	Time-to-grant	270 days
	Time-to-pay	30 days
	Level of adherence to time schedule	Budget committed in the foreseen yearly instalments and calls launched accordingly
	Level of SME participation and benefits	20% IMI2 funding going to SMEs
Efficiency of research programme	Number of publications	On average 20 publications per €10 million funding
	Impact factor of journals where articles are published	As from 3 rd year; average impact factor 10% above EU average
	Impact of publications	Citations 20% above average for EU publications
	Number of patents	On average 2 patent applications per €10 million funding

For the interim evaluation a list of nine milestones to measure the IMI2 achievements at the interim evaluation were identified (Box 3).

Using these milestones however, did not enable an assessment of IMI2 JU in an objective and straightforward manner, because most of these milestones were not based on quantitative data and merely reported for individual projects.

The robustness and monitoring system in IMI2 JU can be analysed from three perspectives which is corresponding largely to the proposed indicators in table 4 above:

- i) Progress monitoring: a KPI system to monitor progress, outcomes and impact in the program as a whole and within individual projects;

- ii) Processes monitoring: means to assure efficiency of the processes and procedures in IMI2 JU with respect to calls for proposals, time to grant, spending efficiency etc.;
- iii) Monitoring and control of eligibility and compliance of all IMI2 JU activities, including individual projects.

Progress monitoring

With respect to monitoring the progress, several stakeholders were interviewed on this particular topic, and it was the subject of repeated expert group discussions. A new Performance Measurement Framework - under discussion for approval by the GB at the time of the evaluation - was presented by the IMI2 JU Executive Director, Pierre Meulien. This framework was built according to a coherent intervention logic. However, the expert group felt that the proposed framework was not relying on the so called SMART (Specific, Measurable, Achievable, Relevant and Time phased) KPIs and encouraged the IMI2 JU Programme Office and the GB members to rework the framework so as to make the performance assessment process straightforward and relying on objective and measurable indicators.

More specifically, the KPIs should be aligned better with the stated objectives of the IMI2 JU, such that every objective is reflected by a simple measurable KPI. KPIs that address a mixture of (qualitative indicators) examples and numbers (with no target for what should be achieved) should be avoided. Examples may be used merely to illustrate progress towards the final goals of IMI2 JU.

The expert group regretted that the development and testing of an accountable Performance Measurement Framework including SMART KPIs has been delayed since the launch of IMI JU in 2008 and that no baseline metrics have been identified even after the repeated recommendations by different independent expert reviews pointing out their absence as a major weakness of IMI1. The final evaluation report on IMI1 summarised this.

The lack of baseline metrics was still seen as a major gap and the expert group was convinced that baseline metrics in many cases could still be retroactively integrated and used in IMI2 JU.

The KPIs should also indicate the targets to be reached during the running time and after the completion of the initiative. Short-term, mid-term and long-term perspectives may be indicated. The baseline metric would be the number of the defined target achieved during the preparatory phase and beginning of the initiative. The mid-term target would be the target available at the time of the interim review. The long-term target would be the indicator available at the final review of the initiative and may be used as an argument for a follow up initiative. Additional target numbers may be considered beyond the running IMI programme.

The framework may indicate which KPIs may be used to inform specific target interest groups such as the EP, patients or others. However, the Performance Measurement Framework should be presented as a complete unified framework.

The expert group found it particularly difficult to analyse the socio-economic impact of the actions taken since the establishment of the joint undertaking in 2008, based on the Performance Measurement Framework presented. The inclusion of baseline metrics would improve analysing progress. The socio-economic assessment report could be used to identify relevant SMART KPIs.²²

Within the Innovative Medicines Initiative Logic Model and Performance Framework 2016 document published on the IMI website, the IMI2 JU lists two critical expected impacts on:

- Better innovation capability of EU firms; and
- Increased competitiveness of European industry (incl. SMEs, start-ups and scale-ups) in areas related to societal challenges.

²²www.imi.europa.eu/sites/default/files/uploads/documents/Publications/SocioeconomicImpactAssessment_FINALMay2016.pdf

The joint undertaking has so far failed to provide a set of SMART KPIs to measure these outputs. Moreover, as outlined in section 7.5 on the added value of IMI2 JU implementation, data on the participation of SMEs in IMI2 JU projects indicate a regression rather than a positive impact of the JU implementation in this area with a decrease of participation rate from 16% in IMI1 to under 12% in IMI2 JU projects and from over 13% to 10% of EU contribution received under IMI1 vs. IMI2 JU. The identification of a positive impact since the establishment of IMI was difficult and more time will be needed especially as none of the IMI2 JU projects have been finalised by the time of this first interim evaluation. The development of an adequate progress monitoring system is needed to allow making a reliable quantitative assessment.

Processes monitoring

When monitoring the efficiency of the functioning of the IMI2 JU Programme Office, the data provided by the Programme Office indicated that the IMI2 JU office staff was meeting or exceeding its targets. This aspect is analysed in more detail in section 7.2.3 of this report.

The processes in place to monitor and control eligibility and compliance of IMI2 JU activities and projects seemed to include adequate controls to assure eligibility of costs as well as efficient budget use and limit fraud.

A process that included a potential risk, brought to the attention of the expert group, was that there seemed to be a difference in obligations between EFPIA members and the beneficiaries under IMI2 JU with respect to commitments made to project implementation. In IMI2 JU there was no regulation in place to prevent that a company would withdraw prematurely from the project, thereby not delivering on its earlier contractual commitment. Some of the interviewed members of the governing and executive bodies of the IMI2 JU identified this as a system deficiency as premature withdrawal of an EFPIA member from a project can have big implications, not only in the content of the project, but also on the budget commitments made and actions should therefore be anticipated. EFPIA proved in the past to function as a broker to find an equitable commitment among existing or new consortium members

There was also no mechanism in place to enforce the industry commitments made at the start of a project. Companies not fulfilling their commitments cannot be penalised. In fact, EFPIA itself, as representing member in the GB did not appear to have an enforcement system in place for their members.

Progress monitoring and use of funding

As part of the control system, expert audits were zooming in on eligible costs of beneficiaries and EFPIA partners. As part of the two-level control there was an ex-post control, which could lead to adjustments. This procedure was also followed for the in-kind part of the contribution. The audit included verification of all forms of in-kind contribution, which was calculated on the basis of the fulltime equivalent (FTE) commitments and timesheets and other eligible cost categories such as consumables, infrastructure use or other costs in conformity with market prices.

In several interviews with IMI2 JU staff, it was mentioned that some EFPIA companies were reluctant and often refused to make time sheets available, claiming that it violated their confidentiality on engagement in other non-IMI projects and could lead to unpermitted disclosure of information. It is not clear, however, whether or not this would indeed implicate a risk of competitive loss for those companies, as timesheets may involve project names without revealing the targets and part of the audit may be kept strictly confidential. Many stakeholders that were interviewed, such as representatives of academia and IMI advisory bodies, agreed that more transparency and openness in this area would be desirable. The European Parliament and IMI2 JU SRG have been insisting on increasing transparency of the calculation rules and composition of in-kind contributions by pharma companies. The demand for thorough financial auditing became stronger after a publication in *Der Spiegel*, in which it

was questioned whether IMI2 JU in-kind contributions were allocated well, and was perceived that transparency and monitoring were inadequate or lacking.^{23,24}

The SRG was also monitoring the budget spending in addition to the return on investment (contribution) to the respective countries. Since the launch of Horizon 2020, IMI2 JU should enable a similar verification possibility, with detailed breakdown analysis of participants.

It should be noted that the in-kind budget in line with the legal basis in IMI2 JU needs to match the EU contribution at programme level, while differences at the project level are acceptable. To ensure that the in-kind (industrial) contributions are matching the public cash contribution for a given programme, a legal/financial mechanism in case of mismatch towards the end of the programme would be desirable. Surprisingly, no such mechanisms were available to guarantee that the industrial commitments of in-kind contributions were made, while there is a strict financial follow up system at project level.

According to IMI2 JU representatives interviewed, there were no controls or mechanisms in place to prevent a gap between the industry in-kind commitment and the public cash allocations. It was indicated by an IMI executive official that if pharmaceutical companies would not fulfil their commitments, they would still be eligible to participate in future projects. There was a risk that at the end of the programme there will be a gap between the public cash funding and the in-kind contributions, which would likely have political consequences. In the expert group's view, a major mismatch of in-kind versus cash funding would indicate a failure of the joint undertaking's programme to mobilise private investment in pharmaceutical research in Europe, despite the fact that it may be acceptable if the outcomes of the programme were impressive. On the other hand, also overspending in IMI2 JU projects was possible, although in the period covered by the interim evaluation there were no such examples.

Progress monitoring at project level including the periodic analyses of the outputs correlated to the budgets spent and the deliverables expected should support continuous adaptation of projects as continuous adaptation of projects when appropriate is advisable to projects operating in platforms with multiple deliverables as under IMI2 JU.

At the time of the writing of this report no IMI2 projects had been stopped. Stopping a project would mean a bigger loss, and appropriate adaptation of projects is the preferred approach.

Some of the interviewed IMI2 JU beneficiaries and other stakeholders advocated for milestone-based payments, aligned with the periodic reports and deliverables. According to IMI2 JU rules milestone payments would in principle be possible, but it cannot be a standard procedure. It would need to be on a case-by-case basis as in some cases there could be a need for significant investment and very often larger budgets were spent towards the end of a project. Others favoured creating a reserve budget at the project initiation and launching open calls during the course of a project to bring new partners on board once the projects were running. It would improve flexibility at the benefit of faster progress of projects.

7.2.1.4 Analysis of the funding streams to achieve the objectives

Sources of funding can be divided into four sub-categories:

- 1) Direct beneficiary funding by the European Commission;
- 2) Matching in-kind contribution by the EFPIA members and Associated Partners;
- 3) Sustainability funding generated from various sources (public or private, contribution or revenue driven);
- 4) Funding generated by consortia or their individual members from sources outside of IMI2 JU.

²³www.spiegel.de/international/europe/imi-in-eu-project-citizens-count-corporations-cash-in-a-1025550.html

²⁴<http://sciencebusiness.net/news/77013/Reprieve-for-under-fire-EU-pharma-partnership-after-Parliament-vote>

Direct funding/ contribution to academic, SMEs, patient organisations, coming from the European Union follows the same rules of eligibility and control as other programmes under Horizon 2020. Similar to IMI1, EFPIA in-kind contributions in IMI2 JU show high variability and cannot be correlated to the size of the company or its general budget allocations to R&D. Moreover, in IMI2 JU the activities of the SGGs were considered as in-kind contributions from the industry, enabling higher contributions of allocated FTEs that are not directly related to a specific research project but rather to a thematic (disease) area under which groups of topics are developed.

At the end of 2016, the overall contributions committed in the 25 signed grant agreements originating from calls 1 to 6, as well as in nine additional full proposals originating from calls 7 and 8 but still under the process of selection and grant preparation, amounted to: approx. EUR 663.9 million, with EUR 337.42 million (50.8%) representing the EU contribution, EUR 312.04 million (47%) representing EFPIA contributions and EUR 14.43 million (2.2%) representing the Associated Partners contributions. To date there was a 2% imbalance between the public (EU) commitment and the EFPIA plus Associated Partners commitment. However, of more concern was a very low contribution to the overall IMI2 initiative by the associated partners (other industries, foundations, charities and other NGOs). This was a clear indication of the inability of the IMI2 JU to attract other industry sectors and associated partners in a meaningful way. The situation may be improved in future projects.

In some cases there may be additional complications when in-kind funding comes from activities outside the EU and Associated countries, for which a ceiling was set in IMI2 JU Regulation to 30% of the total in-kind contribution. The limit at the programme level is 30% of EUR 1.638 billion from EFPIA companies, Associated Partners and potential other Members, therefore EUR 491.4 million.

For the 25 first signed grant agreements, the non-EU contribution reached EUR 83.7 million. The non-EU commitment increased to EUR 97.6 million if the additional nine 9 proposals from calls 7 and 8 are taken into account.

The "non-EU" contribution has so far remained proportionate to its limit and is estimated to represent 31.7% of the total in-kind contribution for the first 25 signed grant agreements. So while the threshold from the programme is far from being reached, proportionally the limit has been exceeded by almost 2%. If this trend continues projects funded towards the end of the programme may no longer be eligible to include non-EU in-kind contributions. Another aspect that should be taken into considerations is that the 30% in-kind contribution from non-EU activities, in fact weakens the possible leverage effect of the IMI2 JU funding by 30%, which does not contribute to investment into EU research and European biopharmaceutical eco-system.

Of the 25 IMI2 JU active projects, there have been examples of five consortia that had attracted, or were in the process of attracting, additional funding coming mainly from the industry. In VSV-EBOVAC project, the industrial partner NewLink has invested over USD 16 million to further investigate the safety and immunogenicity of the rVSV-ZEBOV vaccine in a clinical trial conducted in USA, enrolling 512 subjects. In the remaining projects these contributions are only anticipated to represent very small amounts.

At this stage of the IMI2 JU, it is unclear whether the IMI2 funding (combined EU and industry in-kind contributions) was sufficient to achieve the ambitious objectives as set out in the relevant documents. The main concerns related to the decreasing participation of SMEs and the virtual absence of other industry sectors and associated partners.

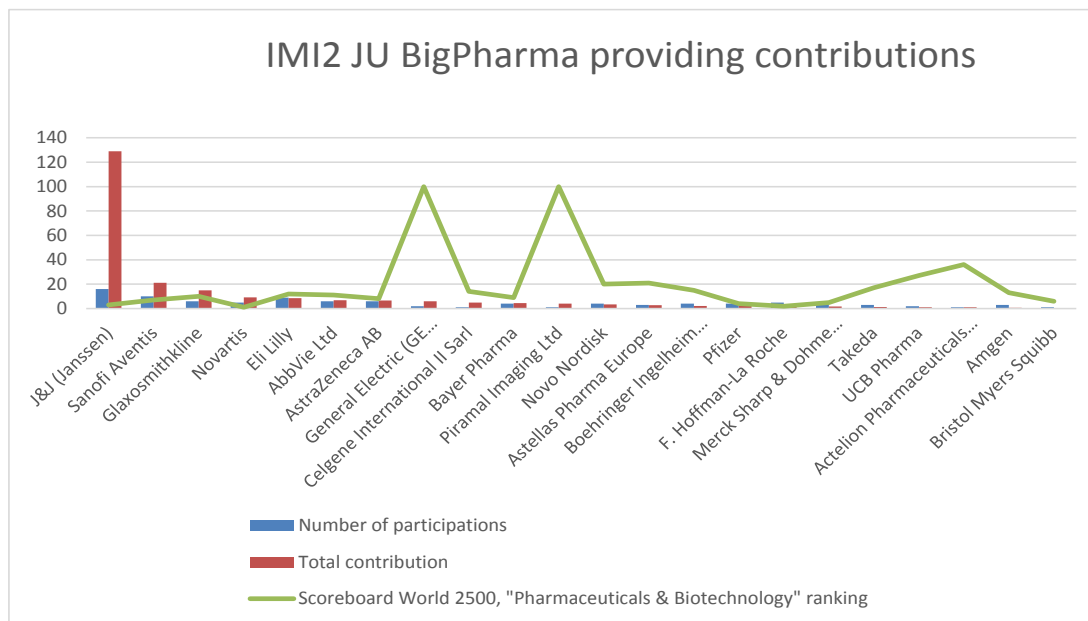
As no cumulative, aggregate data were likely to become available on the amount of additional leverage (beyond the mandatory 50% in-kind or cash contribution from EFPIA and Associated Partners) and sufficient mechanisms were not yet implemented to ensure sustainability of project outcomes, the overall outcome of the first phase of the IMI2 JU may be effected negatively.

Analysis of in-kind contributions in IMI2 JU showed similar variability to that observed in IMI1 among the EFPIA companies. There was no evident correlation seen between the in-kind contribution of the EFPIA companies and their ranking according to their total R&D expenditure (Figure 10). However, this analysis was premature as **the majority of the funding was committed to the vaccines area. IMI2 JU indeed reacted very rapidly and efficiently to the threat resulting from the Ebola outbreak in Africa** (2nd call for

proposals, dealing with Ebola) which represented roughly half of the budget of all IMI2 projects launched and in which Janssen Pharmaceutica (J&J) played the leading and dominant role.

It is nevertheless, worth noting that some of the top five pharma companies on the global R&D scorecard are essentially non-contributors to IMI2 JU.

Figure 10: In-kind contributions vs. rank in R&D spending. Note: GE Healthcare and Piramal are not in the ranking of top 2500 "Pharmaceuticals & Biotechnology" and an arbitrary value of 100 has been assigned to the non-ranked entities in this figure.



In terms of efficiency, an obvious question was whether the objectives of IMI2 JU could have been achieved with lower cost from the public budget and using the regular calls and instruments of the framework programme. A main argument against, was that **IMI2 JU produced a considerable leverage of private funds, which cannot be achieved under the regular framework instruments.** On the other hand, call topics in Horizon 2020 may be closer to the public interest than those identified by the industry. Similarly, arguments have been made by some of the interviewed stakeholders, from the academia and from SMEs, that creating a competitive 'proof-of-concept' funding scheme of the size of one third of the current IMI2 JU budget (that enabled private investors to fund follow-on development on an exclusive basis) would be an unprecedented boost to the competitiveness of the EU-based biopharma ecosystem and have greater efficiency in achieving the desired socio-economic impact as indicated in the IMI2 JU objectives.

7.2.2 Modalities of operation

In general, **IMI2 JU Programme Office has made significant efforts to achieve its ambitious objectives.** The meetings, and webinars and helpdesk were very well appreciated by stakeholders. The interactions with the SRG have improved significantly with respect to reporting on statistics of projects.

However, there were comments from an SC member that sometimes 'artificial consortia' were formed due to an inappropriate focus on gender and geographical balance. In addition, the same interviewee questioned the need for new consortia. According to this source it was less productive than relying on existing consortia that have proven to work effectively and efficiently. However, the expert group fears this would not only prevent from opening to new opportunities and breakthrough ideas coming from outside of the established networks, but also destroy true competition and openness – the key element of innovation.

7.2.2.1 Satisfaction of beneficiaries with the services of the JU

The project coordinators survey had a very limited number of respondents (34) and was over represented by industry (>60% of responders were from industry contributing in-kind). The

findings should therefore be interpreted with caution. Nonetheless the survey does provide some information about the level of satisfaction of some IMI JU beneficiaries.

The positive comments were primarily concerned with the benefits of direct channels of communication with the IMI JU Programme Office (discussed in detail in the previous subsections). In general, the majority of responders were satisfied or very satisfied.

The competency, willingness to help and efficiency of direct interactions with the IMI JU Programme Office was also viewed very positively (74% to 94% of the responders were satisfied with the various forms of interactions and the efficiency of the IMI JU office). There were some comments about how the direct collaboration with the scientific officers has improved over time from IMI1 to IMI2 JU. Furthermore, direct communication with scientific officers was viewed as being much more efficient than getting feedback from financial or legal departments of the IMI Programme Office. There were also comments about the need for more scientific officers due to overload of projects per officer.

Efficiency of time-to-inform, time-to-contract and time-to-grant was viewed with reserved optimism by the responders with 55% to 73% of the responders being satisfied or somewhat satisfied.

The beneficiary view of the proposal submission and evaluation process, including its transparency and feedback from IMI2 JU, tended to be viewed more negatively. For instance, only 35% of the responders strongly agreed that the evaluation process was clear and transparent and 32% "slightly agreed" with this statement but over 20% questioned its transparency and openness. The majority of respondents stated they "agree or slightly agree" with the clarity and transparency of the evaluation process. However, the expert group noted that the number of positive responses was relatively low considering that interviewees are direct beneficiaries of the IMI1 and IMI2 JUs. There were also additional comments about "the role and potential control rights of EFPIA partners in two-stage proposals not being exactly clear" from SME beneficiaries.

There were mixed feelings among the beneficiaries regarding the user-friendliness of the electronic submission tool (44% dissatisfied vs. 41% satisfied), as well as with the user-friendliness of the electronic tools used in the contracting process (38% dissatisfied vs. 29% satisfied) and in the beneficiary validation process (41% dissatisfied vs. 24% satisfied). Half of the beneficiaries who were unsuccessful in previous attempts to secure IMI funding felt that they had not received a clear explanation why their application was not selected for funding. The survey contained additional critical comments about the timing of the proposal submission deadlines (immediately after the new year's / holiday break or after the summer vacation).

Several stakeholders expressed concerns on different aspects of IMI2 JU efficiency, but the main critical voices related to:

- Lack of a mechanism to ensure compliance to commitments made by EFPIA companies and lack of transparency on cost allocations as well as no consequences for defaulting industry partners;
- Top down approach for call topic design making the call topics too narrow and prescriptive, which leaves little room for creative ideas coming from outside EFPIA, and is often preventing SMEs from participating; furthermore it has been suggested that some applicant consortia had contact with the industry consortium prior to the evaluation, and hence may have had an advantaged position in the competitive evaluation process;
- Slow decision making processes in very large consortia and IP/ access rules that generally weaken or destroy the ability to raise private funding for progression of most innovative assets discouraging some of the best research institutions in Europe as well as IP-based asset driven SMEs.

Another problem that was mentioned by several IMI participants both from industry and from academia concerned the sustainability of results or outputs of IMI projects. This concern was also apparent in some comments in the beneficiary survey.

In general **the stakeholders all expressed satisfaction on the interactions with the IMI Programme Office**. Some of the procedures were perceived to generate additional

burden when participating in IMI projects. One of the major barriers noticed was the discussions on IP.

An issue when negotiating the IP was the extra level of complexity introduced by the large consortia and the fact that when the project was closer to the interest of the larger pharma companies, the agreement became very elaborated and technical in such a way which was difficult for academic partners or SMEs to comprehend.

SMEs also indicated that discussions about IP interfered with the speed of progress of the projects and in particular the lack of an SME specific IP regulation to allow exclusive licensing for exploitation was identified as a significant deficiency. While there was evidence that big pharma wanted to have access to all results generated from IMI projects, there were no strategies in place to bring new tools or applications from these projects to the market.

The lack of an IP regulation that allowed exclusive licensing was also reported by some of the major research institutions as a reason for not participating to IMI projects. Many of these research institutions have a role towards innovation and have professional technology transfer offices that have an active role in start-up creation. However, to attract investors, exclusive rights on the IP portfolio were a major prerequisite. It was argued that since the Bayh Dole Act in the US,²⁵ academia obtained a credible technology transfer position to translate more scientific results into innovative applications for society. This has proven instrumental to setup the large numbers of startup and spinout companies from academic research or from activities in large companies that were not pursued by the main company. The creation of an environment in which innovative SMEs can be sustained is increasingly important for large pharmaceutical companies. However, the SMEs depend largely on risk capital which is only provided when there is an exclusivity position protected by IP. The IP-policy in IMI JU does not allow such an exclusivity position on results from IMI projects. This was holding back several potential partners, from academia and SMEs, from participating in IMI JU projects, especially those potential partners that may be predicted to deliver the most important results or with the highest ambitions.

7.2.2.2 Visibility of the EU as partner in IMI2 JU

The EU was generally perceived as an important partner in the IMI2 JU PPP. From the public consultation survey on IMI2 JU, 70% of respondents considered the EU role as critical to overcome the barriers which hinder innovation and drive up costs in the life science sector in Europe. The majority, 90% of the respondents, recognised the need for EU cooperating with industry in the context of a public-private partnership, so that the life science research brings better results to the patients and the market in Europe. Outside of Europe the IMI2 JU has been seen as a flagship initiative, in which the EU plays an important role (confirmed in interviews with US entities, including the NIH). The expert group concluded that the IMI2 JU is a joint EFPIA and EU programme/partnership and that the EC is a key partner and one of its promoters. On the website and in all communications logos of the founding members of the joint undertaking are exposed.

7.2.3 Operational efficiency

7.2.3.1 Efficiency of the management

According to IMI2 JU office representatives **the staffing of the Programme Office was still suboptimal**, especially as the number of projects to manage was constantly increasing. Furthermore, the current overlap with continuing IMI1 projects under FP7 regulations, created a lot of confusion. There appeared to be a significant imbalance in the number of scientific versus the financial and administrative staff. The handling of IMI2 projects was time consuming and complex and would require more scientific officers to effectively manage and support the ongoing projects.

The IMI2 JU Programme Office currently employs 41 staff engaged in operational (26.8 FTEs, including 8.3 project officer FTEs) and horizontal activities (14.2 FTEs). The total salaries of

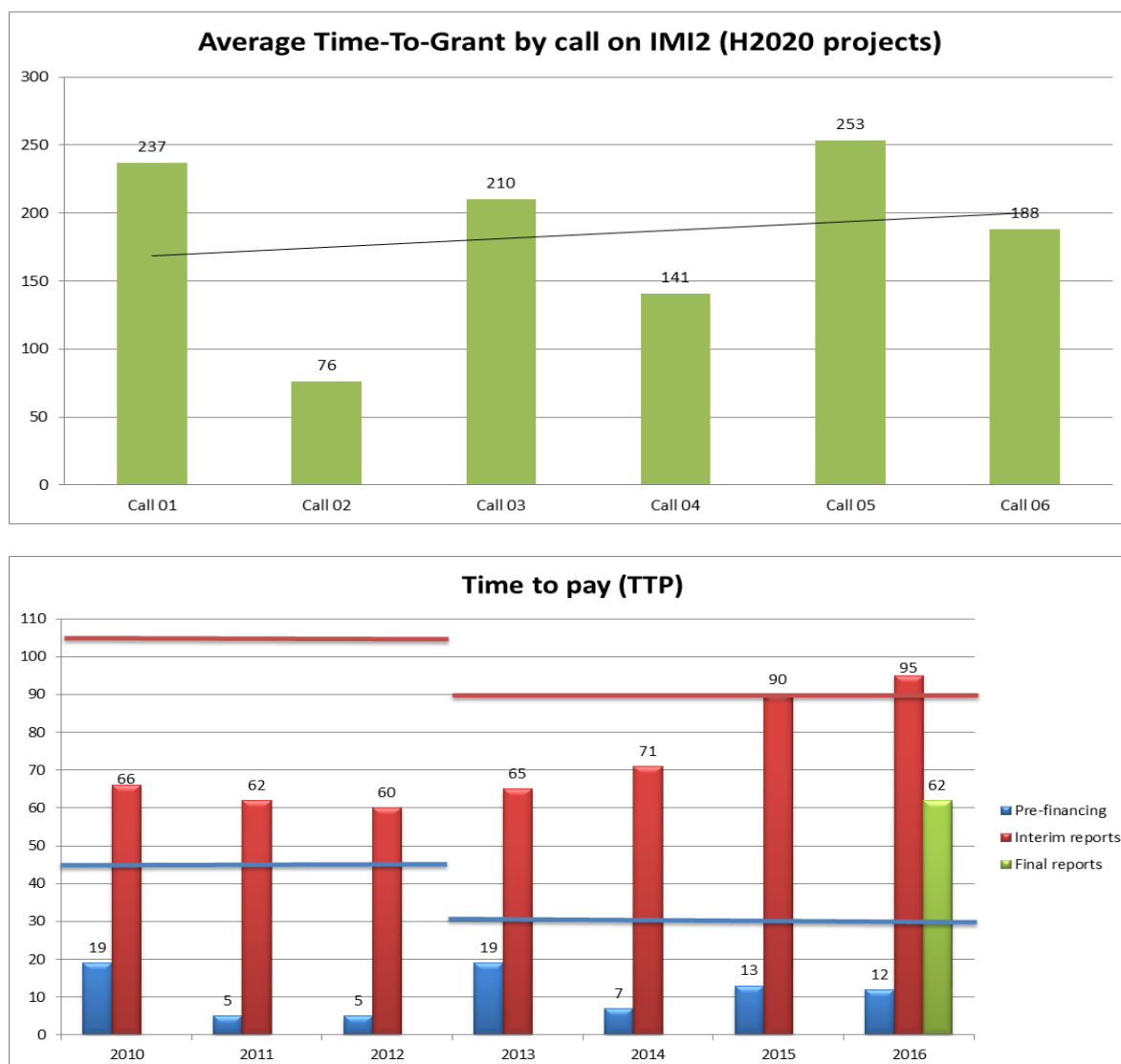
²⁵ https://en.wikipedia.org/wiki/Bayh%E2%80%93Dole_Act: The Bayh–Dole act permits a university, small business, or non-profit institution to elect to pursue ownership of an invention made with federal funding.

these employees add up to EUR 4.8 million, which translates to average annual salary levels of approx. EUR 115 thousand. Considering that this average includes senior level executives, this level seems reasonable. The nine IMI scientific officers were responsible for managing 84 projects, the majority of which, as of the end of 2016, were still IMI1 projects (38 running IMI1 + 21 finished towards end 2016 but not yet closed IMI1 + 25 IMI2 JU). This translated to approximately 10.1 projects per FTE. This appeared to be quite a heavy workload, considering the size and budgets of the IMI projects. In the project selection process, the scientific officers were involved in the logistics as well as selection of the experts evaluating proposals, and moderation of the expert groups, but, in line with their mandate, did not have a task in the selection of project proposals.

7.2.3.2 Timely execution of the functions

Time to grant after the first six calls of IMI2 JU was unfortunately showing an increasing trend, with the last two calls averaging well above 200 days. Except for call 5 all other numbers were below the 245 threshold, but the trend was reversed from the decreasing trend observed in IMI1 (Figure 11) below. In the second part of the figure, the time to pay mostly related to IMI1 projects, as recent IMI2 projects were usually before their interim reports. Therefore the increase above the 90 day threshold on payment following interim report submission set for IMI2 should not yet be a cause for concern.

Figure 11: Time to grant (top figure) and time to pay (bottom figure) vs. targets.



7.2.3.3 Cost efficiency of the management and control arrangements

It is difficult if not impossible to separate the cost efficiency of management for IMI1 compared with IMI2 JU as projects from both are managed and controlled simultaneously by the IMI Programme Office.

Based on the 2016 IMI Annual Activity Report,²⁶ total operational expenditures amounted to approximately EUR 175.2 million while total costs of running the IMI Programme Office amounted to approximately EUR 8.15 million for administration, which therefore represented just over 4.65% of the total EU operational expenditure (reflecting the cumulative project funding for 2016) or 2.3% of the total EU (cash) and EFPIA (in-kind) contributions. These numbers indicated an acceptable, although considerable cost for running the IMI1 and IMI2 JU programmes (in comparison with a typical cost of running a EUR 100 million venture fund was in the order of 2% - 2.5% per annum).

Efficiency of controls (at all stages from submission, evaluation, selection to *ex-post* audit) appeared to be fairly high, with an *ex-post* audit coverage of 31% of the beneficiaries (as of 31 December 2016), for an estimated expense of 22.14% of running costs, 0.96% of the total operational budget and 1.38% of the total operational payments in 2016 (according to Annual Activity Report 2016).

Overall, the expert group concluded that the IMI2 JU is operated and managed very well, although attention should be given to not impose more workload on the scientific officers and take into account the increasing number of projects.

In conclusion, the expert group considers the operational efficiency including the efficiency of management and budget execution as satisfactory for IMI2 JU as well as IMI1 (as these are difficult to separate from the operational management point of view). Time to pay and time to grant have generally been below the agreed thresholds, although under IMI2 JU (unlike IMI1) these two parameters appear to be showing an increasing trend which is something that should be closely monitored and corrective actions may need to be taken to reverse this trend.

Overall satisfaction of the surveyed beneficiaries with the IMI2 JU's services has been higher than 88%, with the majority of responders being satisfied (65%) or very satisfied (23%).

7.3 Relevance

In this section the expert group was asked to analyse and conclude whether the initial identified tasks of IMI2 JU were still valid and sufficient to justify the existence of the public-private partnership and to conclude whether the (original) policy rationale underlying IMI2 JU were still in line with current challenges faced in the specific industrial area.

As outlined in section 3.2 describing the baseline, the urgency to launch an initiative to strengthen the European pharmaceutical industry and increase its competitive position which led to the establishment of IMI JU was still felt to be valid when IMI JU came to the end of its running period. A continuation of the joint undertaking was justified, and the objectives of IMI2 JU have been expanded and specified to certain disease areas, to align with the priority medicines identified by the WHO for which success rates of clinical trials should be increased and to shorten the time to reach clinical proof of concept in medicine development for the specified disease areas. The objectives of IMI2 JU were described in detail in section 3.1.2.

According to the Council Regulation, establishing IMI2 JU, the general objectives of the joint undertaking were to support the Union's competitiveness and industrial leadership and competitive position of European pharma industry. To achieve this, the initiative was set up to address the barriers and bottlenecks in the development of new drugs and therapies and shorten the time to market in this way. All together this strategy was meant to provide socio-economic benefits for European citizens, contribute to the health of European citizens,

²⁶

http://www.imi.europa.eu/sites/default/files/uploads/documents/Publications/IMI_Annual_Activity_Report_2016.pdf

increase the competitiveness of Europe and help to establish Europe as the most attractive place for biopharmaceutical research and development.

To reach its objectives IMI2 JU was “to reach out to new stakeholders towards broadening the network of collaboration in the healthcare family” next to the fostered collaborations between IMI2 JU stakeholders that included industry, public authorities (including regulators), organisations of patients, academia and clinical centres. It is essential that this goal is in phase with the accelerated development of innovation in medicine in particular with the arrival of new industries in the health market such as Google, Samsung, Huawei or Facebook.

The importance of big data in biomedical innovation is growing fast and inducing a transformative shift in biomedical developments. A number of large companies, as well as of SMEs working in these domains are present in Europe and aware of the tremendous potential of the health care market. However, these **IT companies did not participate to IMI2 JU in 2016, while they did participate to other Joint Undertakings or other H2020 programmes**, rather than being associated with EFPIA. The European pharmaceutical industry is losing opportunities when failing to find an answer to this challenge and other industries, for example, Google, Facebook, Samsung or Huawei, are moving further forward to take the lead positions within the healthcare industry.

To include industrial players other than the pharmaceutical industry, EFPIA offered companies outside the pharmaceutical sector to contribute to IMI2 JU as EFPIA’s ‘Partners in Research’, a form of membership to EFPIA. Alternatively, non-pharma companies may join IMI2 JU as Associated Partner.

The IMI2 JU Programme Office is **actively promoting and communicating about opportunities to** increase the participation of the industries other than pharma. **The new calls launched in 2016 reflected the fact that digital technologies play an increasingly important role in research and healthcare.** It resulted in **more EFPIA Partners in Research** with expertise in fields such as diagnostics, medical technology, imaging and data analysis to take an **active role** in the new IMI2 JU Call topics.

The main participants (and in-kind contributors) among non-pharmaceutical companies were GE Healthcare (EUR 5.8 million), Piramal imaging (EUR 4 million) and Somalogic (EUR 2.8 million). The other non-pharma industry contributions were negligible. In contrast, the contribution of some Associated Partners was significant: JDRF (EUR 7.3 million), the Bill and Melinda Gates Foundation (EUR 7 million), the Leona M and Harry B Helmsley Charity Trust (EUR 2.7 million).

However, as outlined earlier, the need to increase and facilitate collaborations with non-pharmaceutical companies remains important. Efforts are needed to overcome the identified barriers to align the different business models, or to negotiate IP agreements to make IMI projects more attractive to other partners and ensure the stimulation of the European competitiveness of several sectors.

The expert group questioned whether the efforts taken were enough to maintain the pharmaceutical industry (and particularly the European industry) at the front edge of innovation. In addition, it was not clear whether the current organisation of IMI2 JU with EFPIA as the leader and coordinator of projects for the industry was able to adequately tackle these new challenges.

The role of EFPIA, as the main driver to address the question of the future in medicine, may need to be modified. It seems improbable that industries from other sectors will join IMI2 JU if EFPIA is the sole industry representative organisation. **It may be needed to consider adapting the structure for the PPP in the future to include other representative organisations to give a voice to specific interests outside of pharma, or to include a representing organisation as an equal counterpart to EFPIA.** Examples may be taken from the other EU Joint Undertakings, such as the organisation of

the bio-based industries, the Bio-Based Industries Consortium (BIC) which is linked to the Bio-Based Industries PPP (BBI).^{27,28}

A success, but simultaneously a limitation, of IMI2 JU was linked to its statutes as a public-private partnership between EFPIA and the European Union. As the representative of the pharmaceutical industry and particularly big pharma, EFPIA and consequently IMI2 JU were not well adapted to attract SMEs which were deemed essential to increase health innovation in Europe.

The involvement of SMEs to strengthen the EU's competitiveness was another challenge that proved harder to address than expected. Both participation and EC contribution rates have dropped considerably since IMI1 (about 30% decrease) and are considerably lower (approximately 25%) compared with non-IMI and non-SME instrument values for Horizon 2020. It was difficult for biotech SMEs that are developing new products to get public funding in IMI2 JU and in H2020, as this type of companies have limited activities in the pre-competitive space. It is questionable whether the focus on precompetitive space for funding is the best way to proceed. On the other hand assets created by IMI2 JU projects may still be beneficial for SMEs. One of the interviewees indicated that SMEs are too defensive to share platforms and tools for the development of advanced therapies.

In general, the pharma representatives interviewed agreed that perhaps the most important achievement of IMI1 and IMI2 JU was that for the first time competing companies are collaborating in precompetitive research. They commonly decided on call topics that address questions a single company cannot answer by itself. IMI2 JU was considered a unique initiative that has not met its counterpart elsewhere.

However, a representative of IMI2 JU Programme Office agreed that it was still unclear whether this, and thus the IMI programme, helped to increase the competitiveness of the pharma industry in Europe. Moreover, the same source pointed out that the joint undertaking has as an objective to facilitate the development of activities for the pharma industry. Although the main actors in the IMI projects may be European based but global companies, there is no guarantee that the IMI projects will lead to the development of therapies in Europe, there was only a hope that IMI1 and IMI2 activities can stimulate this.

IMI projects were establishing resources and facilities to boost drug discovery in Europe. IMI was developing new tools for research and advancing research in important areas like dementia, diabetes, and medicines safety. These tools were expected to help to reduce the use of animals in research. IMI projects were also helping to improve procedures for monitoring the benefits and risks of medicines once they are on the market.

The results that IMI2 JU projects were delivering, confirmed the importance of the public-private partnership model in the wider research landscape. The added value of the IMI public-private partnership was evident from these results, which were helping to address some of the biggest challenges in health research, at the same time the scientific excellence and results of IMI projects as reflected in publications were specific in a context of precompetitive research and interesting.

Through the IMI2 JU programme, the pharmaceutical industry was committing EUR 1.4 billion for collaborative research in Europe, which was matched by an equal budget from the Horizon 2020 budget. The latter provide an extra EUR 213 million to match the additional budgets from other industries. Compared with other EU-funding sources this was a relatively significant investment, the industry budgets concern in-kind contributions and represented only a small fraction of their total R&D expenditure even though under IMI2 JU the focus was on precompetitive research and thus not covering the entire scope of research and development.

To date, since the establishment of IMI, the fast response to the Ebola outbreak in the IMI2 JU projects and progress made towards the development of an Ebola vaccine is the only example of bringing new, safer and more effective therapies or products to patients, and of

²⁷ <http://biconsortium.eu/>

²⁸ www.bbi-europe.eu/

reducing the time to develop such new products. However, specific achievement such as faster validation and approval of biomarkers because of early involvement of regulatory agencies or realising a reduction of time to reach clinical proof of concept as one of the objectives that would contribute to improving the European pharmaceutical competitiveness cannot yet have been achieved because of the early stage of IMI2 JU. IMI2 JU has no finished projects yet and just 25 projects were running at the time of the interim evaluation. In this respect the added value of the PPP-construction for patients or society in general was currently hard to demonstrate.

Nevertheless, it was believed by IMI2 JU representatives that if the JU did not exist, there would be other joint ventures securing cash financing for companies. However, the model has not been replicated in other parts of the world, although it was reported by those same representatives that IMI2 JU was envied elsewhere.

In conclusion the expert group agreed that **the reasons to create a PPP to strengthen the European pharma industry remained valid and the goals were justified. However, the framework conditions may need further modifications in the future to achieve specific objectives like in IMI2 JU.**

It is too early to bring a definitive appreciation on the role of IMI on boosting the competitiveness of European pharmaceutical industry. To demonstrate the socio-economic impact of IMI2 JU, a robust performance assessment system including SMART KPIs reflecting the goals and objectives of the joint undertaking should be established. The expert group considered the lack of such a system to be a serious omission, because the targets put forward were not specified and may reflect a lack of ambition.

Moreover, the lack of a KPIs system made it hard to assess whether the goals of increasing competitiveness of the European pharma industry had been met and were within reach. If the European pharma was not increasing its activities and investment in Europe it can be questioned whether the goals to shorten the time of drug development could not have reasonably been achieved in another way, such as through stronger promotion of European SME involvement that may be considered the engine of European economy.

7.4 Coherence

In this section the expert group sets out to analyse whether the IMI2 JU programme was coherent within Horizon 2020 and with other EU policies and interventions. In addition, the expert group assessed to what extent IMI2 JU was coherent with other programmes that have similar objectives, whether the initiatives were complementary, created synergies or were overlapping.

7.4.1 Coherence with Horizon 2020

The H2020 and the European Research Agenda establish that collaboration among countries and among programmes can maximise the contribution of R&D to achieving smart, sustainable growth in Europe. The main goals of H2020 are outlined in box 5.

Box 5 OBJECTIVES of H2020*

Horizon 2020 pursues three priorities, namely

- generating excellent science (“Excellent science”),
- creating industrial leadership (“Industrial leadership”), and
- tackling societal challenges (“Societal challenges”).

H2020 is 8th Framework Programme for Research and Technological Development, which runs for seven years from 2014 until 2020 with a total budget of nearly EUR 80 billion that reflects the high priority of research in Europe.

* <http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:52011PC0811>

By coupling research and innovation, Horizon 2020 is aiming to achieve the goals through emphasising on excellent science, industrial leadership and tackling societal challenges. The goal is to ensure that Europe produces excellent science, removes barriers to innovation and makes it easier for the public and private sectors to work together in delivering innovation.

In line with the H2020 objectives, the IMI2 JU should support excellent science and create industrial leadership. In addition to these more general goals, IMI2 JU has also more specific and concrete objectives as outlined in Box 1.

Another main goal in line with H2020 is that IMI2 JU should encourage the European international competitiveness while promoting research that supports EU policies.

This vision was taken into account by the expert group when testing whether IMI2 JU projects were coherent with the objectives mentioned and whether IMI2 JU projects were coherent and complementary with projects funded by the different European programmes, including projects implemented by the Commission Directorate General (DG) for Health and Food Safety (SANTE).

In addition, the expert group analysed and compared IMI2 JU with other international initiatives that may have similar goals. The opinion of the expert group relied on the input from different stakeholders and members of the various IMI bodies for their views on coherence and complementarity in the various H2020 initiatives, in addition to reviewing of the published documents and annual reports.

Several interviewees advocated a stronger alignment of IMI2 JU projects with projects financed through Horizon 2020. Increasing the complementarity of IMI2 JU and the framework programme could ensure that projects that successfully started in Horizon 2020 were taken further in the development process towards an IMI2 project, as there is currently a gap in investment for projects between Horizon 2020 and IMI funding, which is indicated also on the figure 12. Also results from IMI2 JU projects may need follow-up in a setting for which the Horizon 2020 approach is better suited.

In general, a stronger emphasis on integrating results from projects funded from different sources should further reduce fragmentation and avoid duplication, while new added values may be created. A member of the SC agreed very much with this vision and advocated for better coordination with framework projects and building on synergies. These suggestions would of course need better coordination across programmes. The SGGs may have an important role to achieve this.

7.4.1.1 Support excellent science and create industrial leadership

It was difficult to assess whether IMI2 JU has realised this goal as it started only two years ago and obviously results were limited. Nevertheless, to achieve these combined goals it was crucial to engage all stakeholders in collaborative projects. There was general consensus that this was the main achievement of the joint undertaking that was realised already in IMI1.

Academia made the largest group of participants and the scientific excellence was reflected in the publications. The scientific output realised under IMI2 JU confirms that the scientific level relative to the focus on precompetitive and translational research was achieved similar to IMI1. By the end of 2016, seven scientific papers had been published – all in the field of Ebola (one in EBODAC, five in EBOVAC 1 and one in VSV- EBOVAC) but no impact analysis of highly cited citations has yet been made.

The participation level of academic organisations plus non-profit research organisations remained around the same level as in IMI1 (Out of all participations including in-kind contributors: IMI1: 52.6% vs IMI2 JU: 55.3%; Out of all EU-funded participations: 74.8% in IMI1 vs 74.0% in IMI2 JU). This was reflected in the EU contribution to academic organisations and non-profit research organisations that also remains more or less around comparable levels (IMI1: 83.5%, vs. 79.8% in IMI2 JU).

The participation of SMEs was crucial to create European industrial leadership as evident from the analysis by Linker *et al.* 2014.²⁹ In the period 2010-2012, SMEs were the source of 27% of new medicines in Europe. However, the SMEs participation has dropped so far from 15.96% of all EU funded participations under IMI1 to 11.78% in IMI2 JU. The share of the total EU contribution to SMEs in IMI2 JU has also decreased so far from 13.25% to 10.33% of the total EU funding, although the average amount received by SMEs has remained stable.

When comparing IMI with the other parts of the framework programme and in particular the Health theme under FP7 and Societal Challenge 1 (SC1) under Horizon 2020, SME participation decreased both under the framework programme (from 15.86% in the Health theme excluding IMI1, to 13.83% in SC1 excluding IMI2 JU and SME-instrument) and under IMI (from 15.96% in IMI1 to 11.78% in IMI2 JU).

As IMI1 received high appreciation by EFPIA members within IMI2 JU, and IMI2 JU may be the more mature programme, it was surprising to the expert group that there was a clear decrease in the participation of the pharmaceutical industry in IMI2 JU with only 24.6% of all participations, while this was still 29.6% in IMI1.

Under IMI2 JU there was a **new category of 'Associated Partners' that were representing other organisations contributing to IMI2 JU objectives**. In IMI2 their participation level was 0.6%, which also contributes in kind to the activities of the joint undertaking.

If it is correct that the European pharmaceutical industry proved to be more resilient against crisis than others industry sectors as mentioned by representatives of the EFPIA and IMI, and that pre-IMI disinvestment was switched to new investments in European biomedical research in pharmaceutical companies, IMI2 JU would have made a main achievement to meet the H2020 objectives. However, these statements were hardly documented in an objective way. Even if pre-IMI disinvestments had been compensated with new investments it was hard to prove that these investments have been triggered by IMI.

According to EFPIA figures until 2014, the most recent available figures, **the European industry has kept its market share both on products developed and sales**. The gap with the US did not change and the trade balance was clearly positive with a slight increase. **This did not mean though, that these data were due to the IMI intervention**. The fact that the gap with the US had not increased in the last 15 years may be explained by several factors. A very important factor may be that the US spends 16% of its GDP on health care, whereas this was only 8.8% in Europe. The trade balance is stable and positive for both.

7.4.1.2 Promoting research that supports EU policies – tackling societal challenges

One of the general goals within the framework programme was to address the grand societal challenges. As half of the IMI2 JU budget came from the framework programme these goals were also tested by the expert panel. To specifically address the societal challenges, the Joint Programming Initiatives (JPIs) were established to pool national resources and coordinate efforts. **In the IMI2 JU the same societal challenges like in the JPIs on Neurodegenerative Diseases (JPND) and on AntiMicrobial Resistance (JPIAMR) are addressed**. To reduce fragmentation and integrate efforts to address the societal challenges, it was expected that the different public funded initiatives are aligned.

However, according to JPND representatives there was limited interest from IMI counterparts to join forces. It was reported that the work of JPND on standardisation protocols in the biomarker generation³⁰ was largely ignored by IMI partners. JPND regretted the absence of dialogue in order to interact and learn from each other and combine relevant results from mainly academia to advance faster towards solutions for neurodegenerative diseases. The expert group considered that closer collaboration, and may be integration of consortia, from both initiatives may be worthwhile.

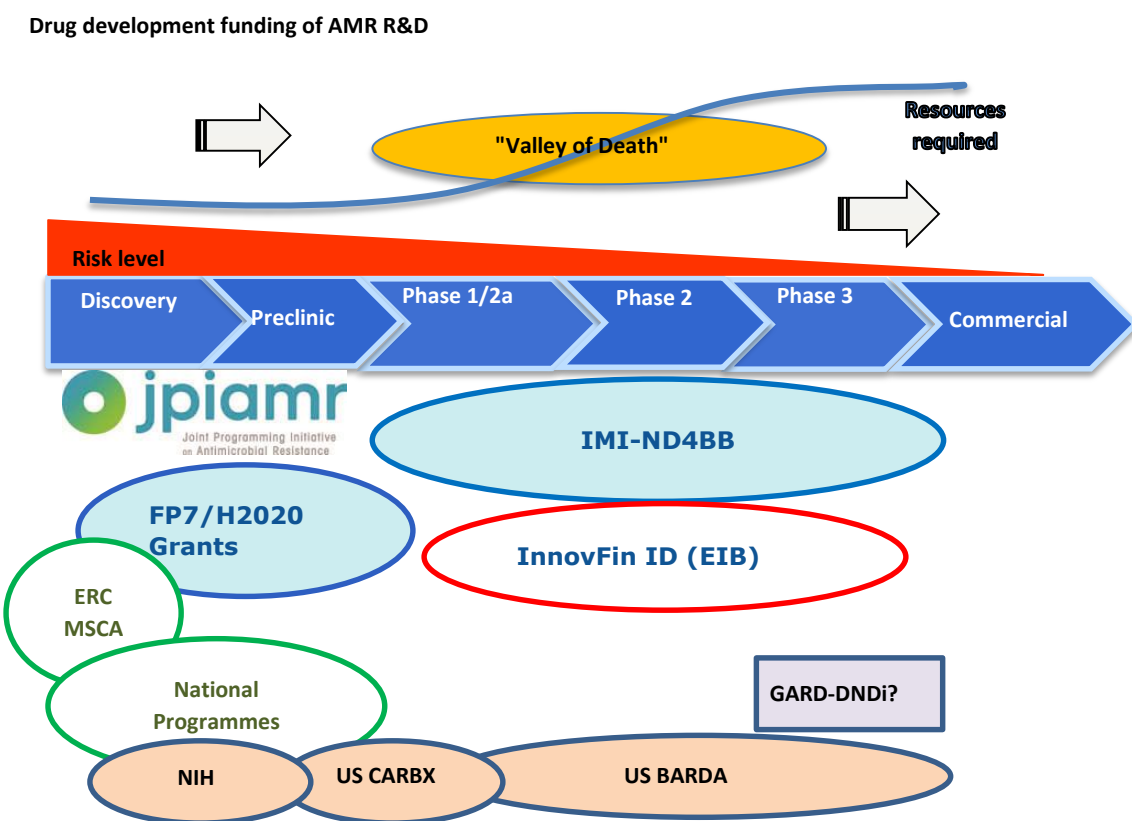
²⁹ Linker *et al.*, 2014 Nature Reviews Drug Discovery **13**:92-93

³⁰ www.neurodegenerationresearch.eu/initiatives/annual-calls-for-proposals/closed-calls/biomarkers-transnational-call/results-of-biomarker-call/

The same question was raised for the projects that address antimicrobial resistance and the development of new antibiotics. In the IMI2 JU there have not yet been projects that address antimicrobial resistance and the development of new antibiotics. Topics addressing antimicrobial resistance and the development of new antibiotics are in the planning however. Although both IMI2 JU and JPIAMR are addressing the same societal challenges the efforts seem complementary as the JPIAMR is focussing on research that is situated earlier in the development process. Figure 12 gives an overview of where IMI projects relative to AMR projects funded by other sources are located in the value chain. As outlined in the final evaluation report of IMI1, a representative of the JPIAMR participated to the SGG on antimicrobial resistance, which is likely to enhance the exchange of information.

Furthermore, duplication of work by the joint undertaking and the JPI was actively prevented by the "EC-JPI AMR-EPPFA-IMI" group that was set up for this purpose. They have organised three workshops: EC-IMI-JPIAMR Antibiotics workshop 04 April 2014, Brussels; Transatlantic collaboration on Clinical trials related to antimicrobial resistance 21-22/1/2016, Stockholm and Early Discovery of New Antibiotics in Paris, 12-13 January 2017, Paris. Nevertheless, contacts could be more intense to stimulate interactions and to build on for example the mapping information gathered by JPIAMR, especially as the threat of AMR can only be addressed properly by a holistic approach that integrates academia, healthcare professionals, regulators, and industry. Fragmentation between initiatives under IMI and JPIAMR would not improve the current threat.

Figure 12: Overview of the relative position of IMI projects and projects funded from other sources in the value chain in the field of antimicrobial resistance



JPI projects mostly address issues that are earlier in the development process using smaller more dedicated projects. IMI projects in contrast were much **larger** and could bring **an overarching structuring effect**. JPI representatives considered **the IMI projects often too much top-down determined by industry**, allowing very little flexibility and creativity. The fear was that such projects would less likely lead to general true innovation. **The JPI projects were more curiosity driven**, and less prescriptive. This approach has generated some very challenging projects that may generate breakthrough results.

Another difference seen was that IMI projects were better designed to address regulatory issues than the JPI type of projects.

7.4.2 Encouraging the European international competitiveness while promoting research that supports EU policies

It may be too early to assess whether IMI2 JU has encouraged the European international competitiveness as results from projects were not yet available, which made it difficult to judge on the outcomes.

EU-based companies noted an annual percentage growth from 1.16% in 2013 to 17.62% in 2015. However, the annual percentage growth of R&D investments of US-based companies was significantly higher and increased from -2.96% in 2013 to 24.60% in 2015.

Similarly, when zooming in on the R&D investments by the pharma and biotech EU-based top-15 companies a negative annual percentage growth of 0.26% in 2013, was reversed into a positive percentage growth of 17.38% in 2015. Non-EU-based companies grew more and went from a negative growth of 4.6% in 2013, to 20.51% in 2015.

It was difficult to draw conclusions from these numbers as these should be linked with the overall performance of the economy. In addition, the annual growth of R&D investments does not specify where these investments are made. As these concern global companies, the investments are allocated to where the headquarters of the companies are located, but this may not be the actual geographical location where the investments occurred.

Nevertheless, at the time of the evaluation it was not possible to demonstrate that the development of a public-private partnership to make Europe more attractive for investing in pharmaceutical R&D had a noticeable effect.

The expert group also tried to address the coherence with the programmes under DG SANTE. However, there was no information available to assess whether there was any sort of interaction and coherence with other health programmes.

7.4.3 Synergies with similar international, national and intergovernmental programmes

No one will deny that synergies with international, national or intergovernmental programmes should be actively sought. As mentioned earlier, broadening the SRG with representatives from regions may help to align with regional strategies and policies. Alignment with bio-clusters, specific laboratories or infrastructures in combination with access to structural funds may further broaden the participation and contribute to the realisation of the IMI JU objectives. Such an alignment is possible under IMI2 JU regulation as it is mentioned that "the chairperson of the SRG may invite other persons to attend its meetings as observers, in particular representatives of regional authorities...".

Under IMI1 such **alignment with national or regional policies or strategies has been limited**. It is expected that this point be improved under IMI2 JU.

Synergies with international initiatives were also rather limited. There were several international initiatives that were similar to IMI2 JU, although IMI2 JU was more ambitious in scale and scope than all other initiatives.

In February 2015, the US House of Representatives issued a white paper on the "21st Century Cures initiative". Launched by the House Energy and Commerce Committee, it studied what steps can be taken to accelerate the discovery, development and delivery of cures. It recognises that what is missing in the USA is a public-private partnership that would bring together the various stakeholders and would need to be "modelled after the Innovative Medicines Initiative³¹".

³¹<https://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/files/114/FINAL%20Cures%20Discussion%20Document%20White%20Paper.pdf>

The organisation that was most similar in its mission to IMI JU is the USA based **Critical Path Institute (C-Path)**³² set up by the FDA in 2004/5. C-Path specifically refers to IMI in its Mission Statement. IMI JU has a very constructive collaboration with C-Path, illustrated by the annual joint meetings. The third meeting will be organised this year.

Nevertheless, C-Path's funding model is very different from IMI although some similar actors were involved, including industry, government (through FDA) and other partners such as patient advocate groups and philanthropic organisations such as the Bill and Melinda Gates Foundation (BMGF).

The annual budget of C-Path reached USD 15 million, while the approximate annual budget of IMI JU was about EUR 300 million from both the public and private sectors: one third of the budget is coming from the FDA, one third from industry membership fees and one third from charities/philanthropy (most of this comes from BMGF).

C-Path was mainly regulatory focused which was reflected in their main performance measures that were related to advances in qualification of biomarkers in specific diseases from the perspective of the regulatory body. The objective of the collaboration with C-Path Institute remained to foster synergies in areas of common interest such as modelling and simulation, and to maintain the collaborations between specific projects and research. The collaboration also focused on data standardisation to enable leveraging data on both sides.

The collaboration between C-Path and IMI encouraged the FDA and EMA to collaborate and increases the probability that both agencies will make similar decisions.

From table 5, that gives an overview of most relevant international initiatives with similar goals to IMI JU, it is clear that IMI JU has the largest budget and broadest scope. More detailed information on the respective initiatives is given in annex 9.

³² <https://c-path.org>

Table 5: Comparison of different international initiatives

	Acronym	STARTING YEAR	BUDGET GOALS	BENEFICIARIES	HEALTH TARGETS	FINANCING PARTNERS	LOCATED
Innovative Medicines Initiative	IMI-1	2008	2.000M€ / 6years	Private-public consortia	Metabolic disorders; neuro-degeneration; prevention and treatment of immune-mediated disease, and advancement in prophylactic and therapeutic vaccines for infectious & non-infectious diseases; infection control including incentives for reinvestment in antimicrobials, antivirals, and vaccines; translational Safety	European Union (50%); EFPIA (50%);	EUROPE
Innovative Medicines Initiative 2	IMI-2	2014	3.276M€ / 11years	Private-public consortia	Antimicrobial resistance; Osteoarthritis; Cardiovascular diseases; Diabetes; Neurodegenerative diseases; Psychiatric diseases; Respiratory diseases; Immune-mediated diseases; Ageing-associated diseases; Cancer; Rare/Orphan Diseases; Vaccines;	European Union (50%); EFPIA (42,5%); other life science industries or organisations (7,5%)	EUROPE
Critical Path Institute	CPATH	2004/5	15M\$ / year	Industry; academy; regulatory agencies;	Alzheimer; accelerate clinical research; parkinson's; tuberculosis; pediatric trials, multiple sclerosis; regulatory science, etc.	1/3 FDA; 1/3 Industry; 1/3 Charities	USA
Global Health Innovation Technology Fund	GHIT	2017	96M\$ from starting	Life science companies, universities and research institutions	HIV; Malaria; Tuberculosis; Neglected Tropical Diseases;	Bill and Melinda Gates Foundation; Wellcome Trust; Pharma industries and non-pharma japanese companies; japanese government	JAPAN
Accelerating Medicines Partnerships (AMP-NIH)	AMP	2014	230M\$ / 5 years	Scientists from NIH and Industry	Alzheimer; Type 2 Diabetes; Rheumatoid Arthritis and Lupus;	NIH; FDA; Biopharmaindustries; non profit organizations	
Combating Antibiotic Resistant Bacteria X	CARB-X	2016	350M\$ / 5 years	Product developers from any country	Antibacterial products, not just therapeutics.	US government; Wellcome trust UK; AMR centre UK;	USA

With the data available, it was not possible to compare the outcomes of the projects funded by the different international initiatives. In some cases, this was because the consortia started fairly recently and thus were young. In other cases, because in spite of being mature consortia, the results of R&D need time to be confirmed by the scientific community, and for example, to be accepted from a regulatory point of view with the idea of being useful in the development of new medicinal products.

7.5 EU Added Value

It was rather early to demonstrate the added value of IMI2 JU in terms of its leveraging effect and scale of resources to attract additional financing or to induce a multiplication effect as it just started in June 2014 in succession of IMI1. Nevertheless, some trends were becoming visible.

The EU funding for IMI2 JU was increased from EUR 1000 million under IMI1 to EUR 1.425 billion, and matched by the equivalent in-kind contributions from EFPIA and Associated Partners.

An important difference with IMI1 was **that the EU contribution included a budget of EUR 213 million to match in-kind contributions from other 'Members, Associated Partners, or from their constituent entities or their affiliated entities'**. This budget reflected the ambition to broaden the participation of partners from different sectors, such as biomedical imaging, medical information technology, diagnostic, animal health industries, IT companies, food industries, etc. This was a key element since it was meant to ensure the involvement of other industries next to the pharmaceutical industry to address the challenges of medicine in the future, which **may constitute determining added value for the IMI2 JU programme**.

The first IMI2 JU projects started in the beginning of 2015 and reported for the first time in 2016. As of 31 December 2016, 25 IMI2 JU projects have been launched with EUR 275.88 million in EU funding, and commitments of EUR 249.15 million from EFPIA, and EUR 14.43 million from Associated Partners. The table 6 provides an overview of contributions from EU, EFPIA and Associated Partner to IMI2 JU projects.

Table 6: Overview of contributions from EC, EFPIA and Associated Partner to IMI2 JU projects

IMI2	Projects	EU		EFPIA in-kind		Associated Partners	
		(EUR million)		(EUR million)		(EUR million)	
Call		Committed	Reported and accepted	Committed	Reported and accepted	Committed	Reported and accepted
1	1	17.63		12.75		5.58	
2	8	114.09	12.9	100.68	47.2		
3	5	49.06		43.94		7.0	
4	1	1.13		1.98			
5	6	47.48		44.27		1.85	
6	4	46.5		45.54			
Total	25	275.88	12.9	249.15	47.2	14.43	

Of the EUR 263.58 million committed by EFPIA and Associated Partners, EUR 83.75 million (or 31.8%) of all in-kind contribution came from outside the EU and H2020 associated countries. A significant part of the non-EU contribution came from Switzerland; it was expected that this percentage will decrease once Switzerland becomes again a H2020 Associated Country on 1 January 2017, but then on the other hand, the UK leaving the EU may balance that effect or even induce an increase of the non-EU contributions depending on the future status of UK vis-à-vis the Framework Programme.

Another advantage of **IMI2 JU** was that it **leveraged additional funding for medicines research and development at a time when research funding was reduced in most of the European countries**. Through IMI2 JU, the EU already invested a total of EUR 275.88 million in the first 25 IMI2 projects. On top of this, EFPIA companies committed EUR 249.15

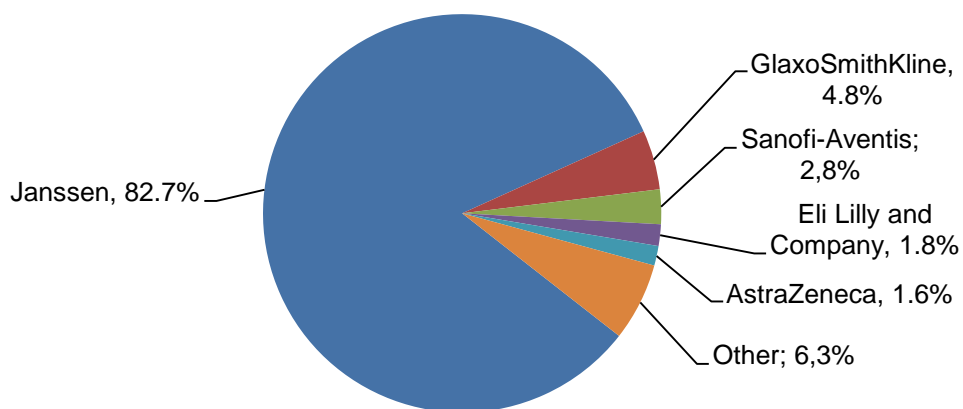
million to the projects, and Associated Partners committed EUR 14.43 million. It can thus be concluded from figures drawn from the first 25 projects launched "that every euro invested in IMI by European taxpayers leveraged an additional EUR 0.96 from EFPIA companies and Associated Partners. In addition to this direct leverage, a further EUR 30.5 million came from "other sources".

The expert group wants to emphasise that care will have to be taken to not exceed the 30% of in-kind contributions from outside of the EU and Associated Countries as the PPP was installed in the first place to secure investments in biomedical research in the EU. Although the expert group was aware that the 30% of the in-kind contributions from outside the EU was accountable to the whole programme, already after these first two years, the share foreseen in the 25 first grant agreements has slightly exceeded this limit of 30%.

In addition, the commitment from Associated Partners for which the EC reserved a matching budget of EUR 213 million seemed to be lagging behind in these two first years of the programme. When the budget would have to be distributed evenly over the ten years the joint undertaking was running, already about EUR 40 million should have been committed by Associated Partners. This situation could be significantly improved once grant agreements under call 10 are signed. Given the transition towards an era in which biomedicine is relying more and more on other technologies than pharmaceutical developments and big data plays an increasingly important role, it may be expected that the participation of Associated Partners will increase significantly.

As illustrated in figure 13, 82.7% of the total IMI2 JU in-kind contribution already reported (or EUR 69.2 million) was provided by one single EFPIA company, Janssen Pharmaceutica, (a Johnson & Johnson affiliate). This was due mainly to its involvement in the Ebola vaccine projects from call 2. The remaining 17.3% came from 29 different organisations.

Figure 13: IMI2 JU in-kind contributions by organisation



Organisations included under 'Other' are: AbbVie, Actelion Pharmaceuticals, Amgen, Bayer Pharma, Biogen Idec Limited, Boehringer Ingelheim, Bristol-Myers Squibb, Company, EFPIA, F. Hoffmann-La Roche, GE Healthcare, Grünenthal, H. Lundbeck, Institute de Recherche Servier, Intervet International, IPSEN Innovation, JDRF International, Merck, MSD IT Global Innovation Center, Novartis Pharma, Novo Nordisk, Pfizer Limited, Piramal Imaging, Takeda Development Centre Europe Ltd., The Leona M. and Harry B. Helmsley Charitable Trust, UCB Biopharma.

7.5.1 Added value through increased collaboration of academia, the creation of specialised research networks and facilities - Overcoming fragmentation of research and innovation efforts

By the end of 2016, IMI2 JU launched ten calls for proposals and today, the IMI community brings together 11500 scientists and experts from across Europe and beyond working in 84 IMI1 and IMI2 JU projects. **55% of the participants in the first IMI2 JU projects were not involved in IMI1 JU**, which was indicative of the increasing success of IMI2 JU. This trend may be followed across the future calls towards the end of the running time.

As outlined in section 7.1, the low participation of SMEs and medium sized enterprises was a major concern since it is a key element for the success of this multidisciplinary approach of innovation in medicine in the future.

Although it has long been recognised as essential for the competitiveness of European health industry, the SMEs participation has not increased from IMI1 to IMI2 JU. It seemed that the leveraging effect of the PPP found its limits to increase the participation of SMEs in the programme and to attract venture capital to support activities in the context of IMI2 JU.

A clear positive result was that IMI projects have been creating long-lasting collaborative networks. This seemed to be confirmed in IMI2 JU; the groups involved in many of the new IMI2 JU projects had never worked together before embarking on the IMI project together.

Although it may provide some measurable added value, it was too early at this stage to evaluate the sustainability of the projects that involve new partners. However, to overcome fragmentation and ensure better sustainability of consortia and outcomes of projects, in 2014 Strategic Governing Groups (SGGs) were set up, which may prove a real added value of the JU.

In conclusion, it was difficult by the end of 2016 to confirm that "thanks to IMI, Europe is an attractive place to carry out pharmaceutical research" and that "the projects have helped to raise the profile and reputation of Europe as a location for medical and pharmaceutical research". This should be the main overall added value of IMI2 JU and the conditions to achieve this goal should be discussed all along the progress of the programme and in view of the future discussion for a potential IMI3 JU programme related to the preparation of ninth Framework Programme.

7.6 SWOT analysis

An analysis addressing Strengths, Weaknesses, Opportunities and Threats was completed by the expert group. The SWOT analysis (Table 7) was used as an illustrative exercise to draw conclusions and recommendations leading to further improvement of IMI2 JU in terms of effectiveness, efficiency and added value for Europe.

Table 7: SWOT analysis

STRENGTHS	WEAKNESSES
<ul style="list-style-type: none"> • Recognised as a world-leading PPP in healthcare, particularly in the US • Unique collaboration model bringing together stakeholders from pharmaceutical industry and academia, SMEs, regulators and patients • Good quality scientific output • Active collaborative networks with growing levels of understanding and trust • Critical mass of expertise to tackle the most complex problems of healthcare needs along the entire R&D cycle • Growing number of individual success 	<ul style="list-style-type: none"> • Low participation from other relevant industry sectors • Continued inability to develop a system of SMART KPIs enabling quantitative monitoring of progress • Decreasing SME participation • Insufficient planning and support for project sustainability • Inefficient level of dissemination and exploitation of project results • Access to results often limited to consortium members

<p>stories and positive perception across IMI project participants and many groups of stakeholders</p> <ul style="list-style-type: none"> • Promising biomarkers and diagnostic tools 	<ul style="list-style-type: none"> • Advisory bodies often not fully informed and not sufficiently engaged • Lack of engagement by Member States leading to lack of alignment with regional and national policies and strategies • Decreasing interest or commitment from EFPIA companies and frequent changes in strategy leading to departures from ongoing projects • Inadequate balance between scientific and administrative tasks of the IMI Programme Office, suggesting a need for more scientific staff
<p style="text-align: center;">OPPORTUNITIES</p> <ul style="list-style-type: none"> • Developing new approaches to encourage the active engagement of other industry sectors with the pharmaceutical industry to capitalise on its expertise in the development of new healthcare interventions • Enhance the visibility and attractiveness of Europe as the environment to develop new healthcare interventions • React in a timely, safe and effective manner to the threat of emerging health threats to the global population • Maximising potential for IMI2 JU as a platform for building a common vision towards maximising the health of the population in Europe • Increasing scope and flexibility to attract non-EU investment for biomedical R&D • Leveraging other potential funding options e.g. via venture capital and/or European Investment Bank loans • Further improvement of the biopharmaceutical R&D environment via removing bottlenecks or improving processes e.g. for clinical trials • Increasing active involvement and role of patients, regulators, payers and health technology assessment agencies • Developing new funding models to exploit results and increase sustainability • Create the momentum for Europe to lead the development of healthcare interventions using big data, patient reported outcomes 	<p style="text-align: center;">THREATS</p> <ul style="list-style-type: none"> • Decrease of political support for IMI2 JU with the absence of quantitative data on outputs • Inability to better accommodate active participation of European start-ups and SMEs • Lack of coherence with other Horizon2020 and national initiatives (i.e. JPI, ESFRI) leading to inefficient use of resources • The UK leaving the EU (Brexit), closing borders, changing foreign policy of USA / China • Inability to engage other industry sectors due to a lack of flexibility of the IMI2 JU governance structure, different business strategies and time to market for new products and different views about the definition of competitive and pre-competitive research • Negative perception of EFPIA among key stakeholder groups (patients, payers, regulators, other industries)

Based on this SWOT analysis recommendations could be set to improve IMI2 JU performance in the future, to support the competitiveness of the European pharmaceutical industry and succeed in realising a significant impact on the health of the population in Europe.

8. CONCLUSIONS

The evaluation set out to address specific questions using the individual criteria of effectiveness, efficiency, relevance, coherence and added value.

Effectiveness in IMI JU was defined in terms of whether the calls and projects are effective to realise the SRA and the IMI JU objectives, the inclusion of all types of stakeholders, from all regions of Europe and whether the budgets have been spent effectively to reach the goals.

Efficiency was defined in terms of whether the activities of IMI JU have been efficient to reach the objectives of the joint undertaking and whether the IMI Programme Office was efficient in supporting these activities.

Answering these questions needs a clear understanding of the initiative. IMI2 JU was created with an overall objective to strengthen the competitiveness and industrial leadership of Europe and to address societal challenges, in particular to move towards the improvement of health and well-being in Europe. IMI2 JU has further specific objectives being: to improve the success rate of clinical trials or priority medicines identified by the WHO; to reduce time to reach clinical proof of concept for cancer, immunological, respiratory neurological and neurodegenerative diseases and to develop new therapies for which there was a high unmet need and limited market incentives; to develop diagnostic and treatment biomarkers for diseases linked to clinical relevance and approved by regulators; reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks; and to improve the drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products. The socio-economic situation justified the development of such public private partnership.

To achieve these goals **EFPIA is due to provide EUR 1.425 billion as in-kind contribution. The EU is due to provide a budget of EUR 1.638 billion, to match the EFPIA contribution and contributions up to EUR 213 million from Associated Partners other than pharmaceutical industry.** The running costs of the Programme Office are shared by both EFPIA and the EU for a maximum of 10 % of the total costs of the programme in cash. Research projects are financed in cash by the EU, while the EFPIA partners and Associated Partners provide in-kind matching budgets.

To achieve the objectives the Strategic Research Agenda from IMI1 was updated. This formed the basis for annual work programmes that defined the topics to be addressed. Calls for research proposals were launched to address the topics. **The expert group agreed that the SRA was relevant, as well as the calls launched. The operational efficiency of the Programme Office was beyond doubt.** However, the communication between the different governing bodies could be improved. **SC and SRG felt that the GB should be more open for their feedback and input and open dialogue,** which was limited.

Effectiveness of communication also needed further improvement to make the results from projects known and accessible outside of the consortia that generated them, especially also for other SMEs. It may be expected that the closeout meetings that were organised to finalise IMI projects may improve this, although it was reported at several moments that most results remain hidden within the consortia.

The expert group believed that the development of thematic Strategic Governance Groups SGGs, may significantly improve the awareness of and communication on results. It may be hoped that this will give an impulse to build further on the outputs of IMI projects and ensure sustainability beyond the project funding period. **Improved communication will also be needed** to align the roles of the SC and SGGs, as these roles may overlap.

In contrast to IMI1, the sustainability of results and outputs from IMI2 projects is taken into account. In the design phase of the IMI2 projects, the sustainability of possible outcomes of the projects are addressed. So far, however there were only a limited number of examples of IMI1 project outcome that were sustained. This may suggest a lack of interest or represent only a low priority for pharma industry (EFPIA). However, as none of the IMI2 JU projects have been finalised it was not possible to assess whether sustainability of projects outputs was easier to achieve because it was part of the IMI2 JU projects from the start.

Related to the perception of a lack of transparency and communication was the frustration that was vented on how the call topics were being developed, as this was a **top down process almost solely in the hands of EFPIA partners**, although there was general agreement that the issues addressed in the SRA were relevant to realise the defined objectives.

The objectives of IMI2 JU were also in line with the objectives of Horizon2020: to generate scientific excellence and industrial leadership and tackle the societal challenges. However, the SME participation in IMI2 JU projects has been decreasing so far from approximately 16% of the EU-funded participations under IMI1, to less than 12%. The effect was similar however, although less pronounced, when comparing with the SME participation in Horizon 2020 Societal Challenge 1. In this programme, SME participation reached close to 16%, but decreased so far by 2% as compared with the participation in FP7. Most likely this change can be attributed at least partly to the popularity of the new SME-instrument that became available under Horizon 2020.

For SMEs, but also for some academic stakeholders, **participation in IMI2 JU projects was not straightforward**. The governance of the large IMI consortia was described as time consuming and complex. In addition, the negotiations on intellectual property were very challenging, as the focus on what is 'precompetitive' research for pharmaceutical companies, was most likely core business for an SME. In addition, there was no room to negotiate on exclusive rights, which is a prerequisite for venture capital providers that are vital for SMEs and start-up companies. Moreover, **SMEs were often not well equipped to negotiate IP rights in the setting of the IMI pharmaceutical companies**. In addition, it was also repeatedly mentioned that the topic descriptions in IMI2 calls were too prescriptive and top-down determined by the large industry. For SMEs, more flexibility was preferred.

Unlike under IMI1, mid-cap companies and companies from other sectors than pharmaceutical can fully participate in IMI2 JU. For mid-cap companies this can be as a partner in the consortium of in-kind contributors, in which they can help designing the call topics and contribute in kind or as a partner in the beneficiaries consortium that replies to the call and are funded.

The involvement of both types of new partners should be enhanced further. Especially the integration of other industries, such as technology providers, diagnostics developers, developers of electronic solutions and big data handlers were instrumental for the development of healthcare of the future. **Failure of IMI2 JU to quickly find a way to meaningfully include other sectors in IMI2 JU projects, would represent a significant long-term threat for the position of the European pharmaceutical and global healthcare system and industry.**

One of the main achievements since the installation of IMI JU on which there was general consensus, was that the PPP led to a new type of consortia, in which competing pharmaceutical companies work together to achieve a common goal. The consortia also induced a mind change in the respective perception of scientists from academia and industry. **Trust and mutual understanding and appreciation were created.**

One of the main weaknesses and risk factors of IMI consortia, was the potential withdrawal of leading industry partners from a running project, even though EFPIA negotiates to find solutions. Although this did not happen often, there were no mechanisms to enforce the engagements made. **Premature withdrawal of one of the central partners in the consortia may jeopardise the entire project** and it imposed significant extra work as work packages need to be rewritten and parts of work need to be taken over by others and adaptations have to be made to align with a potential new partner.

Both IMI1 and IMI2 JU also reached out to regulatory agencies and patient organisations to participate in the projects. Although this was received very well by all stakeholders, the participation of both types of participants could still be improved.

From a geographical point of view, it was clear that IMI2 JU was generally not present in EU-13 countries. Some countries were outperforming significantly in terms of participation in IMI2 JU, when compared to others. This may be linked to traditional presence of biopharmaceutical companies and research.

The coherence of IMI2 JU with the objectives in Horizon 2020 may further be improved not only through specific actions targeting to reach a broader geographical spreading, but also to

align better with other initiatives such as developed by the Joint Programming Initiatives, some of which are addressing the same societal challenge as covered in the SRA of IMI2 JU. Closer interaction and collaboration may enhance innovation in these areas.

The added value of the IMI2 JU, like for the IMI1 final evaluation, was more challenging to evaluate, in particular because, despite recommendations in the two previous interim evaluation of IMI1, no accountable performance measuring system using SMART KPIs is available. The annual reporting and current KPI system under development was not aligned with the impact assessment goals and success criteria that were used in the argumentation to set up a joint undertaking.

The first IMI2JU projects concerned mainly Ebola and related diseases. IMI was able to set up very rapidly and efficiently several calls when it was clear that Ebola virus represented a real threat for Europe. It was appreciated that IMI in spite of what could appear as a huge, rigid administrative structure had been successful in implementing in a very short period of time several projects involving European and African teams and was able to realise four clinical trials in six African countries. For IMI1, the Programme Office reported on commercialisations of project outputs that include new spin-off creations, trademarks, licensing deals, results implemented by industry, sustainability plans, commercialisations, patent applications, although by the end of 2016, only 21 of the IMI1 projects out of 59 had reached the end of their funding cycle. Furthermore, the joint undertaking led to over 2000 direct jobs created, which leverage the creation of other jobs elsewhere in the economy. Next to that IMI projects also realised a significant scientific output as evident from the scientific publications. So far however, there are limited examples that IMI helped to shorten the time of development of new applications or that IMI brought new, safer and more effective therapies or products to patients, but there are promising results concerning the development of a new Ebola vaccine and clinical trials in Africa.

It may be expected that in the future IMI2 JU will induce a further increase of results and outcome; however it was not clear to the expert group whether the joint undertaking induced a stronger boost to the European industrial leadership and competitiveness than the more traditional approach under the framework programmes would have achieved. In particular the SME instrument under Horizon 2020 seems to respond to a significant need.

It would be a major success if IMI2 JU would have a demonstrable effect on making Europe more attractive for investing in biopharmaceutical R&D, but again a long time will be needed to achieve such a goal. Although when compared with other EU-funding sources IMI2 JU mobilised significant private investment, which was not possible in other framework initiatives, it concerned mainly in-kind contributions. Moreover, these in-kind contributions of the pharma companies when compared with their total R&D investments, varied significantly between companies, but are in general always relatively small and cannot be correlated to the overall company R&D budgets, even though under IMI JU the focus is on precompetitive research and thus not covering the entire scope of research and development. There was also still not sufficient transparency on how the in-kind contributions were calculated. Although IMI representatives often mentioned that IMI2 JU was envied in other continents, there was no indication that Europe was becoming more attractive for companies to invest in biopharmaceutical research.

The efficiency of the joint undertaking to support the competitiveness of the European pharma sector can furthermore be questioned when the investments from outside Europe were taken into account in the calculations of in-kind made investments, even though these are global companies. Under the IMI2 JU up to 30% of the in-kind contributions for research projects is eligible to come from outside the EU and countries associated to Horizon 2020. In fact the lever created to increase investments in European pharmaceutical industry and boost European competitiveness is weakened by 30% in this way.

It was clear that a long-term strategy was required before the joint undertaking may realise a demonstrable effect supporting the competitiveness of the European pharmaceutical industry. A particular need identified was to develop new approaches to encourage the active engagement of other industry sectors with the pharmaceutical industry to capitalise on its expertise in the development of new healthcare interventions. In addition, efforts are needed to identify socio-economic benefits from IMI2 JU to analyse and demonstrate the impact of the programme for society, even if more time is needed before health indicators will indicate a change. The interim evaluation of IMI2 JU may be too early to bring a definitive appreciation on the role of IMI2 JU on boosting the competitiveness of European pharmaceutical industry.

These conclusions have been used to formulate recommendations for IMI2 JU and any subsequent IMI2 JU funding stream. These recommendations are now described.

9. RECOMMENDATIONS FOR IMI2 JU

The expert group identified the following recommendations to improve effectiveness, efficiency, coherence and added value of the joint undertaking in the next phase of its running cycle.

- Recommendation 1: A renewed and stronger effort should be made to attract and integrate other industries than the pharmaceutical industry in the collaborative projects.

A new membership category for EFPIA was created to support the participation of industries other than pharma in IMI2 JU. However, the acceptability of EFPIA to industries other than pharma remains problematic and this body needs to adapt to be able to represent the views of other industries. Examples from other European Joint Undertakings, such as BBI JU may provide inspiration to include industries other than pharmaceutical companies.

Furthermore, continued efforts are needed to connect with patient organisations and regulatory agencies.

- Recommendation 2: Create a better eco-system to attract more SMEs.
 - *Expand the scope of projects to attract SMEs developing innovative technologies to capture novel trends in the development of healthcare of the future.*
 - *Make topic description less prescriptive and allow more flexibility for SMEs to come with creative ideas.*

A stronger effort should be made to increase the participation of SMEs as these form the cornerstone of European economy. Not only SMEs in the biomedical development should be included, but the programme should be broadened to capture and include the use of the most innovative technological developments in the healthcare and drug development.

- Recommendation 3: An accountable Performance Measurement Framework, using SMART KPIs should be developed to assess the impacts and socio-economic benefits of the joint undertaking.

An accountable Performance Measurement Framework, using SMART KPIs should be set up and used as soon as possible to allow assessment of the return on invested efforts and compare there with those achieved through other programmes and assess the socio-economic impact generated. Targets to achieve on short, mid-term and long-term related to the ambitions of the programme should be put forward. This recommendation has been standing since the first evaluation of IMI1.

- Recommendation 4: Review the IP policy and make it more flexible to respond to the needs allowing negotiations on exclusive rights.

The IP policy has been a matter of ongoing debate and is now, overall, following the policy of Horizon 2020. Sufficient flexibility should be in place to guarantee that more results from IMI2 JU projects may be translated into applications at the benefit of the society.

- Recommendation 5: Improve and broaden access to project outcomes and assure their sustainability to increase impact.
 - *Develop a platform for open dialogue with and between the different groups in the governance structure of the joint undertaking;*
 - *Develop a brokerage platform to stimulate that results from IMI2 projects and from other programmes are leading to applications;*
 - *Ensure communication to a wider audience to increase awareness of the programme results and outputs.*

To improve the impact of the joint undertaking, results and outputs should be capitalised. This set of recommendations may help to achieve this.

10. RECOMMENDATIONS FOR FUTURE IMI JU INITIATIVES

- Recommendation 1: Make a substantial adaptation to the collaborative and funding model to enable the active engagement of other industry sectors with the pharmaceutical industry to capitalise on their expertise in the development of new healthcare interventions.
- Recommendation 2: Increase the transparency of in-kind contributions as well as the SRA and call topics generation to reflect European interest and interests of stakeholders other than EFPIA.

Transparency on these issues will open up the programme for more creative and innovative thinking and trust amongst the potential participants and stakeholders.

- Recommendation 3: Change the rules on the calculation of the in-kind contributions from non-European entities.

To be consistent with the goal of increasing investments in Europe, in-kind contributions from activities that occur outside of the EU should not be accepted to match with the public funding, but may be accounted as additional contributions or leveraging effects.

11. ANNEXES

Annex 1. Experts short biographies

Annex 2. List of questions asked during the interviews

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Annex 8. Areas addressed under the IMI2 JU during the interim evaluation period

Annex 9. Other initiatives comparable to IMI2 JU

11.1 Annex 1: Experts short biographies

Name of experts	Nationality and Gender	Short biography
André Syrota	French Male	<p>Professor Emeritus at the University of Paris Sud; Former Chairman and CEO of Inserm, (French National Institute of Health and Medical Research); Advisor to the Administrator General of the Cea (French Alternative Energies and Atomic Energy Commission).</p> <p>His research activities were focused on the development of non-invasive functional imaging methods in human, using Positron Emission Tomography, Single Photon Emission Tomography and Nuclear Magnetic Resonance. He is the author of more than 200 articles and 40 book chapters.</p> <p>He has been a member of various boards at the Ministry of research and national institutes. He has also been a member of scientific evaluation committees in the field of nuclear medicine, biophysics and medical technologies such as chairman of the National Consortium in Genomic Research and of the Institute of Structural Biology, (Grenoble). He was a member of the European Strategy Forum on Research Infrastructures (ESFRI) Biological and Medical Sciences Steering Group, (EU), of the ISTC Scientific Advisory Committee (Astana), of CYCERON (Caen) and CERMEP (Lyon) imaging facilities,...). He is now chairman of several boards and represents the French partners of HBP (Human Brain Project).</p>
Kathleen D'Hondt	Belgium Female	<p>Policy Analyst, Senior researcher at Flemish Government in the Department Economy, Science and Innovation. She is actively involved in the development of science policy related to life sciences in Flanders.</p> <p>Formerly working as policy analyst in OECD Working Party on Biotechnology, Nanotechnology and Converging Technologies (BNCT). Former IMI SRG Vice-Chair. In her current position she is Management Board member of the Joint Programming Initiative Neurodegenerative Diseases and the Joint Programming Initiative Antimicrobial Resistance and the Belgian delegate in the Programming Committee for Societal Challenge 1 (Health).</p>
Katherine Payne	UK Female	<p>Katherine was awarded a personal Chair in Health Economics at The University of Manchester in August 2010. Katherine is also a registered pharmacist. She has extensive experience working as an academic health economist with different clinical research groups (pharmacy, psychiatry, genetics, rheumatology, dermatology). Based in the Manchester Centre for Health Economics, established in August 2012, she is now leading a research group that focuses on the evaluation and valuation of genomic technologies and precision medicine. Her research has been funded by a number of different funding bodies including: NIHR (RfPB; PGfAR; HS-DR; HTA); MRC; EU and patient charities. She has substantial experience as a member of funding panels in different jurisdictions (UK; France; The Netherlands; Luxembourg; Canada).</p>
Belen Crespo	Spain Female	<p>Director of the Spanish Agency of Medicines and Medical Products Member of EMA Management Board</p> <p>Previously, a technical Adviser, General Sub directorate of High Inspection and Services in Ministry of Health, Social Policy and Consumer Affairs , (Spain) and Deputy Director of Alert System and Official Controls in Spanish Food Safety and Nutrition Agency. Ministry of Health and Consumer Affairs.</p> <p>Author of more than 50 publications in peer-reviewed scientific journals on: Management of National Health Services, Rational use of medicines, Food safety, Information Systems and Health Regulations.</p>
Marcin Szumowski	Poland Male	<p>MSc, PhD, MBA. Following a successful research career in the United States he has been involved in technology transfer and start-up companies, since 2000 having co-founded and managed three start-ups (US based and Polish consulting businesses and a high technology start-up - Medicalgorithmics Ltd. Currently he is responsible for developing a technology transfer platform for the consortium consisting of three universities and seven Polish Academy of Science institutes, executing a 100 million euro Centre for Preclinical Research and Technology (CePT) project. Now President & CEO in OncoArendi Therapeutics.</p>

11.2 Annex 2: List of questions asked during the interviews

Background of the initiative, objectives and relevance

Question 1: What do you think is the competitive position of the technologies produced as part of IMI JU programme, in three time frames: the short term, the medium term and the long term? In your answer can you indicate how you interpret short, medium and long term in this context.

Question 2: As you know the IMI2 JU programme was set up in 2014. Focussing on the global financial context and economic drivers, what changes have occurred over this time period in terms of the development of new technologies? For example, what are the emerging competitive technologies? What are the likely effects of these changes?

Effectiveness of the Innovative Medicines Initiative

State of play of implementation

Question 3: What types of organisations (academic, regulators, patient organizations, industrial, including SMEs, and research organisation sectors) are taking or have taken part in IMI JU and IMI2 JU? Have you seen an evolution with time? Has this pattern changed in terms of the geographical location of the projects? Do you think the gender balance has changed over time?

Question 4: How would you rate them in terms of their quality, in particular in terms of academic skills, business skills, others? Do the IMI JU and IMI2 JU attract the highest quality organisations/researchers active in the field?

Question 5: Have you seen new sectors joining IMI activities? How IMI is effectively opening to new sectors and bringing in Associated Partners?

Question 6: What strategies have been used to ensure that the highest quality researchers in Europe, from different disciplines, are involved in projects supported by the IMI2 JU? How could this be improved?

Main achievements and extent to which the objectives of the Joint Undertaking have been met

Question 7: What progress has been achieved towards the objectives of the IMI JU and IMI2 JU (as set in Article 2 of the Council Regulation setting up each JU)?

Question 8: Have the research topics published in the calls for proposals sufficiently matched the priorities set out in the Strategic Research Agenda?

Question 9: Are the measures described in the Strategic Research Agenda and the topic descriptions in the calls for proposals texts appropriate to ensure innovation?

Question 10: Has the IMI JU effectively contributed to the implementation of FP7 and of H2020?

Question 11: Have the activities of the IMI JU contributed successfully to the appropriate use of the budget allocated to the programme?

Question 12: To what extent has the IMI JU succeeded in developing effective networks of key stakeholders? This could be in terms of setting up networks between the public and private sectors and/or combining private-sector investment and European public funding?

Question 13: Do you think stakeholders consider the IMI JU to be a useful tool to stimulate research investment in the development of medicines in the long term?

Question 14: Has the IMI JU contributed to the participation/involvement of Small and Medium-sized Enterprises (SMEs) in its supported RTD activities?

Question 15: What changes have occurred in the research and socio-economic context of the medicine development sector since the initiation of the programme? What are the likely effects of these changes? Do you think the objectives of the IMI JU are still valid in light of these potential changes? Do you think the timelines set by the IMI JU are still appropriate?

Question 16: Do you think the Key Performance Indicators (KPIs) of IMI JU are quantifiable? What progress do you think IMI JU has been made in achieving these? Do projects deliverables align with the overall KPIs of the IMI JU?

Efficiency of the Innovative Medicines Initiative

Question 17: Are the activities of the IMI JU carried out efficiently? Efficiently can refer to: The extent to which the IMI JU has been operated efficiently, whether there has been good communication of objectives and progress, and the ability to address problems as they arose.

Question 18: Do the activities of the IMI JU constitute effective methods of achieving the objectives set?

Question 19: Do you think that the project objectives and deliverables are set in a realistic way? How were these monitored (a) at a project level, and (b) at the IMI JU level? How was the overall quality of the projects assessed?

Question 20: Are the levels of resources available to IMI JU and adequate to reach these objectives? Are the in kind contributions from industry appropriate?

Question 21: Is the level of IMI JU supervision appropriate to achieve the effective monitoring of progress in programme implementation?

Question 22: Are the IMI JU's objectives and achievements adequately communicated to and understood by external (within EU 27 and outside) stakeholders?

Question 23: Is the IMI JU effective in terms of knowledge dissemination & exploitation? Is the access to project outputs and outcomes, broad/sufficient enough for the participants from outside the IMI consortia? To what extent has the sustainability of the outputs from the IMI JU been considered in the current projects?

Question 24: Are the IMI JU's activities sufficiently visible to the public?

Question 25: How adaptable is the IMI JU to changing research needs?

Question 26: How adaptable is the IMI JU to changing policy priorities?

Question 27: How are external stakeholders from science, regulation, industry and policy involved in identifying the priorities?

Question 28: In your opinion, are the IMI JU governance and management structures clear? Do you think this is cost effective in terms of achieving outcomes given the budget available?

Question 29: To what extent could the governance and management of IMI JU as a private-public partnership be improved?

Question 30: The JU has developed key processes, for example: call for proposals, mobilising the public and private sector resources needed, involving Associated Partners under IMI2, facilitating coordination with national and international activities in this area, reviewing and making any necessary adjustments to the Research Agenda, etc. In your opinion, are the IMI JU processes clear? Do you think these have evolved adequately and are cost effective in terms of achieving outcomes, given the budget available?

Question 31: According to your experience, are the roles, responsibilities and tasks of the IMI JU bodies clearly defined? Are the roles of the Scientific Committee clear? Are the roles of the State Representatives Group clear?

Question 32: In your view, did the members of the IMI JU contribute to the functioning of the IMI JU timely (in kind contribution/cash/scientific input)?

Question 33: In your view, to what extent does the IMI2 JU operate in accordance with the IMI2 JU Regulation?

Question 34: In your view, to what extent does the IMI2 JU operate in accordance with the Annex of the Regulation (Statutes)?

Question 35: Are the activities of the IMI JU carried out transparently? Do stakeholders have a clear mechanism by which they can input into call topic selection? Do patient groups and other stakeholders have a clear mechanism by which they can input into call topic selection?

European added value

Question 36: At this stage, what are the indications that the research and development activities supported by the IMI JU are of high quality?

Question 37: Did the IMI JU contribute to overcoming the fragmentation of research and innovation efforts and did it facilitate the development of consistent and coherent long-term strategic investment?

Question 38: Did IMI JU contribute towards the main related EU policies in the field of health, biopharmaceutical research, life science research and economic growth?

Question 39: Is the IMI JU perceived as flagship for Public-Private partnership-supported RTD in the world and what more could be done in this respect?

Coherence

Question 40: How well has the IMI JU ensured complementarity with other activities of FP7 and H2020?

Lessons learned from the previous evaluations

Question 41: To what extent were the recommendations from the second interim evaluation taken into account/implemented?

Synthesis, conclusions and recommendations

Question 42: What lessons can be learned from the IMI JU for the future of the Public Private Partnerships?

Additional questions

Question 43: H2020 has aimed to simplify its processes and monitoring procedures? Do you consider that these steps are beneficial for the IMI2 JU?

Question 44: Which is the information that you have of other PPPs in this sector in the rest of the world (mainly USA, Japan, etc.)?

Question 45: What is the current situation with participation of the organisations from EU13 countries? How can more countries and SMEs be engaged in IMI – are there lessons from the more successful countries that could be applied elsewhere?

Question 46: How can IMI JU facilitate the engagement of patient groups?

Question 47: What did the first IMI Socio-economic Impact study produced in 2016 achieve?

Question 48: Do the current Key Performance Indicators (KPIs) reflect the overarching goal of the JU? Are the current KPIs relevant to measure progress? And impact? What are the key KPIs that need to be adopted in future by IMI JU? How should these future KPIs be measured?

Question 49: Does the access policy to IMI project results stimulate broader innovation and benefit entities outside of the consortia members? What can be improved to achieve greater impact?

Question 50: How do you ensure that the information (research data, negative results on safety and efficacy, etc.) are disseminated among the participants of all IMI projects to avoid duplication of efforts?

Question 51: Are there opportunities for improvement in the IMI2 JU communication strategy? What are the targets for the media agency employed? What is being done to encourage/facilitate use of social media by the existing projects?

Question 52: Are there opportunities for improvement in the IMI communication strategy with respect to technology transfer and innovation?

Question 53: Are very large consortia the most effective way to move new therapies benefiting patients really the best tools? What are the main risks and inefficiencies observed?

Question 54: What is the involvement of Joint Programming Initiatives, ESFRI Research Infrastructures and other sectors (e.g. bio-imaging, diagnostics, use of converging technologies, etc.)?

Question 55: Will all available budget be spent in the required time frame – what are the challenges?

Question 56: Are there any gaps in terms of the skills and capabilities in the IMI executive office?

Question 57: What are the main strengths of the IMI office?

Question 58: How do you ensure that decisions taken by IMI2 both on the content of the calls and on the results of the evaluation are transparent?

Question 59: What are your experiences with IMI? Would you consider participating again in the future? Does IMI address the needs in your area?

Question 60: Do you think stakeholders consider the IMI JU to be a useful tool to stimulate research investment in the development of medicines in the long term?

Question 61: How could we qualify and define the achievements in the calls for the JPI AMR, or if there has not been enough time to develop, ... What kind of achievements are being expected?

Question 62: Given the different and clear characteristics of both the IMI and the JPI AMR, which of the two options would you consider to be more productive (resources used more efficiently for delivering achievements) in the case of research in the area of antibiotics and AMR. Why?

Question 63: Do you consider that both mechanisms IMI and the JPI AMR are consistent with each other? Are they coordinated? Are the results between the two permeable? Is there an established mechanism of communication between the two?

Question 64: What strategies does the JPI AMR use to attract researchers? Does the JPI AMR selects more high-quality researchers with track record (and funded by other means) or does it direct its resources to researchers with potential for development and perhaps less likely to compete with consolidated groups? Is there a specific target in JPI AMR project funding?

Question 65: In relation to the IMI DRIVE project on economic models to encourage research into new antibiotics, would you have an opinion on whether the approach is the best possible or if the economic resources used in the project are the best investment for that topic? Are all the stakeholders necessary? Do the 3-year duration and other characteristics of the project make it a useful and above all productive effort?

Question 66: It seems that there is a deficit of technological SMEs in IMI projects in general. What strategies could be used to attract SMEs and involve them in IMI projects related to antibiotics and the AMR problem?

Question 67: Are the public-private partnerships established through the IMI Program and the combination of public and private investments a success?

Question 68: In JPI-AMR, calls are focused on small groups of applicants and finance a significant number of projects. Is there a strategy of favouring small collaborations between a few entities (3-6 entities), or is this a limitation due to the resources available? If the budgets available were to be increased, would this strategy change or remain? Also, how do you consider the open or limited JPI AMR calls closing the option to certain research groups?

Question 69: Are the descriptions and objectives of the topics under IMI adequate to ensure innovation in AMR? Do you consider them very open, or very limited?

Question 70: In relation to the previous question, what is the situation for JPI AMR?

Question 71: Within the possibilities of the two initiatives, IMI and JPI AMR, are their activities sufficiently visible to the general public, e.g. society?

Question 72: In the case of the JPI AMR, are stakeholders involved and informed about the selection of topics? How is the process of topics selection made transparent?

Question 73: How does EMA participate/ contribute to IMI projects? What is the added value for EMA? And for IMI partners (industry and academia)?

Question 74: According to some of the previous interviewees, one of the best IMI achievements is to have provided the regulators such as EMA with biomarkers for several diseases, new methods for medicines production, guides of good practice and standards. Could you please give us examples? Which is the case in which the benefit for the patient has been the most significant?

Question 75: Do you think that the Public-Private-Partnership model of IMI is delivering better social benefits than the traditional public funding (such as in other parts of H2020).

Question 76: From the viewpoint of a regulator, which are the strengths and weaknesses of IMI?

Question 77: Can you indicate if there are any interactions between Advisory Group for Health and IMI2 JU? What is the role of the Advisory Group for Health and what is the difference with the Scientific Panel for Health? How do these groups interact on IMI2 JU issues?

Question 78: According to you, did the IMI office operate efficiently during all stages of the project follow-up, i.e. evaluation, negotiation, contract finalisation, payments, monitoring, etc.?

Question 79: Are you satisfied with the role of the Strategic Governance Group? What could be improved?

Question 80: According to you, which are the indicators demonstrating that the research and development activities supported by the IMI JU are of high quality? Does the IMI JU make a difference to achieve goals that would not have been possible without the IMI JU?

Question 81: If there was no IMI or IMI2, what alternative mechanisms do you think could also be effective in stimulating development and improving access to safe and effective new therapies for European patients?

Question 82: Do you think drug discovery biotech companies focused on development of new assets can benefit directly or indirectly from IMI JU? How?

Question 83: Identify one weakness of IMI JU that in your view needs the most attention.

Question 84: Name a practical example in which IMI has facilitated the authorization of a drug in oncology and its access to patients.

Question 85: Do you think that the drug regulation, concretely, regulation of drug safety and efficacy benefits from the IMI Program?

Question 86: What do you think about the 2-stage selection process for the IMI consortia?

Question 87: Could the selection process of the consortia be improved to increase competition and innovation?

Question 88: How are external stakeholders from science, regulation, industry and policy involved in topics design?

Question 89: Do you estimate IMI is a good programme to improve and accelerate the development of new drugs and therapies? How do you feel about VIB participation in IMI projects? Do you see an added value in the PPP construction of IMI?

Question 90: Why was VIB participation in IMI limited so far (1x in IMI JU; 1x in IMI2)? What would need to change to increase participation?

Question 91: What alternative strategies for stimulating innovation and competitiveness in life sciences could be implemented in place of IMI (PPP in early stage VCs? Loans for SMEs that could be written off in case of program failure?)?

Question 92: What would be your main concerns related to IP protection, value creating and technology transfer in the context of participation in an IMI project?

11.3 Annex 3: List of relevant background documents

(1) Financial management and setting-up joint undertakings

– *General Financial Regulation*

Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L 298, 26.10.2012, p. 1)

Commission Delegated Regulation (EU) No1268/2012 of 29 October 2012 on the rules of application of Regulation (EU, Euratom) No966/2012 of the European Parliament and of the Council on the financial rules applicable to the general budget of the Union (OJ L 362, 31.12.2012, p.14.3.2).

– *Framework Financial Regulation for Joint Undertakings*

COMMISSION DELEGATED REGULATION (EU) No 110/2014 of 30 September 2013 on the model financial regulation for public private partnership bodies referred to in Article 209 of Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council (OJ L 38, 7.2.2014, p.2)

Financial Rules of the Innovative Medicines Initiative Joint Undertaking

Financial Rules of the Innovative Medicines Initiative 2 Joint Undertaking

– *Establishment Act*

Council Regulation (EC) No 73/2008 establishing the Innovative Medicines Initiative Joint Undertaking

Council Regulation (EU) No 557/2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking

(2) Horizon 2020

Regulation (EU) N° 1291/2013 of 11/12/2013 of the European Parliament and of the Council establishing Horizon 2020 – The Framework Programme for Research and Innovation (2014-2020);

Council Decision 2013/743/EU of 3 December 2013 establishing the specific programme implementing Horizon 2020 - The Framework Programme for Research and Innovation (2014-2020);

Regulation (EU) N° 1290/2013 of the European Parliament and the Council of 11 December 2013 laying down the rules for the participation and dissemination in Horizon 2020 - The Framework Programme for Research and Innovation (2014-2020) and repealing Regulation (EC) No 1906/2006;

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 OJ L 174, 13.6.2014, p. 7-11

Commission Decisions adopting the JUs work programmes under Horizon 2020 (WP 2014-2015, WP 2016-2017);

Communication from the Commission of 21.9.2011 to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, Partnering in Research and Innovation COM(2011) 572 final

(3) Decision related to JUs

COMMISSION DECISION on the appointment of Commission representatives to the Governing Board of the IMI Joint Undertaking

COMMISSION DECISION of 27.6.2014 - appointing the Commission representatives to the Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking and repealing Decision C(2008)761

COMMISSION DECISION 2008 constituting a financing decision for implementing the budget of the IMI Joint Undertaking during the preparatory phase

COMMISSION DECISION 2009 constituting a financing decision for implementing the budget of the IMI Joint Undertaking during the preparatory phase

(4) Documents related to the work of JU

IMI JU's Annual Implementation Plans (2008 to 2014)

IMI JU's Annual Activity Reports (2008 to 2013)

IMI2 Annual work plans (AWP) 2014, 2015 and 2016

IMI2 Annual Activity Reports 2014, 2015 and 2016 (draft)

(draft budget N+1, PDB N+2, Staff Establishment Plan)

IMI JU revised Scientific Research Agenda (2011)

IMI 2 Strategic Research Agenda (2014)

(5) Documents on the working arrangements between the Commission and JUs

General Financial Agreements between the Commission and the IMI JU, Annual Financial Agreements between the Commission and the IMI JU

Delegation Agreement between IMI2 JU & the European Commission (Ares(2016)2582379)

Annual Transfer of Funds Agreement between IMI2 JU and the European Commission

IMI JU's Model Grant Agreement

IMI2 JU's Model Grant Agreement

(6) Previous Evaluations and other studies

Assessment of Economical and Societal Effects

COMMISSION STAFF WORKING DOCUMENT - Accompanying document to the Proposal for the Council decision on the setting up the Innovative Medicines Initiative Joint Undertaking Analysis of the effects of a Joint Technology Initiative (JTI) in the area of INNOVATIVE MEDICINES

1st Interim Evaluation report (2010)

2nd Interim Evaluation of IMI (2013)

COMMISSION STAFF WORKING PAPER - Report on the first interim evaluation of the Innovative Medicine Initiative Joint Undertaking

Report from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions

Second Interim Evaluation of the Clean Sky, Fuel Cells and Hydrogen and Innovative Medicine Initiative Joint Technology Initiatives Joint Undertakings

Report of the Independent Expert Panel Accompanying the Commission report - Assessment of European Innovative Medicines Initiative 2

COMMISSION STAFF WORKING DOCUMENT IMPACT ASSESSMENT Accompanying the document Proposal for a Council Regulation on the Innovative Medicines Initiative 2 Joint Undertaking

(7) Socio economic reports for the budget discharge and Audit reports

IMI's added value Project outputs linked to early socio-economic impacts

IMI Socio-economic Impact Assessment Expert Group

(8) Minutes of the IMI JU and IMI2 JU Governing Boards meetings

(9) Call texts and relevant documentation (e.g. Rules for submission and evaluation of proposals), including statistics;

(10) Reports from IMI and IMI2 projects;

(11) Any other IMI and IMI2 JU-specific relevant document, such as: reports of independent observers for the IMI and IMI2 call evaluation;

(12) Bibliometric analyses of ongoing projects

11.4 Annex 4: List of stakeholders interviewed

Adriana Maggi, Vice-Chairperson, Joint Programme Neurodegenerative Disease (JPND); Professor of Pharmacology and Biotechnology, University of Milan, Italy

Anders Olauson, Honorary President of the European Patients Forum

Antoine Cuvillier, Head of Administration and Finance, IMI2 JU Programme Office

Beatriz Silva Lima, Chairperson of IMI2 JU Scientific Committee; Professor of Pharmacology and Pharmacotoxicology, Lisbon University, Portugal

Carlos Segovia, Chairperson of the Management Board, Joint Programming Initiative on Antimicrobial Resistance (JPIAMR); Head of the unit of Accreditation of Health Research Institutes at the national Institute of Health Carlos III, Spain

Christopher Austin, Director, National Center for Advancing Translational Sciences at National Institutes of Health, USA

Corinne De Vries, Head of Science and Innovation Support, European Medicines Agency

Daniel Pipeleers, Professor, Brussels Free University, Belgium

Ferrán Sanz Carreras, Lead of managing entity of IMI JU project "eTOX"; Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Barcelona, Spain

Françoise Meunier, Former member of IMI JU Scientific Committee; Director Special Projects, European Organisation for Research and Treatment of Cancer

Hüseyin Firat, Cofounder and CEO, Firalis company, France

Jérôme Van Biervliet, Senior Business Development Manager, Vlaams Instituut voor Biotechnologie (VIB), Belgium

Johan Cardoen – Managing Director, Vlaams Instituut voor Biotechnologie (VIB), Belgium

Liselotte Højgaard, Chairperson of the Danish National Research Foundation; Professor, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Magda Chlebuś, Director of Science Policy, European Federation of Pharmaceutical Industries and Associations (EFPIA)

Marc de Garidel, Chairperson of IMI2 JU Governing Board; Vice-President, European Federation of Pharmaceutical Industries and Associations (EFPIA)

Marta Gómez Quintanilla, Chairperson of the IMI2 JU States Representative Group; Centre for Industrial Technological Development, Ministry of Economy and Competitiveness, Spain

Michel Goldman, Former Executive Director, IMI JU; Institute for Interdisciplinary Innovation in Healthcare, Université Libre de Bruxelles, Belgium

Nathalie Seigneuret, Scientific Project Manager, IMI2 JU Programme Office

Olivier Arnaud, European Director for Research, JDRF

Pierre Meulien, IMI2 JU Executive Director

Ruxandra Draghia-Akli, Vice-Chairperson, IMI2 JU Governing Board; Deputy Director-General, Directorate General for Research and Innovation (DG RTD), European Commission

Stefan Jaroch, Coordinator of the IMI JU project "ELF"; Head of External Innovation Technologies, Bayer Pharma AG

Stefan Scherer, Leader of the IMI2 JU Strategic Governing Group on "Oncology"; Vice President, Global Head Correlative Science, Novartis Pharmaceuticals

11.5 Annex 5: Funded projects and total project cost

IMI2 JU Call	Project acronym	Total project cost (Eur)	Requested EU contribution (Eur)	Total number of participants (EU beneficiaries)	Average project cost per participant (Eur)	Types of participants
1	INNODIA	35,952,508	17,630,000	33 (26)	1,089,470	4 EFPIA; 2 associated partners; 1 SME; 24 academic/research; 2 other
2	EBODAC	25,740,856	20,328,856	5 (4)	5,148,171	1 EFPIA; 1 SME; 1 academic/research; 2 other
2	EbolaMoDRAD	4,300,935	4,300,935	18 (18)	238,941	14 academic/research; 3 SME; 1 other
2	EBOMAN	48,666,204	1,023,325	3 (2)	16,222,068	1 EFPIA; 1 SME; 1 other
2	EBOVAC1	92,082,643	58,336,885	4 (3)	23,020,661	1 EFPIA; 3 academic/research
2	EBOVAC2	36,671,060	22,790,820	8 (7)	4,583,883	1 EFPIA; 6 academia/research; 1 other
2	FILODIAG	2,260,105	2,260,105	4 (4)	565,026	1 SME; 2 academia/research; 1 other
2	Mofina	1,162,622	1,162,622	6 (6)	193,770	1 SME; 4 academia/research; 1 other
2	VSV-EBOVAC	3,887,260	3,887,260	13 (13)	299,020	1 SME; 9 academia/research; 1 patient organisation; 2 other
3	PERISCOPE	28,125,114	14,000,000	24 (22)	1,171,880	2 EFPIA; 2 SMEs; 20 academia/research
3	PRISM	16,559,551	8,080,000	23 (16)	719,980	7 EFPIA; 5 SMEs; 10 academia/research; 1 patient organisation
3	RADAR-CNS	24,322,379	11,000,000	27 (22)	900,829	5 EFPIA; 2 SMEs; 16 academia/research; 4 other
3	RHAPSODY	15,012,049	8,130,000	27 (23)	556,002	4 EFPIA; 2 SMEs; 20 academia/research; 1 other
3	VAC2VAC	15,978,429	7,850,000	20 (14)	798,921	6 EFPIA; 10 academia/research; 4 other
4	ADAPT-SMART	3,109,131	1,130,000	32 (10)	97,160	22 EFPIA; 3 academia/research; 2 patient organisations; 5 other
5	AMYPAD	24,233,836	11,999,886	15 (12)	1,615,589	3 EFPIA; 2 SMEs; 9 academia/research; 1 patient organisation

5	PREFER	12,000,000	6,000,000	33 (17)	363,636	16 EFPIA; 2 SMEs; 9 academia/research; 3 patient organisations; 3 other
5	ADAPTED	6,796,740	3,510,000	13 (10)	522,826	3 EFPIA; 4 SMEs; 6 academia/research
5	MOPEAD	4,010,251	2,043,000	14 (12)	286,447	2 EFPIA; 2 SMEs; 7 academia/research; 2 patient organisations; 1 other
5	BEAT-DKD	28,624,037	15,085,937	34 (27)	841,883	6 EFPIA; 1 associated partner; 2 SMEs; 24 academia/research; 1 other
5	PHAGO	17,930,496	8,838,000	19 (11)	943,710	8 EFPIA; 3 SMEs; 8 academia/research
6	RESCEU	29,171,790	14,498,125	18 (12)	1,620,655	6 EFPIA; 1 SME; 10 academia/research; 1 other
6	ROADMAP	7,766,976	3,998,250	22 (15)	353,044	7 EFPIA; 2 SMEs; 10 academia/research; 1 patient organisation; 2 other
6	HARMONY	39,294,265	20,000,000	52 (45)	755,659	7 EFPIA; 3 SMEs; 36 academia/research; 1 patient organisation; 5 other
6	Trans-QST	15,802,874	8,000,000	21 (13)	752,518	8 EFPIA; 3 SMEs; 10 academia/research

11.6 Annex 6: Lists of EU-15 and EU-13 Member States, and of Associated Countries Membership of the EU

EU-28 countries	EU-15 countries	EU-13 countries
Complete list of member states	Countries in EU before the accession of ten candidate countries on 1 May 2004	Countries which joined EU after 2004
Austria Italy Belgium Latvia Bulgaria Lithuania Croatia Luxembourg Cyprus Malta Czech Republic Netherlands Denmark Poland Estonia Portugal Finland Romania France Slovakia Germany Slovenia Greece Spain Hungary Sweden Ireland United Kingdom	Austria Italy Belgium Luxembourg Netherlands Denmark Portugal Finland France Germany Greece Spain Sweden Ireland United Kingdom	Latvia Bulgaria Lithuania Croatia Cyprus Malta Czech Republic Poland Estonia Romania Slovakia Slovenia Hungary

Associated Countries

Association to Horizon 2020 is governed by Article 7 of the Horizon 2020 Regulation.

Legal entities from Associated Countries can participate under the same conditions as legal entities from the Member States. Association to Horizon 2020 takes place through the conclusion of an International Agreement. As of 31 December 2016, the following countries are associated to Horizon 2020:

Iceland

Norway

Albania

Bosnia and Herzegovina

The former Yugoslav Republic of Macedonia

Montenegro

Serbia

Turkey

Israel

Moldova

Faroe Islands

Ukraine

Tunisia

Georgia

Armenia

Please note that at the end of 2016 Switzerland was not Associated as concerned the Societal Challenge 1 of Horizon 2020 that covers IMI2 JU. Switzerland is fully Associated again to Horizon 2020 since 1 January 2017

11.7 Annex 7: IMI 2 progress against targets in impact assessment

In 2013, the Impact Assessment accompanying the Commission proposal for a Council Regulation on IMI2 Joint Undertaking, identified on its page 46 a list of 9 key milestones that could constitute a measure of the IMI2 achievements, at interim evaluation.



SWD IMPACT
ASSESSMENT Accomplishments

These 9 milestones are:

- two clinical trial networks to be established by 2016;
- all projects for arriving at taxonomy of disease started by 2017;
- six projects for validating novel targets started by 2016, further 3 projects started by 2017;
- trials for developing novel treatments started by 2017;
- projects for developing diagnostic markers started by 2017;
- infrastructure to gather data on disease incidence and medico- and socio-economic burden of major infectious diseases established by 2016;
- projects for developing novel biomarkers to predict vaccine efficacy and safety started by 2016, results on one markers by 2017;
- projects for developing of adjuvants started by 2016;
- projects for developing efficacy and safety models for vaccine research started by 2016, results for one model by 2017.

Below is a list of IMI2 progress against these 9 targets.

1. Two clinical trial networks to be established by 2016

- INNODIA project (from Call 1) envisions that a pan-European clinical trial and translational research network will be established
- Clinical trial capacity building in Africa through the EBOLA program (EBOVAC1 and EBOVAC2 projects ongoing, from Call 2)
- PRISM project (from Call 3) is setting up clinical networks in Schizophrenia, Alzheimer's Disease and Depression
- Topic developed for Pan European Paediatric Clinical Trial Network (Call 10 topic)
- Topic developed for Autism research including clinical trial networks (Call 10 topic)
- Topic for Clostridium Difficile- research network including clinical trial component (Call 9 topic)

2. All projects for arriving at taxonomy of disease started by 2017

- INNODIA project (from Call 1) - New approaches to research in Type 1 Diabetes
- PRISM project (from Call 3) - stratification of patients with Schizophrenia, Alzheimer's and Depression
- RHAPSODY project (from Call 3) - new strategies in type 2 diabetes
- ADAPTED project (from Call 5) - new biomarkers in Alzheimer's disease
- BEAT - DKD project (from Call 5) - new biomarkers and stratification of Diabetic Kidney Disease Patients
- HARMONY project (from Call 6) - using the analysis of big data to understand patient stratification in Haematological malignancies

- Dry Age Related Macular Degeneration – clinical endpoints and stratification (Call 7 topic)
 - Immune Tolerance in Rheumatic Disease (Call 9 topic)
 - Biomarkers in Non-Alcoholic Liver Disease (Call 9 topic)
 - Biomarkers in Hypoglycemia (Call 10 topic)
 - Biomarkers in Chronic Pain (Call 10 topic)
 - Big Data in Prostate Cancer helping to stratify patients for more appropriate treatments (Call 10 topic)
- 3. Six projects for validating novel targets started by 2016, further 3 projects started by 2017**
- INNODIA project (from Call 1) - target identification in T1DM
 - ADAPTED project (from Call 5) - researching APOE gene as a target for intervention in Alzheimer's disease
 - PHAGO project (from Call 5) - development of tools and methods to study the workings of TREM2 and CD33 and whether they are targets for intervention in Alzheimer's disease
 - BEAT-DKD project (from Call 5) aims to deliver tools and knowledge that will facilitate the development of personalised treatments for DKD
 - RESCUE project (from Call 6) - new targets for RSV induced respiratory disease
 - Target identification based on solute carrier gene family (Call 10 topic)
 - Immune tolerance therapies in rheumatic disease (Call 9 topic) - identification of new drug targets and pathways in RA
- 4. Trials for developing novel treatments started by 2017**
- 5. Projects for developing diagnostic markers started by 2017**
- FILODIAG project (from Call 2) - new rapid diagnostics for filoviruses
 - EbolaMoDRAD1 project (from Call 2) - diagnostic methods in Ebola
 - INNODIA project (from Call 1) - biomarkers to identify patients at high risk of T1DM
 - BEAT-DKD project (from Call 5) - will identify and validate biological markers (biomarkers) in diabetic kidney disease
 - RHAPSODY project (from Call 3) - biomarkers for patient stratification in T2DM
 - Call 9 topic – non-alcoholic fatty liver disease (NAFLD) identification and qualification of diagnostic biomarkers for NASH and across the spectrum of NAFLD
 - Call 9 topic – Immune tolerance therapies in rheumatic disease – diagnostic markers in RA
 - Call 10 topic – How big data could support better diagnosis and treatment outcomes for prostate cancer – identification of diagnostics to help understand patient disease
- 6. Infrastructure to gather data on disease incidence and medico- and socio-economic burden of major infectious diseases established by 2016**
- RESCEU project (from Call 6) methods to improve RSV surveillance in Europe
 - Clostridium Difficile burden of disease (Call 9 topic)
- 7. Projects for developing novel biomarkers to predict vaccine efficacy and safety started by 2016, results on one markers by 2017**
- EBOVAC 1 and 2 projects (from Call 2)
 - VSV EBOVAC project (from Call 2)
 - PERISCOPE project (from Call 3) - pertussis vaccine project

8. Projects for developing of adjuvants started by 2016

9. Projects for developing efficacy and safety models for vaccine research started by 2016; results for one model by 2017.

- VAC2VAC project (from Call 2) - cell based models and alternative non-animal assays for consistency testing of vaccines
- PERISCOPE project (from Call 3) - pertussis vaccine research and animal and human models
- Call 9 topic - Joint influenza vaccine effectiveness

Note:

It should be noted that IMI2 has the mission of covering several disease areas. Most of the targets proposed above, however, are associated with infectious disease and /or vaccine projects. In addition IMI2 has the mission to engage with patients and patient advocacy groups and to involve them in meaningful ways in projects specially designed with this in mind. We have several projects launched or planned in this area but they do not fall into the categories above as no targets were developed at the time. In the same vein, big data plays a major role in our projects today and again no targets were identified in this regard.

11.8 Annex 8: Areas addressed under the IMI2 JU during the interim evaluation period

Results in six different areas have been obtained from the first projects launched until the end of 2016.

1. Identification and validation of new drug targets and novel hit and lead discovery

Project title	Description of result(s)
INNODIA (diabetes)	Discovered novel beta cell targets of the early autoimmune attack in diabetes (citrullinated proteins and splice variants).

2. Establishment of robust, validated tools for preclinical drug development

Project title	Description of result(s)
INNODIA (diabetes)	Developed a robust method for large-scale production of 3-dimensional islet-like aggregates from human pluripotent stem cells. These have a high content of insulin- and glucagon-positive cells and are able to respond to physiological and pharmacological stimuli.

3. Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)

Project title	Description of result(s)
EbolaMoDRAD (Ebola and related diseases)	Developed a way to inactivate the Ebola virus in blood samples so they can be safely processed in the field or easily transported to other centres without the need for high containment facilities.
FILODIAG (Ebola and related diseases)	Patent application covering superparamagnetic particles which are used to speed up the diagnosis of Ebola.
INNODIA (diabetes)	Discovery of miRNA's that regulate human pancreatic beta cell death in diabetes.
INNODIA (diabetes)	Identified Interferon-alpha as a key regulator of early markers of beta-cell dysfunction/death in human diabetes, suggesting this inflammatory cytokine could be a target for novel clinical interventions to prevent diabetes.
INNODIA (diabetes)	Developed and progressing with validation of an oral vaccination strategy for type 1 diabetes prevention.
INNODIA (diabetes)	Development of a dry blood spot method for C-peptide measurement in the home setting.
Mofina (Ebola and related diseases)	Device designed to test for the Ebola virus and other related Filo viruses has been successfully tested in three European reference labs and has also passed initial field studies in Sierra Leone. The device is now ready for product registration and the data obtained from lab and field tests is being submitted to the regulatory authorities
VSV EBOVAC (Ebola and related diseases)	A series of new biomarkers of VSV-ZEBOV vaccination were identified.

4. Clinical trials - improved design and process

Project title	Description of result(s)
EBODAC (Ebola and related diseases)	Supporting the EBOVAC-Salone trial in Kambia, Sierra Leone. 9326 individuals were engaged using public meetings, house visits, drama and radio. Biometric Identification tools collected iris scans and fingerprints for nearly 900 volunteers to ensure that trial participants receive both vaccines. Mobile messaging has supported 419 rural participants to vaccinate on time.
EBOMAN (Ebola and related diseases)	The investment by the contract development and manufacturing organisation (CDMO) extends its aseptic fill and finish capability by around 300% and reinforces its ability to support early phase biologic supply needs for Phase I and II clinical trials.
EBOVAC1 (Ebola and related diseases)	Data from the Phase 1 clinical trial in the UK (87 trial participants) with the Janssen prime-boost Ebola vaccine regimen showed the regimen is safe, well tolerated, and induces durable antigen-specific antibody and cellular immune responses. Results published in the Journal of the American Medical Association. Phase 1 clinical trials in Kenya, Uganda, and Tanzania have completed 12 months follow up with 144 subjects enrolled. In the northern Kambia District of Sierra Leone, staged trial gathering immunogenicity and safety data is ongoing with 443 adults currently randomised. Across the different EBOVAC trials (including EBOVAC2), 1653 subjects have been enrolled to date.
EBOVAC2 (Ebola and related diseases)	Implementation of the Phase 2 trials with Janssen prime-boost vaccine regimen in Europe and Africa progressing. To date, 423 trial participants (out of 630) have been enrolled in the Phase 2 trial in the UK and France. In Africa, 556 subjects (out of 1188) have been randomised across sites in Burkina Faso, Uganda, Kenya and Cote d'Ivoire. Across the different EBOVAC trials (including EBOVAC1), 1653 subjects have been enrolled to date.

5. Impact on regulatory framework

Project title	Description of result(s)
ADAPT-SMART	Publication of a discussion paper on engagement criteria for MAPPs (medicines adaptive pathways to patients) to aid in debates on how and when a MAPPs approach should be used and for which medicines and diseases/conditions. The paper proposes a set of six questions that will trigger discussions initially at the company level (i.e. medicine developer) and subsequently at interaction meetings between the company and the other stakeholders and will help to drive selection or de-selection of a product for MAPPs. These questions were designed on the basis of input gathered from a wide range of stakeholders, including regulators, payers, HTA bodies, prescribers, patients and companies. The paper is intended to inform and drive future discussions on MAPPs, both within the ADAPT SMART consortium and in the wider scientific and healthcare communities.
EBOVAC1 (Ebola and related diseases)	Pioneering regulatory pathways, adapting to a post-epidemic situation, through numerous interactions with regulatory agencies on potential way forward to licensure for novel Ebola vaccine.

6. Education and training for a new generation of R&D scientists

Project title	Description of result(s)
ADAPT SMART (MAPPs)	Glossary developed providing working definitions including references of standardised terms relevant in MAPPs (working document to be updated during the lifespan of the project). Publication of an animated lay explanation note of the MAPPs concept to explain what is early access and how Medicines Adaptive Pathways to Patients (MAPPs) seek to foster access to beneficial treatments for the right patient groups at the earliest appropriate time and in a sustainable fashion
EBODAC (Ebola and related diseases)	Capacity building in Kambia, remote area of Sierra Leone. Local staff trained in clinical trials, community engagement, data entry, use of biometric identification and other technological tools: 122 clinic-based research staff trained on communications and engagement skills (1 half-day workshop per month), 11 community liaison staff have received 4 formal 2-day workshops on community engagement, with refresher training performed on weekly basis.
EbolaMoDRAD (Ebola and related diseases)	Workshop in Dakar entitled 'ModRAD workshop on Mobile Laboratory' on 4 -5 February 2016
EBOVAC1 (Ebola and related diseases)	Training of local staff in Sierra Leone. Capacity-building in remote area of Kambia in Sierra Leone. Built an emergency room, research laboratory and vaccine depot.
EBOVAC2 (Ebola and related diseases)	Providing training on blood sample handling and extracting a special cell preparation (PBMC) and helping to reduce existing gap between East African sites which have this capacity already well established and West African trial sites not yet familiar with these techniques. Participating trial site in Burkina Faso fully qualified by the Sponsor according to strict quality control guidelines and currently preparing PBMC for the Janssen vaccine trial.
VSV EBOVAC (Ebola and related diseases)	Postdoctoral fellows, PhD students and students enrolled in Masters programmes are trained in the frame of this project

11.9 Annex 9: Other initiatives comparable to IMI2 JU (other than C-Path)

The Global Health Innovation Technology Fund (GHIT)³³

The Global Health Innovative Technology Fund is an international non-profit organization headquartered in Japan that invests in the discovery and development of new health technologies such as drugs, vaccines, and diagnostics. The mission of this public-private partnership is to stimulate Japanese innovation, investment and leadership to address global health issues. GHIT was launched in 2013 and invested so far USD 63.7 million, inducing a leverage effect to an additional USD 32.3 million through partnerships (as of 2015 Annual Report).

They are funding from 20-30 projects at different stages of development and have claimed that they have produced: (as per 2015 Annual Report)

- 18 hit series identified
- 7 preclinical candidates identified
- 7 clinical candidates identified
- 1 proof of concept achieved

The average project size is around USD 1 million over two or three years.

Among the funders one can note: The Bill and Melinda Gates Foundation, The Wellcome Trust, several Japanese and Global Pharmaceutical companies and several large non pharma Japanese companies such as ANA and Fujifilm. The Japanese Government is also a funder and represented on the Board.

The Accelerating Medicines Partnership – (AMP)³⁴

The Accelerating Medicines Partnership is a public-private partnership between the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), 10 biopharmaceutical companies and multiple non-profit organisations to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets for therapeutics. The ultimate goal is to increase the number of new diagnostics and therapies for patients and reduce the time and cost of developing them.

AMP was launched in February 2014, with projects in three disease areas:

- Alzheimer's disease
- type 2 diabetes
- autoimmune disorders of rheumatoid arthritis and systemic lupus erythematosus (lupus)

For each project, scientists from NIH and industry developed research plans aimed at characterizing effective molecular indicators of disease, called biomarkers, and distinguishing biological targets most likely to respond to new therapies.

Through this cross-sector partnership, managed through the Foundation for the NIH (FNIH), NIH and industry partners are sharing expertise and resources — over USD 230 million — in an integrated governance structure that enables the best informed contributions to science from all participants. A critical component of the partnership is that all partners have agreed to make the AMP data and analyses publicly accessible to the broad biomedical community.

10 pharma companies and 12 non-profit organisations are involved and the total budget is USD 230 million over 5 years.

³³ <https://ghitfund.org/en/>

³⁴ www.nih.gov/research-training/accelerating-medicines-partnership-amp

It is too early (first projects launched in 2014/15) for any impact assessment to be made.

Combating Antibiotic Resistant Bacteria Initiative (CARB-X)³⁵

CARB-X, a new global public-private partnership for preclinical antibacterial research, with research funds for the first 5 years exceeding US\$350 million (see Further information). Over the first 5 years of CARB-X, the goal is to accelerate a diverse portfolio of more than 20 high-quality antibacterial products towards entry into human testing. Key funders include the US government (BARDA and NIAID), the Wellcome Trust and the AMR Centre, a public-private partnership located at the Alderley Park research facility near Manchester, UK. The entity is called CARB-X as it sprang from the US government's Combating Antibiotic Resistant Bacteria (CARB) initiative, and will directly address several key goals in the 2015 US CARB National Action Plan. Boston University leads the project.

CARB-X is a global accelerator, designed to provide significant research funding, research support services and business mentoring services with minimal bureaucracy. The goal is to advance products towards clinical studies expeditiously, but with all of the data needed to make good decisions.

³⁵

www.phe.gov/about/barda/CARB-X/Pages/default.aspx

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OPEN DATA FROM THE EU

The EU Open Data Portal (<http://data.europa.eu/euodp/en/data>) provides access to datasets from the EU. Data can be downloaded and reused for free, both for commercial and non-commercial purposes.

The Council Regulation (EU) No 557/2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking stipulates in Art.11(1) that by 30 June 2017 the Commission shall conduct an interim evaluation of the IMI 2 JU with the assistance of independent experts.

The current interim evaluation of the operation of the IMI 2 JU covers the period from July 2014 to 31 December 2016. Its main objective is to assess the performance of the IMI 2 JU and its progress towards the objectives set out in the Council Regulation (EU) No 557/2014.

The evaluation was carried out by a Commission Expert Group registered in the EC Register of Expert Groups under Nr E03454, from October 2016 to June 2017. It is accompanied by a final report of the IMI JU, published under EUR 17538 EN.

Studies and reports