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

Experts Group Report

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

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EUROPEAN COMMISSION

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

Expert Group Report

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LIST OF ACRONYMS

AIPs	Annual Implementation Plans
AMP	Accelerating Medicines Partnership
BMFG	Bill and Melinda Gates Foundation
CoA	Court of Auditors
C-Path	Critical Path Institute
EC	European Commission
EFPIA	European Federation of Pharmaceutical Industries and Associations
ELF	European Lead Factory
EMA	European Medicines Agency
EP	European Parliament
ETP	European Technology Platform
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
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
PPP	Public Private Partnership
R&D	Research and Development
SC	Scientific Committee
SGGs	Strategic Governing Groups
SMART	Specific, Measurable, Achievable, Relevant, Time-phased
SMEs	Small and Medium sized Enterprises
SRA	Strategic Research Agenda
SRG	States Representatives Group
TFEU	Treaty of the Functioning of the European Union
ToR	Terms of Reference
VC	Venture Capital

Abstract

This report summarises the final evaluation of the public private partnership Innovative Medicines Initiative Joint Undertaking (IMI JU) that was created in 2008 and ran until 2014. The overall aim of IMI JU was to improve the effectiveness and efficiency of the drug development process to produce better and safer medicines in Europe. The underlying reasoning was to make Europe a more attractive for investments in the pharmaceutical sector.

An expert group was entrusted with the evaluation task and addressed effectiveness, efficiency, relevance, coherence and added value of the IMI JU. For this purpose numerous documents were consulted and interviews with representatives of the different stakeholder groups to provide deeper insight were conducted. Also the survey of beneficiaries and the public consultation on IMI JU served as an additional input.

The expert group concluded that the IMI JU programme was relevant and justified and positive contributions on the drug development process have been realised. However, the added value, especially with respect to socio-economic outcomes, may need more time to become evident even though the first projects started in 2009 and close to two billion euro public and private money has been invested.

Résumé

Le présent rapport résume l'évaluation finale de l'entreprise commune "Initiative en matière de Médicaments Innovants" (IMI), un partenariat public-privé qui a été créé en 2008, et s'est poursuivi jusqu'en 2014. L'objectif général de l'entreprise commune IMI était d'améliorer l'efficacité et l'efficience du processus de mise au point des médicaments afin de produire des médicaments plus efficaces et plus sûrs en Europe. Le raisonnement sous-jacent était de rendre l'Europe plus attrayante pour les investissements dans le secteur pharmaceutique.

Un groupe d'experts s'est vu confier la tâche d'évaluation, et a abordé l'efficacité, l'efficience, la pertinence, la cohérence et la valeur ajoutée de l'entreprise commune IMI. À cette fin, de nombreux documents ont été consultés et, afin de fournir une réflexion plus approfondie, des entretiens ont été menés avec des représentants des différents groupes de parties prenantes. En outre, l'enquête auprès des bénéficiaires et la consultation publique sur l'entreprise commune IMI ont constitué des contributions supplémentaires.

Le groupe d'experts a conclu que le programme de l'entreprise commune IMI était pertinent et justifié, et que des contributions positives au processus de mise au point des médicaments, ont été fournies. Toutefois, la valeur ajoutée, notamment en ce qui concerne les résultats socio-économiques, peut avoir besoin de plus de temps pour devenir évidente, et ce même si les premiers projets ont débuté en 2009 et près de deux milliards d'euros de fonds publics et privés ont été investis.

Zusammenfassung

Dieser Bericht fasst die abschließende Bewertung der öffentlich-privaten Partnerschaft „Gemeinsames Unternehmen Initiative für Innovative Arzneimittel" (IMI JU) zusammen, die im Jahr 2008 ins Leben gerufen wurde und die bis 2014 lief. Das übergreifende Ziel der Initiative bestand in der Verbesserung der Effizienz und Wirksamkeit der Arzneimittelentwicklung, um bessere und sicherere Arzneimittel in Europa zu entwickeln. Der zugrundeliegende Argumentation war es, Europa für Investitionen im Bereich der pharmazeutischen Industrie attraktiver zu machen.

Eine Expertengruppe wurde mit der Aufgabe betraut und hat die Wirksamkeit, Effizienz, Relevanz, Kohärenz und den Mehrwert des Gemeinsamen Unternehmens IMI beurteilt. Zu diesem Zweck wurden zahlreiche Dokumente konsultiert. Um vertiefte Einblicke zu gewinnen, wurden Interviews mit Vertretern der verschiedenen Interessengruppen durchgeführt. Darüber hinaus dienten die Befragung der Begünstigten sowie die Ergebnisse der öffentlichen Konsultation über das IMI JU als zusätzliche Beiträge.

Die Expertengruppe kam zu dem Schluss, dass das Programm für das Gemeinsame Unternehmen IMI relevant und begründet war und dass positive Beiträge zum Prozess der Arzneimittelentwicklung geleistet worden sind. Es ist aber zu erwarten, dass es länger dauern wird, bis der Mehrwert klar wird, vor allem in Bezug auf die sozioökonomischen Ergebnisse, und dies trotz der Tatsache, dass die ersten Projekte im Jahr 2009 begannen und fast zwei Milliarden Euro an öffentlichen und privaten Mitteln investiert worden sind.

1. EXECUTIVE SUMMARY

This report summarises the final evaluation of Innovative Medicines Initiative Joint Undertaking (IMI JU) conducted by an expert group 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 on the final outcome of the IMI JU under the EU's Seventh Framework Programme (FP7). The term of reference further outlined that the report 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 of JUs.

The IMI JU is a **Public Private Partnership** between the European Union (EU), represented by the European Commission (EC) (public partner), and the European Federation of Pharmaceutical Industries and Associations (EFPIA) (private partner).

The rationale to set up IMI JU originated from the political and socio-economic situation early in the millennium. The pharmaceutical industry is important for the European economy, but the pharmaceutical research and development basis gradually eroded over the period from 1990 to 2005. In that period private R&D investment in the United States grew twice as much as in Europe. Since 1990, over a period of less than ten years, Europe saw the private R&D expenditure in its territory dropping from 73% to 59%. Also public spending in pharmaceutical R&D in the US (0.26% of the GDP) was much higher than in Europe (0.04% of the GDP).[1]

These considerations justified the launch of an ambitious Public Private Partnership between the EC and EFPIA to address the main barriers to drug development to support the competitiveness of European pharmaceutical industry and make Europe attractive again for investments in biopharmaceutical R&D. The focus on precompetitive research in an open innovation model would allow the big pharma companies to collaborate and to support translational research from academic groups and build on innovative developments from micro, small and medium-sized enterprises (SMEs).

The Council Regulation specified a maximum Commission contribution of EUR 1 billion to cover running costs and research activities of the JU. The private partner should provide an equal budget, to cover an equal share of the running costs with cash up to a maximum of 4% of the total budget, and contribute in kind to the research activities developed, matching the same budget financed by the EU. The EFPIA members, i.e. the large pharmaceutical companies, were not eligible to receive financial support from the IMI JU. Only academic groups, SMEs and non-profit organisations were eligible to receive funding in IMI projects.

A further key objective of IMI JU was to remove bottlenecks to significantly improve the effectiveness, quality and efficiency of the drug development process, with the long-term aim that the European pharmaceutical sector produces safe, effective, innovative medicines more rapidly. This focus was meant to leverage research capabilities to stimulate investments in the biopharmaceutical sector in Europe; a sector in which Europe traditionally held a strong position.

The roles of the different **governing bodies** in IMI JU generally appeared to be clear and well defined. The governance structure of the IMI JU main decision making body, the **Governing Board**, comprised equal representation of the founding two parties, i.e. EFPIA and the EC. As both represented parties serve different interests and priorities, this binary situation was sometimes reported to interfere with key decision making processes.

The Executive **Director** and **IMI Executive Office** were responsible for the management of the joint undertaking. The efficiency of the IMI Executive Office was viewed to be satisfactory.

The Governing Board and Executive Office were supported by advisory groups. The first one was the **Scientific Committee** (SC) which was consulted to give input on the topics selection. The other advisory group was the **States Representatives Group** (SRG) served as interface between national bodies and the Joint Undertaking, and was giving feedback in line with national priorities and tested the Annual Work Plan against other programmes to avoid duplication. Feedback was provided by the **stakeholder forum**, which was an annual meeting open to all stakeholders.

[1] www.imi.europa.eu/sites/default/files/uploads/documents/comm_pdf_sec_2007_0568_1_en_documentdetravail_en.pdf

The **communication** between various governing and advisory bodies involved in IMI JU operations was critical for the realisation of the goals. However, the communications between the different governing and advisory bodies have been the subject of criticism. Opportunities may have been lost, to include national and regional developments and priorities, because of the limited involvement of and interaction with the SRG. Also satisfactory reporting on the relevance and impact of feedback from the SC seemed limited or lacking.

The first IMI **Strategic Research Agenda** (SRA) was published in 2008, updated in 2011 and ended in 2013. The issues in this SRA were addressed by the launching of eleven **calls** for proposals, which were peer reviewed by independent experts. The **process of developing the SRA and call topics was often considered insufficiently transparent.** As this **process was led by EFPIA partners,** this was a source of frustration to many stakeholders, because it was **unclear how to contribute to the SRA development or to the development of the annual work programme**. The **Scientific Committee**, and the **State Representatives Group were consulted to avoid overlap with possible other running projects.** It was the **Governing Board** that had **final decision power to approve the SRA** and **call topics.** The top-down process of call topic description combined with the fact that there could only be one winning consortium, raised questions about the usefulness of the competition process.

Pre-existing networks were a key factor forming the applicant consortia. The reliance on existing networks may in some cases have resulted in missed opportunities to bring new partners together and include some of the best infrastructures, biobanks or scientists.

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

One of the major risks to successful project execution, although this did not happen frequently, was **the premature withdrawal of a leading pharmaceutical company**. Premature withdrawal of a lead company from a project could have substantial implications, not only in terms of the content of the project, but also on the budget commitments made. There were no regulations in place to enforce the industry commitment made at the start of a project. In practice, in such instances there were negotiations within the consortium and with EFPIA to find a solution, but companies that did not fulfil their commitments could not be penalised. In such instances, EFPIA functioned as a broker to find an equitable commitment among existing or new consortium members, such that the projects involved could continue and that the final private and public budgets were matched.

A substantial amount of criticism focussed on the lack of transparency of the in-kind calculations of the EFPIA companies. Although six projects finished their activity by the end of 2016, the final report and IMI contribution was accepted for just three of the projects at the time of writing this assessment. The EFPIA financial report had not been accepted for any of these projects, although many interim reports have been validated in which EFPIA in-kind contributions were reported and accepted for a total amounting to EUR 385.2 million according to Annual Activity Report 2016. EFPIA companies, however, seemed reluctant and refused to make time sheets available for auditing the in-kind contributions, claiming that it violated their confidentiality on engagement with other non-IMI projects which could lead to disclosure of unauthorised information. The actual implications of disclosing time sheets are questionable.

Another key aspect was how the in-kind contributions from activities from outside Europe were calculated. Under IMI JU, it was allowed by the Regulation establishing the JU, to take into account in-kind contributions incurred outside the EU and Associated Countries. In the view of the experts, the efficiency of the joint undertaking to support the competitiveness of the European pharmaceutical sector could be questioned if investments from outside Europe can be taken into account. In the view of the experts, although these are global companies, for future potential initiatives, only costs incurred in Europe should be accounted for the in-kind contributions, while costs incurred outside of the EU may be calculated as an additional leveraging effect, which may be considered a significant socioeconomic impact.

The main achievement of IMI JU on which there was general consensus, was that under IMI JU **collaborations** between different competing global companies, SME's and academia became possible. These collaborations created trust and new partnerships, including partners from different areas of expertise, such as with regulatory bodies, or with patient's representatives groups. Together with the available budget and long term strategy, this was considered an important asset for European pharmaceutical research. IMI actions have also contributed to **access to research infrastructure**. A major success was the **development of an antimicrobial resistance**

infrastructure that provided access to external companies or the European Lead Factory (ELF) project, providing access to libraries medicinal compounds.

The mechanism used to communicate the results and outcomes of IMI projects were considered to be suboptimal. It was apparent that most results from projects were not known or accessible to stakeholders outside of the consortia that generated the results. Access of such findings could be especially valuable for SMEs to encourage new developments. Moreover, it was felt that increased efforts were needed to improve awareness, and to communicate the attractiveness and added value of the initiative.

To understand and collate the key outputs of funded projects, **closeout meetings** of ending IMI JU projects were introduced. These closeout meetings summarised the projects outputs, extracted lessons learned, and identified the challenges for the different teams. These meetings can also be used to support a stronger emphasis on how to better integrate results from different projects, not only from projects under IMI, but also from projects funded through the framework programme. **Coherence** with other FP7 projects, however, in general was limited, as IMI projects focus on precompetitive research and were designed by the EFPIA partners and therefore stronger industry oriented than projects in funded by FP7. There also seemed to be a risk of duplication between IMI projects and the Joint Programming Initiatives (JPIs) JPND on neurodegenerative diseases and JPIAMR on antimicrobial resistance. To avoid this lack of coherence, closer collaboration and communication between the IMI consortia and the JPI initiatives should be encouraged. The dialogue between JPIAMR and IMI consortia addressing antimicrobial resistance was reported to be ongoing, although collaborations have not (yet) been achieved. JPND representatives indicated that there had not been an active dialogue with IMI consortia addressing neurodegenerative diseases to identify possible closer collaborations.

Sustainability of project results and outputs such as databases established during IMI projects needed stronger emphasis. One IMI project continued beyond the funding period with a new consortium agreement. Other projects were under negotiation to try and find a sustainable follow up mechanism. The sustainability of project results and outputs beyond the funding period was not supported by all parties. Also some of the EC and industry representatives were reluctant as they saw IMI more as an instrument to catalyse elements, but not to maintain databases once the projects were finished. To keep databases sustainable, the business plan should have foreseen this from the start. The limited number of project outputs that were sustained beyond the project funding period was interpreted as a lack of interest or low priority for EFPIA and therefore introduced some doubt of the added value generated from IMI projects.

By the end of 2016, only 21 projects out of 59 had reached the end of their IMI funding cycle. From these 21 projects, the IMI Executive Office reported on important project outputs, including 16 spin-off creations, 9 patents, 1071 publications. Furthermore, 2768 full-time jobs were created by the end of 2016, employing and developing highly-skilled personnel directly associated with all IMI projects. Every job in life sciences R&D has a leveraging effect of creating further jobs indirectly elsewhere in the economy. Although these results are significant, they should be evaluated in relation to the results obtained by the various and numerous technology transfer offices in Europe and other financing programmes and in relation to the available budget. The expert group however, did not have access to those data nor the time available to appraise whether these outputs were realised nor the impact of such outputs.

The large scale, the long term vision and strategy of the projects were considered a positive objective for IMI JU, but pose at the same time challenges for management and coordination, which does not favour **SME involvement**. The participation of SMEs in IMI JU was represented by 15.96 % (192 out of 1203) of the participations, compared to 15.86% in the rest of the FP7 health theme. The EU contribution to SMEs was 13.25% compared to 17.93% in the rest of the FP7 health theme; both figures are relatively low. The SMEs are instrumental for the global pharma companies to facilitate access to new applications or therapies.

The participation of SMEs and some academics was further hampered by the complexity of **IP negotiations** and by the fact that **exclusivity rights on results from IMI projects were not negotiable.** IMI projects that involved large consortia added an extra level of complexity to the IP negotiations, which was even more pronounced when the project was closer to the interest of the large pharma companies. The IP agreements became very elaborate and technical, and formed a barrier for non-IP professionals. The discussions on IP issues prior to the start of the projects were also reported to sometimes significantly delay the start of projects. The fact that no exclusive rights could be negotiated on results from IMI projects made it impossible for some SMEs to participate in IMI projects. Another main barrier to the participation of SMEs was the focus on precompetitive research, which for SMEs, may be their core-business and implies that they may prefer not to share the background IP and need exclusivity rights on results.

It was very clear that the creation of an ecosystem of academia, SMEs in biotech and other technologies is crucial, as manifest in the concentration of the pharmaceutical companies around the innovative sites in the US. IMI JU provided interesting new opportunities given the size of the budgets and the focus outlined in the SRA. The innovations bringing new medicines to market and patients were mostly coming from outside big pharma, but some of the main players were missing in IMI JU. Mid-cap companies, although eligible for participating in IMI JU projects, could not receive funding under IMI JU while these types of companies were likely to be valuable partners.

Importantly, at the time that IMI JU was launched, it was already clear that the **development of new medicines in the future would depend on the involvement of other sectors**, such as imaging, diagnostics, medical devices developers, and technology providers using electronics, IT, data management. These missed opportunities to include other sectors and make midcap companies eligible for funding in IMI projects have been addressed in IMI2 JU.

Together with the industrial partners, under IMI JU, also **regulatory agencies** participated in IMI projects. The European regulatory system for medicines, which is based on a network of the national medicines regulatory authorities and the European Medicines Agency (EMA), participated as partner or advisor in IMI JU projects. In total, in addition to 6 participations of EMA in 6 out of the 59 IMI JU projects, six medicines regulators from six EU Member States, and two from two countries associated at that time to FP7 (Croatia and Switzerland) have participated on 15 occasions in 9 out of the 59 IMI JU projects. According to EMA, that created a process to avoid conflicts of interest, IMI played a positive role in breaking down the silos between academia, industry and patients, and by facilitating the dialogue between EMA and the pharmaceutical companies. The increasing involvement of regulators in general has represented a positive trend under IMI JU.

More efforts will still be needed to improve **patient involvement**. The IMI Executive Office was aware of this and considered this a key learning process. The participation of patient organisations in IMI projects has been criticised as an attempt to train patient advocacy groups to lobby for faster approval of new medication. The important financial participation of these organisations including European and American organisations, albeit in IMI2 JU, suggested this criticism was unfair.

The main participants in IMI JU projects involved 845 **academic teams** and over 7000 researchers working in different disciplines across Europe and beyond. **This substantial and diverse level of participation was considered to be a success** since academic researchers may traditionally be less inclined to collaborate with industry and in translational and applied research areas. In the context of precompetitive research the scientific output of IMI can be rated to be very good, although not always comparable with the outputs from projects funded to produce frontline fundamental research.

The major objective of setting up the joint undertaking was to support the competitiveness of the European pharmaceutical industry. However, whether this had been achieved was most difficult for the expert group to assess, mainly because there was still no adequate performance measuring system in place that allowed monitoring of the socio-economic impact generated by IMI JU. An improved performance measuring system could be achieved by introducing SMART (Specific, Measurable, Achievable, Relevant, Time-phased) **Key Performance Indicators** (KPIs) to measure not only scientific output, but also socio-economic impacts. At the time of writing this final evaluation report on IMI JU, work was continuing by the IMI Executive Office and the IMI GB to develop a new set of KPIs.

To date, there were no examples of IMI bringing new, safer and more effective therapies or products to patients or examples of the time to develop such new applications being shortened. In this respect **the added value of IMI JU for patients or society in general was hard to demonstrate**. At the same time, the timelines for pharmaceutical development are very long. IMI projects were nevertheless, already now establishing **resources, training and facilities to boost drug discovery in Europe and are developing new tools for research**. The research topics addressed important areas like dementia, or diabetes, and contributed to medicines safety and the reduction in the use of animals in research.

A major success for IMI JU would have been a demonstrable effect on making Europe more attractive for investment in biopharmaceutical R&D. Through the IMI JU programme, the pharmaceutical industry committed EUR 1 billion for collaborative research in Europe. Although when compared with other EU-funding sources this was a significant investment, it related mainly to in-kind contributions. Moreover, **these in-kind contributions of the pharma companies were in general relatively small when compared with the overall companies R&D budgets and not correlated with them**, even though these budgets cover research far beyond precompetitive research. IMI JU claimed that the IMI budget for precompetitive research, although very small when compared with the R&D budgets of the pharmaceutical companies, had a strong

influence on the industry, but acknowledged that it was difficult to demonstrate whether IMI induced an increase in R&D investments from the European biopharmaceutical industry. The actual significance and impact of IMI JU on the competitiveness of the European pharmaceutical industry can therefore be questioned.

The main rationale supporting the introduction of IMI JU, rather than use the regular calls and instruments of FP7 to support the European pharmaceutical industry, was that IMI JU was leveraging considerable private funds, which could not be achieved using the existing mechanisms. The focus on precompetitive research in the IMI JU also triggered collaborations between companies that would otherwise be in direct competition to address complex challenges that cannot be solved by single companies. Such collaborations would not have been achieved under FP7. The participation of industries was in general low in FP7 and consortia that brought together many industries like in IMI projects did not exist in FP7. The establishment of IMI JU stimulated capacity building, the development of new tools in particular for safety and toxicity, and contributed to the development of shared standards. On the other hand, call topics defined in the regular framework programme, may be closer to the public interest than those identified by the industry and results may be achieved at a lower cost for the public budget.

In conclusion, the expert group agreed that **the reasons to create a public private partnership to strengthen the European pharma industry were valid and the goals were justified** at the time when IMI JU programme was launched. Whether the right framework conditions were met to achieve these goals, is not clear as quantifiable indicators to demonstrate a socioeconomic benefit were lacking. If the European pharmaceutical sector is not increasing its activities and investment in Europe it can be questioned whether the goals to shorten the time of drug development could have been achieved using different mechanisms such as the stronger promotion of European SME involvement as a way to stimulate the European competitiveness.

It was clear that a long-term strategy is required before the joint undertaking can realise a demonstrable effect and support the competitiveness of the European pharmaceutical industry. Currently, no socio-economic benefits from IMI JU activities could be identified. To realise a measurable socio-economic impact or a measurable impact for patients and their health, it was clear that more time was needed. **The expert group concluded that it was, therefore, too early to assess the role of IMI JU on boosting the competitiveness of European pharmaceutical industry.**

2. INTRODUCTION

2.1 Purpose of the evaluation

Council Regulation 557/2014[2] establishing the Innovative Medicines Initiative 2 Joint Undertaking stipulated that the Interim Evaluation of IMI2 JU shall include a final evaluation of the Innovative Medicines Initiative Joint Undertaking (or IMI JU) under regulation (EC) No 73/2008.

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 final outcome of the IMI JU under FP7 as well as the outcome realised so far by the IMI2 JU operating under Horizon 2020.

The term of reference further outlined that it 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 evaluation was outlined in the Terms of Reference,[3] defined by the European Commission after consultation with the IMI JU. The evaluation covers the entire period of the IMI JU implementation from 2008 to 2016[4] and focusses on:

- Effectiveness: the progress towards meeting the objectives set, including how all parties in the public-private partnerships live up to their financial and managerial responsibilities;
- Efficiency: the extent to which the IMI JU was managed and operated efficiently; and on
- Research quality: the extent to which the IMI JU enabled world-class research that helped Europe to establish a leadership position globally, and how it engaged with a wider constituency to open the research to the broader society.

In addition to the legal requirements and in order to allow meaningful comparison between the first and the second generation of JU, the evaluation should also focus on these additional aspects:

- Openness and 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 evaluation period covers the period from the start of IMI JU in 2008 to 31 December 2016. In that period 59 projects were started under FP7. At the end of the evaluation period only 21 have finished their activity, but were not yet closed. The last two IMI JU projects are expected to end in 2021. Projects are concluded with closeout meetings that summarise the outputs of the activities. By the end of the evaluation period only six closeout meetings have been organised although data on projects results are available on the respective project websites, the IMI website, and in annual activity reports. This report is considered the final evaluation of the joint undertaking even though fewer than half of the projects were closed.

The performance of IMI2 JU will be addressed in a specific interim report.

3. BACKGROUND TO THE INITIATIVE

3.1 Description of the initiative and its objectives

3.1.1 IMI JU Legal Basis

The IMI 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 IMI JU was set up by the *Council Regulation for the*

[2] http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32014R0557&from=EN
[3] Terms of Reference of an Expert Group on the Final Evaluation of the Innovative Medicines Initiative Joint Undertaking operating under the Seventh Framework Programme and the Interim Evaluation of the Innovative Medicines Initiative 2 Joint Undertaking operating under of Horizon 2020. Commission DG for Research and Innovation document, 2016.
[4] Cut-of date is 31 December 2016. Some IMI JU projects are continuing until 2021: 25 projects finished by the end of 2016, 17 projects finishing in 2017, 4 finishing in 2018, 5 projects finishing in 2019, 7 projects finishing in 2020 and 1 project by the end of 2021.

implementation of the Joint Technology Initiative (JTI) on Innovative Medicines[5] on the basis of Article 187 of the Treaty on the Functioning of the European Union (TFEU).[6] The 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 as of then it had the operational capacity to implement its own budget. Before the autonomy, the Commission was responsible for the management of the IMI JU.[7]

To realise the objectives the maximum contribution from the European Union (EU) to IMI JU was set to EUR 1 billion to match the contribution of EFPIA. This budget was paid from the budget appropriation allocated to the Theme 'Health' of the Specific Programme 'Cooperation' implementing FP7.[8]

It was furthermore stipulated that the running costs of the IMI JU will be financed in equal parts by EFPIA and the European Union and not exceed 4% of the total budget for the period ending on 31.12.2017.

The research activities were to be covered by funding from the EU and at least to an equal level by in-kind resources (such as personnel, equipment, consumables, etc.) from the research-based pharmaceutical companies that are members of EFPIA. To ensure an equal partnership, the research based pharmaceutical companies that are members of EFPIA were not eligible to receive financial support from the IMI JU. Partners in IMI projects eligible for funding were academia, SMEs and non-profit organisations, including patient's organisations and regulatory agencies.

3.1.2 IMI JU Objectives

The IMI JU objectives were 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 (Box 1). This approach was taken to stimulate investments in the biopharmaceutical sector in Europe so as to leverage research capabilities in a sector in which the EU traditionally held a strong position.[9]

IMI JU projects were focussing precompetitive research to make collaborations possible between the large pharmaceutical companies that are otherwise competitors. Also collaborations with SMEs, academic groups, patient organisations and regulatory agencies were believed to be facilitated when focussing on the precompetitive domain.

[5] Council Regulation No 73/2008 (OJ L30 of 04.02.2008, p.38-51)
[6] 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.
[7] Article 16 of the Council Regulation setting up the IMI JU
[8] http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A52007PC0241
[9] 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 IMI JU according to Article 2 of the Council Regulation No 73/2008 of 20 December 2007

The IMI Joint Undertaking shall contribute to the implementation of the Seventh Framework Programme and in particular the Theme 'Health' of the Specific Programme Cooperation implementing the Seventh Framework Programme. It shall have the objective of significantly improving the efficiency and effectiveness of the drug development process with the long term aim that the pharmaceutical sector produces more effective and safer innovative medicines. In particular it shall:

- support 'pre-competitive pharmaceutical research and development' in the Member States and countries associated with the Seventh Framework Programme via a coordinated approach to overcome the identified research bottlenecks in the drug development process;
- support the implementation of the research priorities as set out by the Research Agenda of the Joint Technology Initiative on Innovative Medicines (hereinafter referred to as 'Research Activities'), notably by awarding grants following competitive calls for proposals;
- ensure complementarity with other activities of the Seventh Framework Programme;
- be a public-private partnership aiming at increasing the research investment in the biopharmaceutical sector in the Members States and countries associated to the Seventh Framework Programme by pooling resources and fostering collaboration between the public and private sectors;
- promote the involvement of small and medium-sized enterprises (SME) in its activities, in line with the objectives of the Seventh Framework Programme.

3.1.3 IMI JU Governance

The IMI JU comprised three bodies (Governing Board, Scientific Committee, and Executive Director with the support of the IMI Executive Office) and was supported by two external advisory bodies (States Representatives Group and Stakeholder Forum) – see figure 1 and table 1. The Scientific Committee was part of the Governance Structure but its role was primarily advisory and it had no role in decision making.

The IMI JU periodically produced or updated the IMI Internal Control Standards, the IMI Staff Policy Plans; the IMI Annual Implementation Plans (AIPs); the IMI Annual Activity Reports and Annual Accounts. The IMI JU was housed in Brussels on the same premises as all other JTI JUs, which under FP7 were Clean Sky, Fuel Cells and Hydrogen, ARTEMIS and ENIAC.

Figure 1: IMI Joint Undertaking Governance Structure

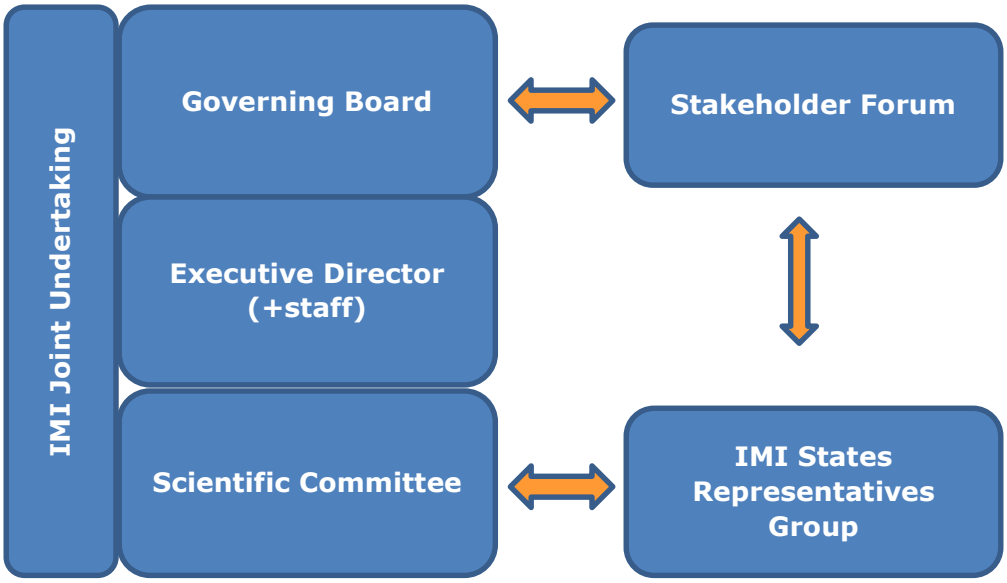

Table 1: IMI JU bodies and functions

Body	Function	Established
IMI JU Governing Board (GB)	Represents Commission and EFPIA. Overall responsibility for strategy and operations of the IMI JU.	3 March 2008
IMI JU Executive Director	Legal representative and Chief Executive responsible for day-to-day management and activities. Total of 41 staff by 31 December 2016	First appointed as of 10 June 2008, and took up duties as of 16 September 2009. The current ED was assigned as of September 2015.
IMI JU Scientific Committee (SC)	Advisory body (e.g. research agenda and scientific priorities)	21 November 2008
IMI States Representative Group (SRG)	Represents Member and Associated Countries. Advisory body (e.g. research agenda and scientific priorities) and interface between stakeholders and IMI JU.	26 June 2008
IMI Stakeholders' Forum	Meeting open to all stakeholders	14-15 June 2010

3.2 Baseline

The objectives of the IMI JU originated from the political and socio-economic situation in 2006-2007. The overriding aim of Innovative Medicines Initiative Joint Undertaking was to significantly improve the efficiency and effectiveness of the drug development process with the long-term aim that the pharmaceutical sector produced more effective and safer innovative medicines.

The basis for the joint undertaking IMI was laid by the work of the Innomed Technology Platform. In the publication of the Communication on Life Sciences and Biotechnology – a Strategy for Europe by the Commission on January 23, 2002[10] life sciences and biotechnology were identified as among the most promising frontier science and technology areas for the coming decades. Life sciences and biotechnology were considered to entail and foster the development of many enabling technologies – like information and nano-technologies – and to cover a wide range of applications with benefits in both the public and private sectors. According to this report, the basis of scientific

[10] http://europa.eu.int/comm/biotechnology/pdf/com2002-27_en.pdf

and technological breakthroughs in previous years, and the explosion of genomic data on living organisms were posed to spur new research and applications in the future.

This strategy was supported by the High Level Group on innovation and provision of medicines in the European Union – the G10 Medicines Group - which brought together stakeholders from the European Commission, government representatives, industry, patients and healthcare providers. The IMI JU finds its origin in the recommendations for actions that were agreed with respect to the research and development environment (G10 Medicines report of 7 May 2002[11]):

- Recommendation 8: The creation of the European virtual institutes of health, connecting all existing competence centres on fundamental and clinical research into a European network of excellence.
- Recommendation 9: To improve the co-ordination of Community and national activities, by:
  - Commission and Member States to co-ordinate and support the conduct of clinical trials on a European scale, establish a database of trials and clinical research results.
  - Commission and Member States to put in place an effective policy in terms of incentives to research and support the development and marketing of orphan and paediatric medicines.
  - Supporting the development of a biotechnology strategy in Europe.

Building on these recommendations, in 2004 the European Commission published the Communication "Science and technology, the key to Europe's future – Guidelines for future European Union policy to support research",[12] in which the need to double the Union's research budget was acknowledged. This paper also emphasised the launch of European technology initiatives and the need for a European level co-ordination of research efforts and for the development of research infrastructures as key factors to stimulate research in Europe.

As a follow-up the concept of a European Technology Platform was developed as an instrument by the European Commission to address major economic, technological or societal challenges enabled by Research and Development. It was intended to foster effective public-private partnerships (PPPs) between all relevant stakeholders and to implement Strategic Research Agendas across Europe. It was anticipated that such a PPP would contribute to achieving the Lisbon objectives, developing the European Research Area and increasing investment in R&D towards the 3% of GDP target.

In this context, the European Commission asked EFPIA's Research Directors Group (RDG) to identify main barriers to innovation in life sciences research in Europe with the objective of establishing a European Technology Platform for Innovative Medicines. The RDG had already identified main precompetitive barriers to innovation, around which industry and stakeholders in the drug development process could collaborate to achieve a first class environment for R&D. A Strategic Research Agenda was to be developed that should mobilise stakeholders in consortia to implement this agenda. In this effort, many possibilities and opportunities were identified that were expected to help Europe towards more efficient drug development. Examples of such opportunities included:

- Leveraging expertise in new technologies for identification and validation of biomarkers;
- Managing and organising data to create knowledge to predict benefit and risk of new therapies to the benefit of all stakeholders in the drug development process;
- Improving the dialogue with regulators during development prior to regulatory approval to help reduce requests for additional data and regulatory questions following submission; and
- Building and supporting pre-competitive research centres and a European network of centres of excellence.

Initiatives such as these needed funding, coordination and targeting to have the maximum impact. The creation of a European Technology Platform (ETP) to manage the initiatives was considered both important and relevant. To be effective, the European Technology Platform was expected to deliver added value to the drug discovery and development process and to individual stakeholders. The collective benefit was expected to come from a transparent, total-systems approach to the discovery and development process. This approach would enable each player to appreciate more

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11 http://ec.europa.eu/health/ph_overview/Documents/key08_en.pdf

12 https://cordis.europa.eu/pub/era/docs/com2004_353_en.pdf

fully the roles and needs of the others and to be able to make non-traditional contributions in areas beyond their own.

Answering this call for technology platforms, the Innomed Technology Platform was set up, bringing together stakeholders from industry, research institutions, the financial world and the regulatory authorities at the European level to define a common research agenda and mobilise a critical mass of - national and European - public and private resources, and focussing on innovative medicines. In 2004, a vision document was published by Innomed.[13] According to the analysis of the technology platform, 'Europe has lost its major place as a global centre for biomedical research. Despite a five-fold increase in the pharmaceutical trade surplus over the last 5 years, investment in R&D is declining markedly in comparison with the US. Over the last decade the US has invested far more in public sector sponsored biomedical research, Europe has not yet matched this level of public sector investment. This is affecting, and will continue to affect, growth and development in Europe to the detriment of both patients and society. The InnoMed proposal addresses the complex issues associated with the future of biomedical research within the EU, and *addresses ways of achieving accelerated development of new, safe and more effective medicines that will help revitalise the European biopharmaceutical research environment.'*

The analysis further indicated that 'The discovery and development of new drugs is very costly and the rate of failure of drug candidates is high. Initiatives to reduce the rate of attrition during later phases are clearly desirable and if successfully implemented will reduce development costs. Then Europe can again become a place where Industry chooses to invest. EFPIA's Research Directors Group has identified pre-competitive barriers to innovation, around which industry and stakeholders in the drug development process can collaborate to achieve this goal. The barriers on which this proposal is focused are the failure of preclinical studies to predict safety and efficacy in the clinic and the regulatory process, which has not kept pace with scientific developments. Improvements in predictive biology and the incorporation of these new concepts into an improved regulatory framework would decrease the cost of drug development and speed (up) the delivery of innovative medicines to patients.'

Under FP6, Innomed received EUR 18 million as a pilot project to prepare for IMI JU and develop governance and IP policy guidelines and a new version of the Strategic Research Agenda.

FP7 introduced the concept of Joint Technology Initiatives (JTIs) to answer to the needs of industry. JTIs were meant to be public private partnerships to pool resources from public and private sector across all R&D entrepreneurs in a specific area.

An impact assessment to analyse the effects of a Joint Technology Initiative in the area of Innovative Medicines was published in 2007.[1]

The assessment confirmed the previous analyses that the pharmaceutical industry continued to be important for the European economy, showing a continued growth over the period from 1990 to 2005. Until 2003, the private R&D expenditure by the Europe biopharmaceutical industry was comparable with the one in the US, but seemed lagging in the biotech segment.

The discrepancy between the US and Europe becomes more pronounced when comparing the public spending in pharmaceutical R&D. In 2004, the Government Appropriation or Outlays on health related R&D (GBAORD) in the US was around 0.26% of the Gross Domestic Product (GDP), whereas in Europe this was only about 0.04% of the GDP. Moreover, the average growth rate of health related GBAORD between 2000 and 2004 was about 10% for the US, while only a third of that in the largest European countries.[1]

Furthermore, while the budget of the National Institutes for Health research in the US doubled since 1998 to 2006 up to USD 23 billion annually, in Europe the R&D funding for health was decreasing in some countries or stagnated in others. The combined contribution of key European research institutions and funding agencies (i.e. MRC UK, MP Germany, INSERM France, Karolinska Institute Sweden, CNRS Italy and the European Framework Programme part) amounted to about EUR 4.2 billion annually in that same period.[1]

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[13] http://ec.europa.eu/research/fp6/p1/innovative-medicines/pdf/vision_en.pdf: 2004 innomed Technology Platform

According to an EFPIA analysis cited in the impact assessment report, R&D investments in the pharmaceutical industry grew almost double in the US between 1990 and 2005 when compared with Europe (Box 2).

Box 2 Pharmaceutical R&D is moving out of Europe

Over the past 10-15 years (i.e. 1990-2005 note by expert panel), Europe's pharmaceutical research and development basis has gradually eroded. Whereas R&D investment in the United States grew by 4.6 times between 1990 and 2005, the corresponding increase in Europe was only 2.8 times.[a] In 1990, major European research-based companies thus spent 73% of their worldwide R&D expenditure on the EU territory, while the figure was only 59% in 1999. According to the biopharmaceutical industry [EFPIA, 2006], companies are increasingly transferring leading-edge technology research units out of Europe, mainly to the United States and recently also to Asia. The industry thus frequently refers to Europe losing the "R&D race". The loss of leading edge technology units could be extremely serious for European competitiveness, as several lines of evidence[b] points to the pivotal role of innovation and cutting edge technologies for long-term economic growth.

The relocation of R&D investment also means that Europe will have weakened scientific environments to nurture and retain talented researchers. This may fuel a European "brain-drain" with loss of skills and experience. In combination with the modest public research spending, this could make Europe even less attractive for pharmaceutical research activities in the future. There are already indications that industry regards Europe as a decreasingly attractive place to locate its key knowledge intensive operations. In 2002, pharma giant Novartis said it would "move the headquarters of its worldwide research organization from Basel, Switzerland, to a new $250 million, 255,000 square-foot laboratory and office facility in Cambridge, Massachusetts." In November 2006, Novartis announced that it would further expand its R&D headquarters in the U.S. by adding as much as 500,000 square feet. Another example is in the EFPIA report to the Commission, where it is clearly mentioned that 5 pharmaceutical companies have recently opened new R&D Centres in China, whereas the associated investments could have been made in Europe.

[a] EFPIA (2006): The Pharmaceutical Industry in Figures, Edition 2006. Brussels, European Federation of Pharmaceutical Industries and Associations.

[b] OECD (2007). Innovation, Growth and Equity. Key Issues. Paris: OECD – Organisation for Economic Cooperation and Development.

The conclusions were clear: the public investments together with more attractive market conditions, such as related to patenting and pricing policies, and the availability of venture capital, made the US the most attractive location for R&D investments of biopharmaceutical companies.

The impact assessment report concluded that the best option was to establish a public-private partnership with the participation of the industry and a specific legal set-up, as a "Joint Undertaking" model on the basis of Art, 171 of the Treaty, based on the Joint Technology Initiative for Innovative Medicines.[14]

It was reasoned that if nothing was done, EFPIA companies were likely to move further out of Europe for their precompetitive research. National actions were estimated as insufficient to decrease the defragmentation of research and regulatory processes, and would remain limited to the national expertise. The traditional framework instruments were in general found to be too bureaucratic and calls would not be designed to support the industry demands. The list of advantages pleading for the establishment of a JTI was convincing not the least, because of the notion that according to diverse studies is was expected that 'a EUR 1 increase in public R&D investment induces overall on average EUR 0.7[15] - 0.93 of additional private sector investment.'[16]

[14] Article 171 The Community may set up joint undertakings or any other structure necessary for the efficient execution of Community RTD programmes

[15] Guellec and Pottelsberghe (2003). "The impact of public R&D expenditure on business R&D", Economics of Innovation and New Technologies, 12(3).

According to the impact assessment report the economic impacts expected when establishing a joint undertaking were significant.

Short term outcomes (i.e. 2-3 years after IMI launch) related to improvements of scientific quality and enhanced knowledge production, network-based R&D capacity building, and human resources development were expected. The *mid-term impacts* (4-5 years after IMI launch) were expected to include concrete results on biomarker validations and toxicology tests, along with shared IT facilities and other data-sharing infrastructure to improve communication and knowledge transfer. For the *longer term* 'wealth and health' benefits comprising improved economic performance, such as increased competitiveness at the European level, securing employment in the pharmaceutical sector, and eventually new medicines and related medical treatments were expected.

In general, it was expected that IMI JU would induce a leverage effect and increase the return of invested FP7 funds and on job creation and will thus deliver a more significant socio-economic impact.

Moreover it was expected that IMI JU would induce the industry to commit to longer-term objectives and investments in new research infrastructures, R&D networks, and the creation of new companies and spin offs. IMI was expected to anchor and increase industry funds in European pharma research.

The impact assessment report also included a monitoring and evaluation system with performance indicators agreed by the industry. The monitoring system will be discussed further in this report.

Together this led in 2007, to the adoption of the IMI legal package by the different EU bodies and finally to the approval of the establishment of the IMI JU by the European Council in December 2007.

4. EVALUATION QUESTIONS

To assess whether the goals put forward when setting up IMI JU and to analyse whether the expectation have been met, key issues on effectiveness, efficiency, research quality and openness and transparency as outlined in section 2.2 of this report.

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. What are the lessons learned from the previous evaluations?
7. Synthesis, conclusions and recommendations

The final evaluation should assess whether the strategic objectives of the IMI JU were relevant, and whether the strategic context and the budget of EUR 2 billion were justified to achieve the goals. For this purpose there was a need to test the budget available and the expenditure with the performance indicators and impact achieved by the JU.

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 outputs and the longer term impact that the IMI JU has realised or was expected to deliver. An intervention logic diagram for the evaluation is presented in figure 2.

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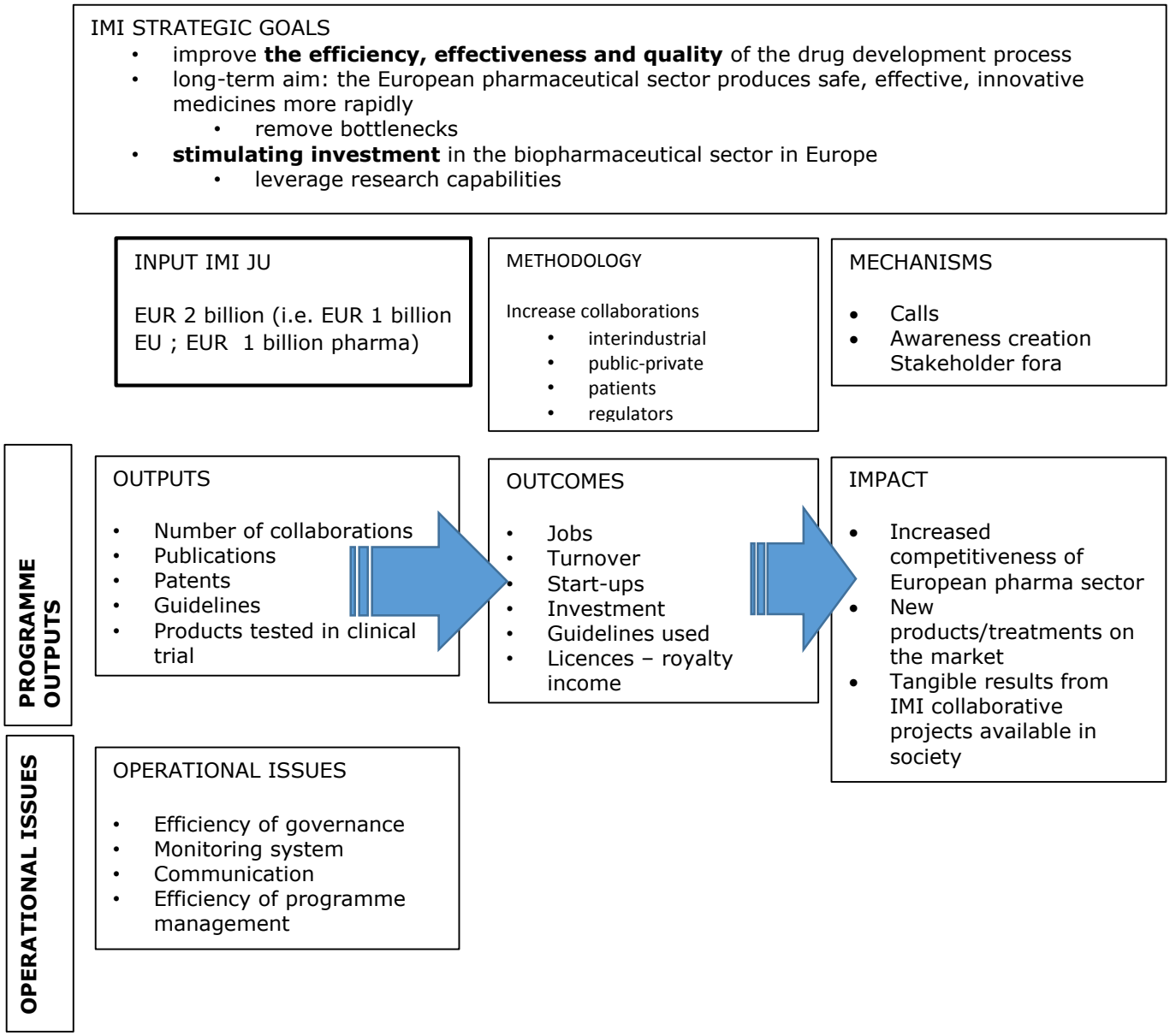
[16] SEC(2004)1397: European Competitiveness Report 2004

In line with the Impact Assessment Report that formed the basis of the IMI JU, primary outputs of the IMI JU activities, the number of collaborations, publications and patent applications can be used. Secondary outputs from IMI 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 IMI JU activities should be analysed. Next to the economic indicators it would be interesting to analyse whether guidelines developed under IMI JU or biomarkers were used outside of the IMI 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 IMI JU will have succeeded if a true impact has been realised, i.e. whether the European pharmaceutical industry is attracting new research activities and investments, and becomes more competitive. New products originating from IMI JU research projects that are available on the market will be 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 Commission in carrying out the final evaluation of the Innovative Medicines Initiative Joint Undertaking (IMI 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. The evaluation started in October 2016 and ended with the delivery of the evaluation report by June 2017. The work consisted of a combination of remote work, conference calls and seven panel meetings in Brussels. The expert group built its assessment on

(i) documents and published information, and on extensive data compilations prepared by IMI Executive Office (see Annex 2 for the list of documents, most of these are available on the IMI website);

(ii) interviews with a wide range of IMI stakeholders, including representatives of both founding members, IMI bodies, participants of on-going IMI-supported research projects, representatives of regulatory bodies, patients' organisations, research and SME associations (see the list in Annex 3). For this purpose, the general evaluation questions were translated into more specific questions, revised during the course of the interviews (the list of questions is available in Annex 4);

(iii) a survey of beneficiaries and a public consultation.

5.2 Limitations – robustness of findings

The expert group was entrusted with the challenging task of the final evaluation of IMI JU, and the interim evaluation of IMI2 JU. This task was challenging because the two programmes had different objectives, different legal frameworks and IP policy. Most of the IMI JU projects were still running, and some projects will continue up to 2021, while the first projects of IMI2 started in 2014.

The information used by the expert group was gathered from interviews with stakeholders, which often represented a mixture of appreciations for IMI JU and for IMI2 JU. A substantial volume of information was available from documentation, but there was no accountable performance monitoring system with Key Performance Indicators (KPIs). Therefore, it was not easy to crystallise the key messages that were specifically relevant to IMI JU. The experts had to rely on their individual background expertise and common sense to formulate a logical and comprehensive analysis, although this limitation will be inherent to any evaluation process relying on an expert group.

The guidance and help of the European Commission office was instrumental, especially in delivering information and pointing to where to find the information, to produce this report.

Most of the interviewees identified by the expert group, readily agreed to participate, which was also an indication of the positive view of the JU. It was harder though to get feedback from members of parliament involved in health although the final evaluation report will be shared with the European Parliament (EP); an interview with a Member of the EP would have been an opportunity to communicate the visions and expectations of the EP. We are grateful that Mrs. Grosstete, as a Member of the EP, agreed to answer the experts group’s questions in writing.

The expert group was further hampered because some pieces of information were missing or came very late in the evaluation process. In particular, it was suggested by EFPIA representatives that the number of clinical trials in Europe had not decreased since the economic crisis of 2008, because of the activities of IMI JU. The expert group compared the number of clinical trials in Europe before the establishment of IMI JU and now, but had no access to data from other parts of the world to put this suggestion in a global context that would allow attributing the resilience against the economic crisis to activities of IMI JU.

There were also no quantitative data available to indicate whether the big pharmaceutical companies were increasing their research investments in Europe, which would be an indication that the Europe had become a more attractive environment for biopharmaceutical research as was the ultimate goal of the PPP.

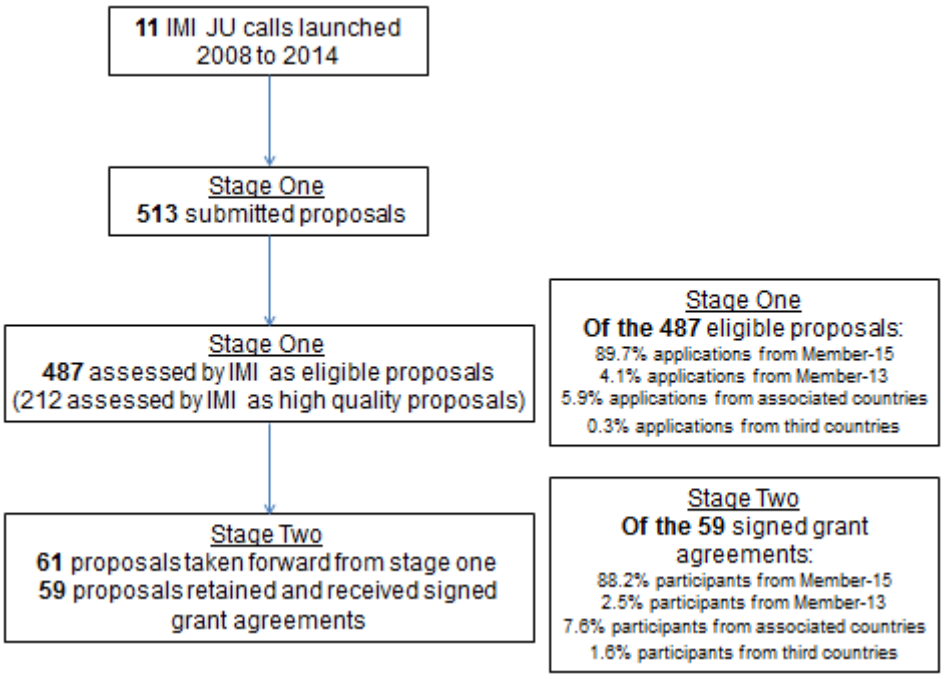
6. IMPLEMENTATION STATE OF PLAY

This section describes how the IMI JU set by the Council Regulation 73/2008 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 provides evidence of if, and how, IMI JU has attracted the main research actors in Europe and, also, highlights the main research and structural trends.

6.1 Overview of calls launched during the period 2008-2013

A total of 59 projects were funded by IMI JU, of which 21 were finished, but 38 were still active as of 31 December 2016. Figure 3 summarises the number of calls and submitted, eligible and funded proposals. Between 2008 and 2011 one call per year was launched, with four calls launched in 2012 and three calls launched in 2013. Each call had a different number of topics launched with the most topics (n=18) for IMI-JU-01-2008 and least topics (n=2) for IMI-JU-04-2012, IMI-JU-05-2012 and IMI-JU-07-2012. The number of proposals submitted per call ranged between 2 (for IMI-JU-10-2013) and 134 (for IMI-JU-01-2008).

Figure 3: Summary of calls and proposals for IMI JU



6.2 Participation patterns broken down by country and region

A total of 24 of the EU-28 Member States were represented in the 487 eligible short proposals submitted to stage one of the IMI JU calls, including Croatia (that was associated to FP7 before 2013 and that joined the EU in 2013). In terms of the proposals assessed as 'eligible' the UK was the EU Member State that took part in the largest share (19.2%) of the total number of applications in the eligible short proposals (n=5027). Italy and The Netherlands were also commonly represented in the applications for 14.0% and 12.8%, of eligible short proposals, respectively. However, the pattern in countries represented in terms of the success rates for proposals retained in stage one differed from the submitted proposals. A total of 23 of the EU-28 countries were represented in the 59 projects funded as part of the IMI JU, including Croatia that joined the EU in 2013. Among EU-28 Members States, the largest share of EU-funded participations in signed grant agreements was represented by the UK (23.6%), followed by Germany (16.5%) and France (12.6%). In terms of the funding awarded, out of the EU-28 countries, the highest

share in signed grant agreements was represented by the UK (26.1%), followed by The Netherlands (17.9.1%) and France (16.2%).

The types of countries represented in the 59 IMU JU funded projects can be grouped under four headings: EU-15; EU-13; associated countries and third countries (Annex 5 defines these headings). Figure 3 also shows the share of funded projects under these four headings. These figures show that the EU-15 states participated in the majority of funded proposals. This is also reflected by the overall success rate between applications in eligible proposals and participations in signed grant agreements:

- 22.8% success rate for EU-15;
- 9.5% success rate for EU-13;
- 26% success rate for associated countries; and
- 40% success rate for third countries.

6.3 Participant patterns per 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. All of the 59 signed grants had some EFPIA representation. Of the 59 funded proposals, with signed grants, there were 1711 participations in total (of which 1204 were EU-funded participations):

- 51.9% (n=887) of the participations came from academia, secondary and higher education establishments, and non-profit research organisations;
- 11.2% (n=192) came from SMEs;
- 29.6% (n=507) came from EFPIA;
- 5.7% (n=97) came from an entity categorised as other; and;
- 1.6% (n=27) represented patient organisations.

Within these 59 funded projects, there were 647 individual participants in total, including 40 individual EFPIA companies. This means there were 607 individual participants, within the 59 signed grants, who received EU-funding as part of IMI JU.

6.4 Characterisation of the academic players

Two ranking systems were used to assess the status of the universities taking part in IMI JU, i.e. the European Multirank and the Shanghai ranking system. Both of these ranking systems showed that more than 50% of all participations and EU contribution was for organisations ranked amongst the 200 (or 150 according to the Shanghai ranking) first Universities. Nearly three quarters (72%), of the Universities participating in IMI JU were in the overall World top 500 and 12% of the universities were in the overall World top 100, dependent on the ranking used.

A substantial number (n=201) and variety of key non-university research organisations have participated in IMI JU proposals. These represent a mixture of academic and non-academic institutions such as research active hospitals and national research organisations. Most of these entities came from the EU-15 states.

6.5 Characterisation of the industrial players

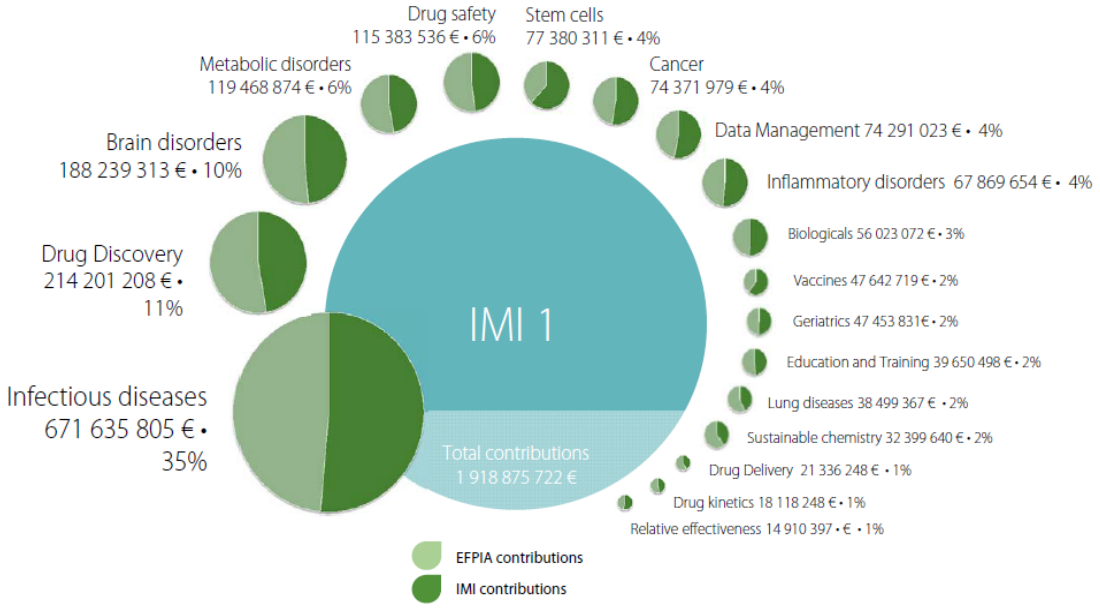
Forty distinct EFPIA companies representing industry participated in IMI JU. Of these, 19 had headquarters outside of the EU. Of the 21 companies with headquarters within the EU, 15 were in the top 40 ranking of the Pharmaceutical and Biotechnology section of the Scoreboard EU 1000. Six of these companies with headquarters within the EU did not appear in this ranking. Using the Pharmaceutical and Biotechnology section of the scoreboard World 2500 ranking, the majority of the companies (n=29) were in the top 100. Eight of the companies did not appear in this ranking.

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 18 defined scientific areas. The data summarised in Figure 4 also show the contribution to the total funding awarded from EPFIA and

IMI respectively. Of the total funding awarded (EUR 1,918,875,722) for the 59 signed grants agreements, over two thirds (EUR 671,635,805 or 35%) was directed towards projects in the area of infectious diseases. The scientific areas of 'drug discovery' and 'brain disorders' were awarded 11% and 10%, respectively, of the total funding awarded. The remaining 15 scientific areas were awarded 44% of the remaining funding but were each awarded less than 10% of the total funding awarded.

Figure 4: Distribution of funding per scientific area - update January 2017 (IMI Executive Office)



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

The average success rate for eligible short proposals in stage one of the calls for IMI JU was 14.2% but ranged from 7.6% for IMI-JU-02-2009 to 100% for IMI-JU-10-2013. The call IMI-JU-02-2009 comprised nine topics with a range of focus including the identification of biomarkers through to the use of electronic health records. One call (IMI-JU-10-2013; developing an immunological assay for use in influenza vaccine production) attracted only two applications of which one was deemed eligible and then subsequently awarded funding, which led to an obvious success rate of 100%. More than half of the calls (n= 7 calls) had a success rate above the mean value of 14.3%.

The average success rate in terms of contribution to the retained (and funded) proposals was 3.3% (range: 0.6% for IMI-JU-02-2009 to 100% for IMI-JU-10-2013). The majority of the funding awarded per call (n= 11 calls) were above this mean value of 3.3%. There was no clear pattern across the calls and associated topics in terms of the observed success rate.

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

The total contribution (EU and EFPIA) for the 59 projects was EUR 1,918,875,722. Of that, the total EU contribution was EUR 965,730,983. The mean EU contribution was EUR 16,368,322 per project. In terms of the individual projects, the EU contribution per project ranged from EUR 2,270,000 for WEB-RADR (call IMI-JU-09-2013 on the topic 'leveraging emerging technology for pharmacovigilance') to EUR 109,433,010 for COMBACTE-NET (call IMI-JU-06-2012).

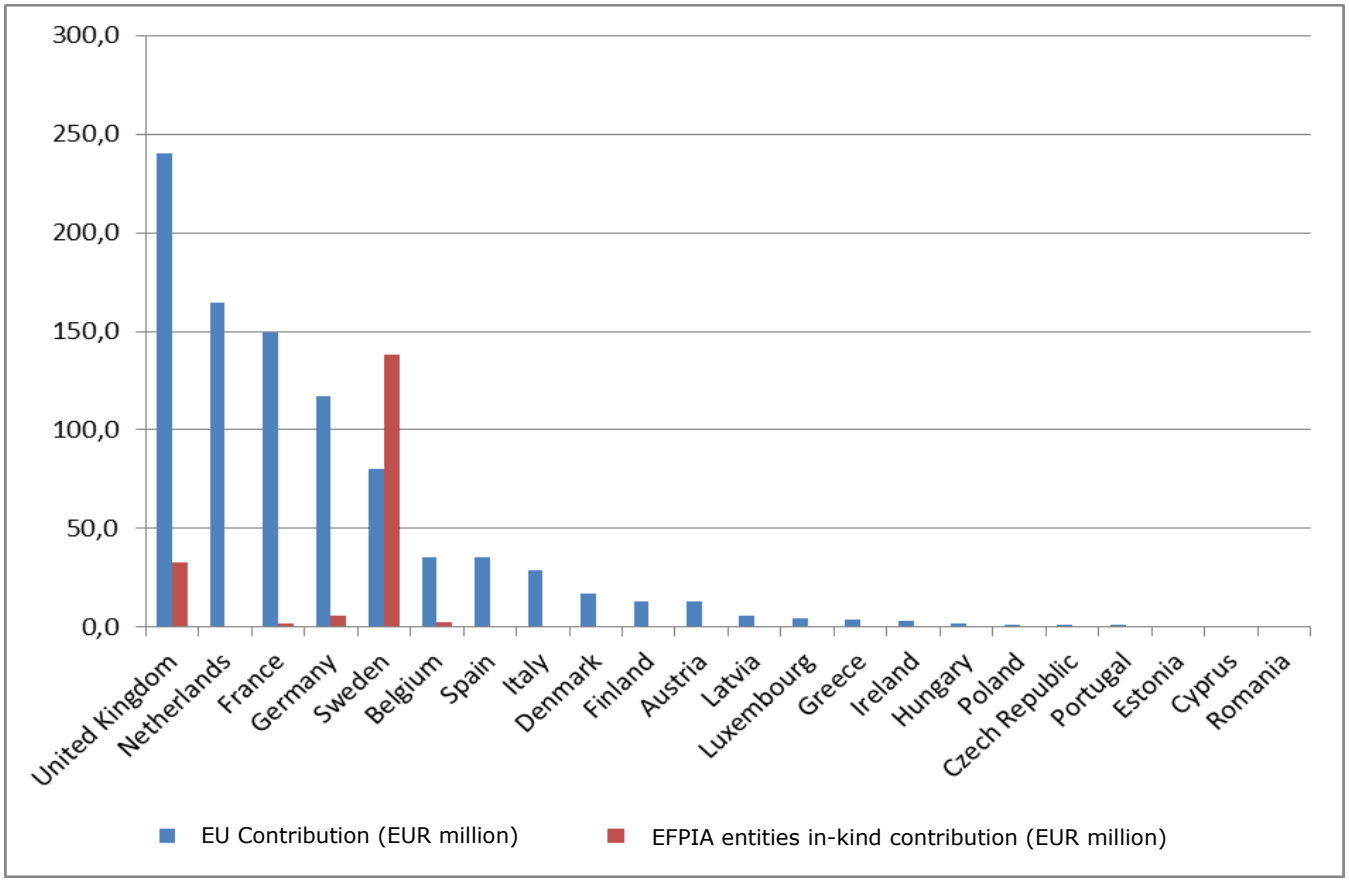
The EFPIA contribution was EUR 953,144,739 (amounting to 49.7% of the total funding in the signed grant agreements). This total EFPIA contribution included EUR 213,617,349 which was in-kind contributions from outside the EU and Associated Countries.

Figure 5 illustrates the distribution of total funding received per country. The highest total contribution was received by the participants based in the UK (EUR 240.2 million) followed by The Netherlands (EUR 164.7 million) and France (EUR 149.1 million).

The total EU contribution (% share) to participations distributed over the different country categories was:

- EUR 907.3 million (93.9%) for EU-15;
- EUR 45.6 million (1.3 %) for associated countries;
- EUR 12.1 million (1.3%) for EU-13; and
- EUR 0.7 million (0.1%) for third countries.

Figure 5: Distribution of funding per country



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

Table 2 summarises the number of the different types of participations in the IMI JU projects, with the respective requested IMI JU contributions and the in-kind contributions from EFPIA. The numbers indicate that the public and private budgets are almost matching.

Table 2: Types of organisations and the budget distribution for the 59 projects

Type of organisation	Number of participations in IMI	Requested EU Contribution (EUR)	EFPIA in-kind contribution (EUR)
Academia, Research Organisations	888	802,395,744	0
EFPIA	507	0	953,144,739
Patient Organisations	26	5,672,638	0
SMEs	192	127,994,480	0
Others	98	29,793,249	0
Grand Total	**1711**	**965,730,983**	**953,144,739**

Annex 6 shows the funding awarded for each project with the number of participants and type of participants. Of the 59 funded projects within IMI JU, the total value of the funding was EUR 1918.8 million, of which EUR 953.1 million was contributed in-kind by EFPIA partners and EUR 965.7 million from the EU contribution. Within the 59 funded projects, there were 40 EFPIA companies participating. As of 31 December 2016, EUR 385 million of the reported in-kind contribution of EUR 487.7 million had been formally validated and checked by IMI JU Executive Office staff and/or audited by external auditors.

Annex 6 shows the 59 funded projects which had a total of 1711 participations. The total number of individual EU funded participants was 607. The mean EU funding awarded per participant was EUR 1.59 million.

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 IMI JU, a dual approach to monitoring the IMI JU was proposed.[1] Firstly, a quantitative approach using key measures on a large scale, which are conducted in a comparative and systematic manner and, secondly, a qualitative approach by conducting case studies and surveys done by expert panels and scientific committees. It was advised to perform a series of baseline studies which should focus on the state of affairs in the pre-IMI area (2005-2006-2007) in order to help assess IMI's additionality effects during its life time.

According to the impact assessment report that accompanied the proposal for a IMI Joint Undertaking, performance indicators were agreed by industry (Box 3).[8]

Box 3 Some of the most important performance indicators as agreed by industry are the following:

1. To measure the impact of IMI on EU competitiveness:

- The number of pre -competitive pharmaceutical collaborative research projects established in the EU as a proportion of those established globally;
- The investment in EU pre-competitive pharmaceutical collaborative research projects as a proportion of the investment in these projects globally;
- Number (and/or budget) of clinical projects performed in the EU: e.g. conduction of phase I, II and III clinical studies in Europe required to support safety and efficacy projects;
- Per year, the number of pre-competitive pharmaceutical collaborative research projects established in the EU;
- Per year, private investment in pre-competitive pharmaceutical collaborative research projects in the EU;
- Over the duration of IMI, evolution of the private investment in pre-competitive pharmaceutical collaborative research projects in the EU;
- Over the duration of IMI, evolution of the investment of the biopharmaceutical industry in R&D in the EU in comparison with the rest of the world;

2. To measure the impact of IMI Scientific Environment:

- Per year, the number of validated biomarkers including chemical, toxicological and imaging that have been established and used in clinical trials;
- Per year, the number of new or amended EMEA guidelines related to the use of new technologies in drug discovery and development;
- Per year, the number of new EMEA guidelines including surrogate end points;
- Per year the number of recalls and restrictions in use due to safety reasons;
- The change in median time to approval by therapeutic area.

To monitor the overall performance of IMI JU and draw conclusions about the achievements was difficult because of the lack of an accountable performance monitoring system that used SMART (Specific, Measurable, Achievable, Relevant and Time phased) Key Performance Indicators (KPIs).

At the time of this evaluation, work was ongoing within the IMI Executive Office and the IMI GB to develop and agree on a new set of KPIs. As these were still under development, the system will not be relevant for the IMI JU final evaluation. The need for a review and adaptation of KPIs was a recommendation from previous IMI evaluation rounds. The new set of KPIs is discussed further in section 7.2.1.3.

Moreover, the advice formulated in the Impact Assessment Report to perform a series of baseline studies to establish the state of affairs in the pre-IMI area (2005-2006-2007) in order to help assess IMI's additionality effects during its life time was not taken up; there was no overview available that gave a year by year evolution of the proposed indicators, so that at the time of the final evaluation there were no targets nor baselines of indicators defined, which made it difficult to assess the impact of the allocating a significant budget to the PPP activities.

The final evaluation of IMI JU therefore had to rely on the "IMI Socio-economic Impact Assessment" report published in May 2016,[17] on statistics on calls and projects information, and on interviews.

The "IMI Socio-economic Impact Assessment" report is the result of an analysis that focussed on the outputs of nine individual IMI JU projects, which were reaching the end of the funding period. The report summarises the **socio-economic impacts**, under the headings of 'Mediators and Intermediate Outcomes' (e.g. Peer reviewed publications) and direct socio-economic impact such as building research capacity.

Some high impact project results, such as on drug discovery and development, early disease prediction and diagnosis, personalised medicine, biomarker development, tools for drug development, novel clinical approaches, drug safety, data sharing and sustainability or capacity building in Europe were reported in the latter report.

The IMI Executive Office also provided the expert group with a list of "Examples of impactful project results". The list of examples, however, indicated that, although the results are certainly important and (very) promising, in most cases their impact has not been shown as yet and more research efforts will be needed to realise real impact.

Specific achievements that were reported were faster validation and approval of biomarkers because of early involvement of regulatory agencies, although this was not evident from the quantitative data available nor from feedback from EMA.

There were examples of projects from IMI JU that are expected to last and become increasingly important as IMI2 JU is continuing its activities. Building on the closeout meetings that started under IMI JU is expected to support this. It can also be expected that the establishment of thematic Strategic Governing Groups (SGGs), although under IMI2, will contribute to the sustainability of important project outputs.

The "IMI Socio-economic Impact Assessment" report stated in general that the IMI JU should eventually impact on the medicines development process and result in improvements in factors such as cost savings, time savings, reductions in risk, reductions in attrition rate, and a reduction in the use of animals in research. The real impact on the European pharmaceutical industry thus remains to be demonstrated. According to the same report EFPIA estimates that the process 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. It was stressed by all IMI, EFPIA and GB representatives that a long-term strategy was required before IMI JU could have a demonstrable effect to enable the competitiveness of the European pharmaceutical industry.

Although socioeconomic impact needs more time to be demonstrable, IMI JU projects in general contributed to some novel scientific insights. The number of publications was impressive with 1,678 unique Web of Science publications linked to the Thomson Reuters citation databases. All

[17] www.imi.europa.eu/sites/default/files/uploads/documents/Publications/SocioeconomicImpactAssessment_FINALMay2016.pdf

publications were published in the period from 2009 to the end of 2015. There were 1,661 papers (articles and reviews; 99%); 17 other document types (13 editorials, two meeting abstracts, one letter and one news-item; 1%). Between 2009 and 2015, the citation impact for IMI project papers (1.93) was nearly twice the EU's citation impact (1.1) in similar journal categories.

IMI project publications appeared most frequently in PLOS ONE (83 publications), followed by Annals of the Rheumatic Diseases (50 publications).

In the TOP 20 journals ranked by impact, there was only one IMI-related publication in the New England Journal of Medicine, two in The Lancet, two in Nature Reviews Drug Discovery, one in Nature Biotechnology, five in Nature, one in Nature Reviews Cancer Nature Reviews Genetics, and one in the Journal of the American Medical Association. The number of patents per EUR 10 million EU-funding was 0.51 for IMI JU, while for the rest of the Health theme of FP7 this amounted to 1.49. In contrast, for the same amount of EU-funding, 0.9 of spin-off companies were established as a result of IMI JU projects, but for the Health theme of FP7, this was only 0.24 spin-offs per EUR 10 million EU-funding.

One of the main achievements of IMI JU about which there was general consensus, among the stakeholders interviewed, was that under IMI JU **collaboration** between different competing global companies, SMEs and academia became possible. Together with the budget and long-term strategy, this was considered to be an important asset for European pharmaceutical research that may strongly support its future. The fact that companies from the US and Japan wanted to join in IMI projects was considered to confirm this notion.

The new type of collaborations were said to have created **trust** and new partnerships, including with partners from other areas of expertise, such as regulatory bodies, and patient representative groups, to bring new and better products or treatments faster to the patients. The new collaboration models may have lasting effects beyond the existence of the IMI funded projects, as the added value of working cross disciplinary, becomes more obvious.

Moreover, EFPIA and IMI representatives reported that IMI JU also induced a **mind change** in academia to move away from "blue skies" research, while industrial partners became less sceptical and agreed to work with academia. The fact that IMI generated opportunities for academia, SMEs and industry to collaborate and created a broad platform to make technologies and patient material accessible, bringing academia and SMEs in the clinic is a major achievement. This kind of **platform collaboration** was believed to be a prerequisite to address complex diseases such as cancer and created opportunities to learn from patient treatment in clinical practice and not only in the clinical trial setting. The increased opportunities for contacts of academia and SMEs with clinicians was reported to improve clinical trials design, based on input on the working mechanism of molecules, more appropriate development of databases of patients cohorts, and stratification of patients. This synergy, aimed to better adapt the medication to prolong the periods between treatment episodes, reportedly reduced the number of days in hospital.

The **sustainability** of project results and databases established during IMI projects also needs to be considered. Under IMI JU this was not in the objectives, which made it difficult to see benefits now. Project participants contacted were asked about examples of sustainability of results and outputs beyond the end of the project. One project (PRO-ACTIVE) is continuing beyond the funding period with a new consortium agreement, including aspects on rights and obligations, operational aspects, membership fees, license fees, etc. The consortium did not receive other external funding. The goal of the continuation of the consortium was to gather data to support the use of a tool developed in the IMI funded project and to allow third parties to use this output. Another example of a project that has a sustainable outcome was eTox (see Box 4).

Box 4 Towards sustainability of IMI project results - example

The eTOX project aimed to develop a drug safety database from the pharmaceutical industry legacy toxicology reports and public toxicology data and innovative in silico strategies and novel software tools to better predict the toxicological profiles of small molecules in early stages of the drug development pipeline.

The eTOX IMI grant finished on Dec 31th, 2016. eTOX is entering into its sustainability phase in which partners are committed with the eTOXsys maintenance. eTOXsys consists of a worthwhile database, a mature and professional software platform and a collection of useful models that makes attractive the commercial exploitation. Lhasa and Molecular Networks are managing such exploitation. The exploitation model is based on affordable fees for profit users and symbolic fees for academic institutions. An eTOXsys Sampler version with subset of data and models will be public.

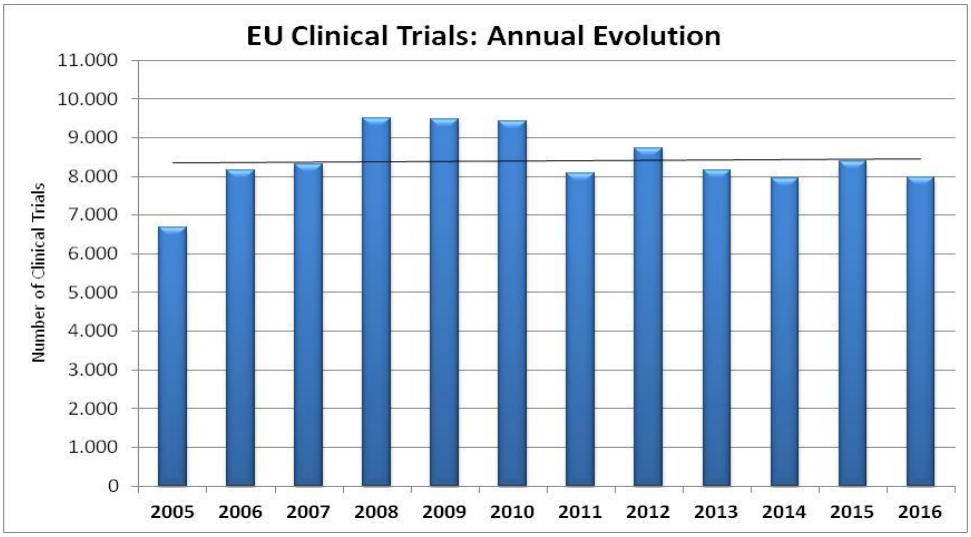
Another IMI JU project was exploring options to find a sustainable follow up initiative under IMI2 JU. The European Lead Factory (ELF) brought together a collection of compounds from industry and newly synthesised molecules from academia. The collection was made accessible to academics and SMEs to allow screening for interesting targets. This mode of operation provides a potentially good example of reaching added value as a result of joining forces and a strong argument to use the European platform for follow up studies.

The sustainability of project results beyond the funding period was not supported by all parties, including some EC representatives and industry representatives that considered IMI was more of an instrument to catalyse development towards better and safer medicines, but not a mechanism to maintain databases once the projects were terminated. It was therefore suggested that a more complete appraisal would be needed to inform which project results should be sustained. In this respect it was noted that when there was no budget allocated to maintain databases, was an indication that industry was not sufficiently interested in this aspect. To keep databases sustainable, the business plan should foresee the need for a database from the start of the project. This requirement was considered systematically under IMI2 but not under IMI JU. In addition, calls are being planned in IMI2 JU to maximise the use of results from IMI JU when appropriate.

The closeout meetings that were held to conclude the first IMI JU projects, were used to summarise the outputs from the projects and were extracting lessons learned from the projects and identified the challenges for the different teams. One IMI scientific officer considered that all projects did 'deliver to a certain degree'. Results from the closeout meetings in combination with the thematic Strategic Governing Groups that were installed under IMI2 JU, were expected to increase the likelihood that relevant project outcomes will be granted a sustainable future and access to results for further use will be guaranteed.

IMI JU may have contributed to resilience of the European pharmaceutical industry, as the number of clinical trials and research remained stable across Europe in the period following the crisis of 2008, according to one of the interviewees. Although there was a decrease of clinical trials after 2010, the number reached about the same level as just prior to 2008 according to an analysis of the numbers of clinical trials in the EU from the EudraCT Data base (Figure 6).[18] It was not possible, however, to compare the number of clinical trials in Europe globally, as the expert group had no access to such data. Therefore, it was impossible to attribute the suggested resilience of the European industry against the economic crisis, to the activities of IMI JU.

Figure 6: Annual number of clinical trials in the EU



In addition, the same interviewee also stated that pre-IMI disinvestment was switched to new investments in European biomedical research in pharmaceutical companies, including a focus on difficult research areas such as dementia diseases. However, there were **no quantitative numbers available to support this**. It is also difficult to attribute these achievements to IMI JU as no comparison could be done with countries from outside the EU.

[18] https://eudract.ema.europa.eu/

One of the interviewees with expertise in technology transfer did not believe that IMI JU had delivered on the criterion of improving the competitiveness of European pharmaceutical companies or increased their investments in R&D in Europe. Instead, the interviewee felt that disinvestment in R&D facilities in global pharmaceutical companies continued, while public financing increasingly supported R&D in academia and SMEs. In fact the SMEs are instrumental for the global pharmaceutical companies to get access to new applications or therapies. The creation of an ecosystem that brings together academia with SMEs in biotech and other technologies was demonstrated to be crucial for the pharmaceutical companies and manifested in the concentration of the companies around the innovative sites in the US. IMI provided an interesting financial model in terms of the size of the budgets and the focus outlined in the SRA. However, the creation of such an ecosystem that put a stronger emphasis on the importance of the European SMEs combined with a possibility for exclusive right, albeit negotiable, to the results from projects would enhance the participation of successful SMEs and of some of the research institutions with ambitious tech transfer activities.

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

This section addresses the progress towards meeting the IMI JU objectives and how all parties in the PPP had lived up to their financial and managerial responsibilities. The objectives spelled out in the Council Regulation are summarised in Box1.

7.1.2.1 Extent to which the IMI JU achieved the objectives set in Article 2 of the Council Regulation establishing IMI JU - Formulation and implementation of IMI JU Research Activities

The key objective of IMI was to address bottlenecks in pharmaceutical R&D with the aim of leading to faster discovery and development of better medicines for patients and the enhancement of Europe's competitiveness.

The first **Strategic Research Agenda** (SRA) was released in March 2008.

Four research pillars were identified as Efficacy, Safety, Knowledge Management and Education & Training. These themes made up the horizontal lines within a matrix of research pillars, while a number of 'selected diseases' (cancer, brain disorders, inflammatory diseases, infectious diseases) constituted the vertical dimension within this matrix.

An overview of the 30 projects launched following the first three calls were in accordance with the four research pillars. For example,

- **SAFETY** was addressed by SAFE-T, PROTECT, MARCAR, and E-TOX;
- **EFFICACY** was addressed by IMIDIA, and PREDECT;
- **KNOWLEDGE MANAGEMENT** was addressed by OPEN-PHACTS, and EHR4CR;
- **EDUCATION & TRAINING** was addressed by EU2P, and PHARMATRAIN.

A revised version of SRA was released in June 2011. Revision of the SRA was done by the SC in consultation with the SRG and approved by the GB. The IMI Scientific Committee proposed that "IMI should consider focusing overarching strategic initiatives on 'game-changing' ideas and areas where the maximum number of companies can join forces". From this, the strategic themes were added to already existing IMI Research Priorities:

- Safety sciences,
- Research on metabolic diseases,
- Knowledge management, and
- Central Nervous System disorders.

Scientific Committee members observed that since the drafting of the original SRA, the drug development industry was facing growing external pressures towards personalised medicine. In addition, pricing issues, demographic shifts and consumerism, all have created new challenges but also opportunities. Where patients have traditionally been relatively passive participants in health delivery, they were now being empowered by technological progress (such as internet, smart phones) to have a much more active role in management of their health care. This led to the replacement of the Research Pillars by seven Areas of Research Interest. The revised SRA considered that the areas that cover most of the relevant aspects of drug research were:

- The Patient in the Focus of Research;
- Diseases – Drug Efficacy;
- Knowledge and Knowledge Management;
- Strategies;
- Beyond Drug Discovery: Drug Development and the Regulatory Framework;
- Tools and Techniques;
- Education and Training: Science Communication at various levels;
- Strategic Themes for IMI Research.

This in turn led to entirely New Research Priorities and reassessed the 'Established Research Priorities'. Some of these areas that had not been identified in the 2008 IMI SRA were included in the revised SRA:

- Pharmacogenetics and Taxonomy of Human Diseases (Areas of Interests: Patient, Diseases, Knowledge);
- Rare Diseases and Stratified Therapies (Area of Interests: Patient, Diseases, Knowledge);
- Systems Approaches in Drug Research (Area of Interests: Strategies, Diseases);
- 'Beyond High Throughput Screening'- Pharmacological Interactions at the Molecular Level (Area of Interests: Strategies, Tools);
- Active Pharmaceutical Ingredients (APIs) Technology (Drug Compound Development) (Area of Interest: Development);
- Advanced Formulations (Areas of Interest: Development, Diseases);
- Stem Cells for Drug Development and Toxicity Screening (Area of Interest: Tools);
- Integration of Imaging Techniques into Drug Research (Areas of Interests: Tools, Disease).

This framework which identified ten key Research Priorities ('pillars' plus 'disease themes') that IMI had selected was used for its strategic planning, in conjunction with the new Research Priorities described above:

- Safety Sciences (Area of Interest: Development);
- Increasing Practicability of Biomarkers and Biobanks (Areas of Interest: Tools, Knowledge);
- Coping with Regulatory and Legal Hurdles (Area of Interest: Development);
- Knowledge Management (Areas of Interest: Knowledge, Patient, Development);
- Science Communication (Areas of Interest: Knowledge, Diseases, Tools);
- Neuro-psychiatric Disorders/Brain Diseases (Area of Interest: Disease);
- Inflammatory and Immune-Mediated Diseases (Area of Interest: Disease);
- Cancer (Area of Interest: Disease);
- Metabolic Diseases including cardiovascular diseases (Area of Interest: Disease);
- Infectious Diseases (Area of Interest: Disease).

This SRA is complete and it was noted that "these areas cover most of the relevant aspects of drug research". It may therefore not come as a surprise that the eight next calls of IMI JU and respective projects funded were in line with the revised SRA. Nevertheless, major sectors that are relevant to the design of new drugs and to the competitiveness of the European pharmaceutic industry were not explicitly addressed, such as diagnostics, imaging, medical devices, bioinformatics, IT, big data management and safety. Although these domains have been listed in some projects (EMIF, eTRIKS, GetReal or Stembancc) it is only since IMI2 JU was installed that these topics were fully included.

Every year, IMI draws on its legislation and the SRA to set out annual research priorities. These form part of the Annual Implementation Plan (AIP), which is approved by the Governing Board. AIPs were prepared by the IMI Executive Office needed approval of the GB, and were published online. The AIPs covering IMI JU are available on the IMI website.[11]

These annual priorities are based on the need for collaboration in complex areas of biomedical research and innovation.

The priorities were addressed by the launching of eleven calls for proposals between 2008 and 2013.[19] The last call was launched on 11 December 2013 and eight projects started in the beginning of 2015.

Call topics were defined by EFPIA companies which were committed to participate in a specific research area. The call topics were consulted with the SRG, the SC and experts in the field through workshops.

Since the establishment of IMI JU, critics have been coming from many different angles and mainly targeted EFPIA and the role of the big pharma companies as call topics were defined by these. Several times putative stakeholders from academia, SMEs and SRG mentioned the lack of transparency in defining the call topics.

The IMI JU representatives indicated that the first step in the process was to agree to collaborate on projects and to commit significant budgets. Over time, the mutual understanding between industry and academic partners has grown. As the pharmaceutical companies contribute in kind to the projects, thereby allocating significant budgets to the projects the companies believe it is justified they determine the content of the call topics. Moreover, it was reasoned that the call topics were open for discussion in the SRG and for advice in the SC. Both these advisory bodies indicated that a more interactive process would have contributed to better understanding of how the provided feedback had been processed.

7.1.2.2 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 next section summarises how IMI JU projects have brought the main stakeholders together from industry, academia, patients' organisations and regulators to work towards common goals.

The participation of **SMEs** in IMI projects was of major importance as the SMEs are a key component to drive the competitiveness of the European health industry. The SMEs have a potential to become future mid-size enterprises and potentially new big European pharmaceutical companies in the future. The transformation from SME to large companies that has often been seen in the US (Amgen, Celgene, Genentech, Genzyme, Gilead,…) is a model.

IMI has made efforts to facilitate the participation of SMEs. Several IMI projects supported the activities of SMEs. For example, the European Lead Factory and ENABLE provided open platforms that allowed SMEs to follow up on interesting drug targets and candidate molecules. Since the start of the project, 39 of the 60 applications to enter ENABLE with a programme came from SMEs. At the time of writing this report fifteen SMEs directly participate in ENABLE.

The participation of SMEs in IMI JU has represented 15.96% (192 out of 1203) of the participations, compared with 15.86% in the rest of the FP7 health theme. In IMI JU the percentage of EU contribution to SMEs was 13.25%, compared to 17.93% in IMI in the rest of the FP7 health theme; but both levels of participation are relatively low.

The majority of the SMEs specialised in biotech and IT / data management and have been able to benefit beyond their expected contribution to projects. IMI reported the important results obtained by some of them and it can be found in Annex 7.

The development of the highest possible number of SMEs in Europe was of the highest importance to support the competitiveness of the health sector (not only of the pharmaceutical industry). However, the participation of SMEs in the IMI projects did not always seem straightforward. The barriers for SME participation have been described succinctly in an IMI workshop in May 2016[20] and were confirmed by information assessed by this expert group. **Several barriers** were identified in this workshop, in particular:

[19] www.imi.europa.eu/content/overview-imis-calls-how-participate
[20] http://www.imi.europa.eu/sites/default/files/uploads/documents/Events/SMEworkshop_notes.pdf

- SMEs lacked human and financial resources for intensive and time consuming consortium negotiations, especially on IP issues. They perceive IP rules designed to the benefit of big pharma, and which are unfavourable for the SMEs;
- The rules and call conditions were too rigid because they were not initially designed for SMEs, and the deadlines for application are too short;
- Topics were defined top down and too narrow so that SMEs are obliged to follow the lead of big pharma.

Furthermore, Venture Capital (VC) funded SMEs were more adverse to risk-taking strategies than owner-capital SME in a highly competitive funding environment. VC-funded SMEs were strategically more narrowly focussed and if the call is not aligned with the SME strategy, these types of SMEs will be less likely to participate. Owner-capital SMEs tend to be more flexible in this respect.

The timeline projections before a return on investments can be expected, should also be taken into account. According to existing believes driven by evidence from EFPIA it can take 13 years from the scientific investigation into a disease to identify potential treatments for that disease through to the availability of a medicine to patients. An average biotech project may take 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 over the duration of the project.

An SME representative reported how they found the IMI projects in general interesting to participate in, especially when the topic addressed the SME's goals. This representative also saw the benefit of SME's, large pharma and academic groups being brought together. The available funding was indicated to be the main reason for participation in an IMI project and when compared with other opportunities in the framework programme. However, such other opportunities from the framework programme were appreciated as potentially better options to support innovation.

Some SMEs indicated they were badly equipped in the consortium negotiations, as often human and financial resources were insufficient to invest in time consuming and hard negotiations especially with respect to Intellectual Property (IP) issues. Testimonials from SMEs in the interviews indicated that there was a perception that the IP rules were customised for big pharma and unfavourable for SMEs, leaving SMEs with little room to manoeuvre. SMEs could always fully have a role in the negotiations or fully contribute to the design of the projects.

The focus on precompetitive research is for most SMEs their core business, which may not be compatible with sharing background IP and interfered with the need of SMEs for exclusivity rights for exploitation.

Similar sentiments to those expressed on IP issues were reported about the IMI JU 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 road of big pharma, while often SMEs needed more flexibility than that offered.

The issues on topic design, consortium negotiations, including the aspects of IP were shared by major academic partners, mostly from research institutions with strong tech transfer activities.

The participation of SMEs in IMI JU may have been hampered further because this funding stream 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 Eurostars programme and the efforts of FP7 to increase involvement of SMEs in its projects were strong competitors for collaborative projects.

Unlike in IMI2 JU, **mid-cap companies** could participate in IMI JU projects but could not receive EU-funding. In the area of biomedical development sector, which is extremely capital intensive, the definition handled for SME[21] was too narrow as compared with other sectors. It was realised that this was excluding important expertise, and was therefore changed under IMI2, which now allows 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

[21] Definition SME: http://ec.europa.eu/growth/smes/business-friendly-environment/sme-definition_en

consortium receiving financial contributions. A major incentive to be part of the biopharma consortium was that this allowed an active role in the planning and preparation of the project.

The inclusion of stakeholders representing **sectors other than the biopharma sector** was not a clear IMI objective in IMI JU. This may have been a missed opportunity, which was also addressed when establishing IMI2 JU with modified objectives.

IMI JU also aimed to encourage the participation of **patient organisations**. Integration of patient organisations in an IMI project seemed straightforward, as these organisations do not bring IP nor research infrastructure. **Twenty one patient associations have participated to IMI JU**. Examples of IMI projects in which patient groups participated under IMI JU are given in Annex 8. IMI was able to attract private foundations from outside Europe such as Autism Speaks.

A strong engagement with patient organisations was evident from the participation of those organisations in different projects and participation in the Scientific Committee. Patient organisations were also well represented in the annual stakeholder forum and other IMI events as speakers and panellists, but did not contribute to the agenda setting. IMI projects also frequently focus on patients' needs for personalised treatments, but more efforts are still needed to improve patients' involvement as full partners. Feedback or contribution of patient organisations in call topics in particular depended on *ad hoc* procedures so far. This has already been addressed by the GB but consensus on which patient groups may be representative and criteria for their input without creating a bias or conflict of interest has not yet been reached.

The participation of patient organisations in IMI projects was criticised as an attempt to train patient advocacy groups to lobby for faster approval of new medication. The important financial participation of these organisations (from Europe and US), albeit in IMI2 (because it was not possible in IMI JU), suggested this criticism was unfair. This was confirmed in the interview of the president of an international patient association.

The efforts of IMI Executive Office ensured that the patient involvement was growing, but the efforts need to be continued.

The **regulatory bodies** were seen as key stakeholders to align with, or to be included in the IMI projects. There was consensus that researchers, academics, small and medium-sized enterprises, the pharmaceutical industry and regulatory agencies need to work together to ensure that medicines were authorised in a shorter timeframe and were safer. Involvement with the regulatory bodies brought added value as these could provide the regulatory tools needed to achieve greater effectiveness and efficiency in the drug development process.

The institutions constituting the European regulatory system for medicines, which is based on a network of the national medicines regulatory authorities, and the European Medicines Agency (EMA) participated as a partner or advisor in IMI JU projects.

EMA was participating in IMI at three levels: as a member of the SC of IMI JU; a participant in stakeholders meetings; or at the Regulatory Summit. In some projects EMA was also a partner and its involvement was increasingly solicited.

In order to reach a broader audience, EMA encourages that the organisation should be approached early in the development of the projects. It was recommended that any advice given in such consultations should become publically available as such advice is often generic and can serve as a model in different projects. It was noted that briefing meetings at the start of a project may be helpful, which applies to future IMI2 JU projects or to other EU projects addressing biomedical research. The EMA requested that projects have an advisory board so that the EMA can actively participate. IMI was considered to be a useful mechanism to improve the dialogue between industry and regulators, and to raise awareness of academic partners about the importance of considering regulatory needs.

In total, in addition to 6 participations of EMA in 6 projects out of the 59 IMI JU projects, six medicines regulators from six EU Member States, and two from two countries associated at that time to FP7 (Croatia and Switzerland) have participated on 15 occasions in 9 projects out of the 59 IMI JU projects (Figure 7).

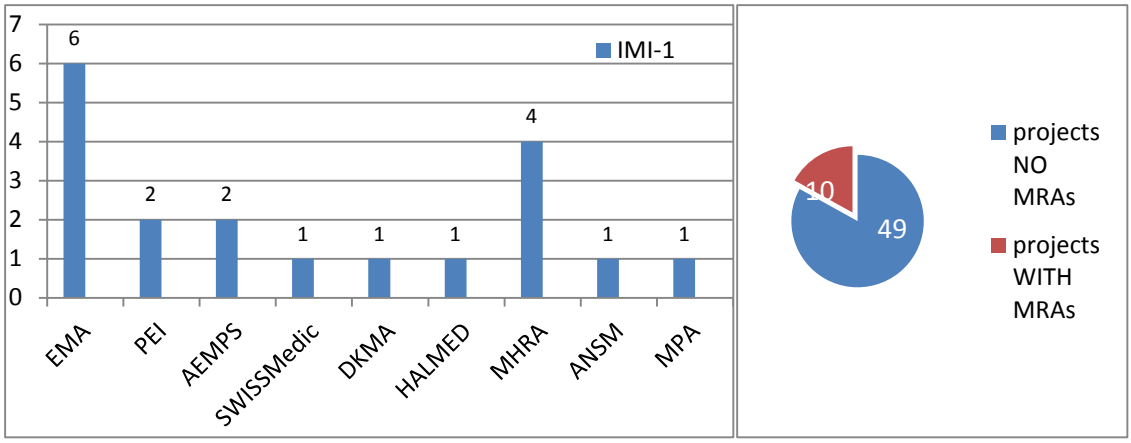
Progress has been made, but there was still room for improvement and specific actions were required to increase the participation of regulators. These actions should aim primarily to showcasing positive results from the collaboration between industry and regulators among

the European regulatory system for medicines, and at enabling regulatory agencies to participate in the definition of priorities and topics.

To increase the involvement of regulatory agencies, transparency among stakeholders and the absence of conflicts of interest will be crucial. The EMA has introduced an explicit process and internal rules to avoid conflicts. It is also vital that free access to the research results, whether positive or not, should be available for the entire network of regulators and not only for the regulatory agency that participated in the project.

The increasing involvement of regulators in general has represented a positive trend under IMI JU, together with better strategy for project sustainability (i.e. ELF) and more transparent access policies to project outcomes. However, this needs to be a widespread solution and not be limited to a few selected projects.

Figure 7: Participation of 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 Nederlands
ANSM	Agence Française de Sécurité Sanitaire des Produits de Santé, Saint-Denis Cedex, France
MPA	Medical Products Agency, Uppsala, Sweden
MRA	Medical Regulatory Agency

The most common group of stakeholders driving the research projects in IMI JU came from **academia** either from universities or from research organisations as outlined in section 6. Together academia made up more than 50 % of the participations (including the in-kind contributors) and more than 70% of the EU funded participations. The United Kingdom had the largest number of academia and research organisations participations in grant agreements (189), Germany (143), France (105), Netherlands (100), and Spain (56). Countries in Eastern Europe and Portugal had very few participations. In terms of financial contribution from EU contribution to academia and research organisations, the winner was again the UK with EUR 198 million, Netherlands (147), France (128), Germany (91) and Sweden (73). On the other hand Poland received EUR 1.5 million.

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

One of the major undeniable achievements of the IMI JU was that **IMI collaborations have enhanced trust between academic and industry partners**. There has been a mind shift that has led to better understanding of each other's needs and values. Some projects

resulted in the development of infrastructures and making them accessible for other research projects. The expert group agreed that there was also exchange of knowledge from outputs such as high level scientific publications. Furthermore, the project closeout meetings provided a powerful mechanism to develop knowledge warehouses.

Some criticisms identified from the interviews focussed on the size of the consortia which were considered too large and hence difficult to manage. Other criticisms considered the topic descriptions too prescriptive and rigid, therefore not allowing flexibility and creativity. These views were shared by several academic researchers as well as by SME participants. The size of the consortia potentially slows down the progress of the projects. Although the outputs of some IMI JU projects were significant, so far even after closeout meetings, none of results have been used to realise patient benefits.

There was consensus about a need for collaborations with researchers, academics, SMEs, the pharmaceutical industry and regulatory agencies to shorten the medicines development time, i.e. produce more effective and safer medicines obtaining authorisation in a shorter timeframe. Regulators will be able to provide the regulatory tools needed to achieve greater effectiveness and efficiency in the drug development process.

7.1.2.4 Effectiveness of the implementation

Formulation and implementation of IMI JU Research Activities

As described in section *7.1.2.1* the call topics drawn from the SRA were mainly defined by EFPIA members that wanted to commit to the scientific priorities. After consultation with the SC and SRG, the GB had the final say on the text that went in the call. During the consultation process of SC and SRG, potentially similar projects or calls planned were identified, within IMI or in other parts of FP7, to avoid overlap and duplication.

The strong commitment of the industry in the IMI JU led to an IMI specific approach in which industry consortia consisting of EFPIA members were formed around the respective identified call topics. In IMI JU all calls followed a two-stage procedure, except the call to 'Explore New Scientific Opportunities' (ENSO). This one-stage call was continuously open until December 2013 with two cut-off dates per year.

The calls described what the industry consortia wanted to address and what the respective industry partners could offer to the project, which was then translated into the corresponding in-kind contribution. Applicants wishing to join forces with the industry consortium responded to the calls with an "Expression of Interest" and offered complementary expertise to address the topic goals.

After an eligibility check, the applicant proposals were reviewed and ranked by independent experts. The consortium that submitted the top-ranked proposal was invited to submit a full proposal merging the industry and the applicant consortium. The full proposal was then reviewed by independent experts.

The independent experts were selected by the IMI scientific officers based on the subject matter competence for a given topic, maintaining gender balance and geographic distribution and following the same rules of eligibility as in FP7. According to an IMI Executive Office representative a minimum of three, but mostly five to seven experts per project evaluation were consulted. EFPIA members could provide input on the competences required but were not involved in the selection of experts. Also the SC was invited to review the expert lists.

EFPIA members and the GB were not involved in the evaluation of the proposals to avoid a conflict of interest, since they designed the annual implementation plans and identified call topics.

The applicant consortia and the industry consortia were not in contact before the evaluation. The industry consortia through the coordinators had some insight into the relevant applicant proposals. This insight allowed the coordinators to explain during the evaluation what they wanted to achieve in the project and what was interesting or missing in the applicant proposals. The industry consortium however could not participate in the evaluation of the applicant proposal. Only one applicant proposal was selected to merge with the industry consortium.

Several interviewees have indicated that as a consequence, opportunities may have been missed as other consortia could have been formed to address the call topic, and as such valuable expertise may have been excluded. Some have advocated the (partial) merger of

applicant proposals in the final consortium so that additional and complementary expertise would be brought into the final consortium.

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, if that leads to the exclusion of some of the best infrastructures and scientists, or largest biobanks. In some cases efforts were then (partially) duplicated by the IMI consortium.

The selection of the winning applicant consortium was perceived to lack transparency, although the independent observers of the review process were generally very satisfied with the evaluation process. However, several sources reported contacts prior to the evaluation between the leading industrial partners and the applicant consortium, which was denied by IMI representatives. Pre-evaluation contact would generate a competitive advantage for that applicant consortium as more information and details on the specific expectations of the industry consortium may have been communicated. It was indicated that some of the best assets were not used in some of the IMI consortia, suggesting that some opportunities may have been missed. Some of the best European research groups indicated they hesitated to reply to calls for applicant proposals as there was a view that informal preformed consortia already existed. If certain partners were preferred, this should be transparent and indicated in the call.

The issue of the pre-evaluation contacts between lead companies in a call topic and an applicant consortium has also been suggested as perhaps (part of) the reason why the participation of eastern European countries was significantly lower than that of countries which have a tradition of collaborating with big pharmaceutical companies or are home to, or hosting, the lead companies. The participation of eastern European countries in FP7 was 5.45%, while for IMI JU this was only 1.75%, which is more than 30% lower than in FP7.

The call topic selection and development were considered too top-down and industry driven with insufficient inclusion of input from the academic, research and clinical centres, regulators and patient groups, which resulted in call topics that were considered too narrow and not allowing sufficient flexibility for participation of SMEs and academia. As the industry consortia were to be formed around the respective topics, thereby allocating in-kind contributions, EFPIA members found it logic that they were determining the call topics.

The call topic selection process was not considered to be sufficiently transparent, even though the SRG and SC were consulted for advice. It was generally unclear what happened to the feedback from the advisory bodies. The involvement of patient groups in providing feedback was only recently (under IMI2) implemented and also regulators were not involved early enough in the process of call formation and identification of currently unmet needs. Wider involvement of various stakeholder groups, especially the academic research and clinical centres in the call topic development could enhance the absorption and implementation of more innovative ideas to solve some of the more complex research problems in the areas of unmet medical needs.

So far six of the 21 finished IMI JU projects were finalised with a closeout meeting. The closeout meetings were installed to summarise the projects outcomes, extract lessons learned, and identify the challenges for the different teams. The closeout reports give a good overview of the project outputs, which may stimulate the uptake in future projects.

An overview of the financial contribution per scientific area was given in figure 4. At the time of writing, the final reports on the IMI funding were accepted for only three of the finished projects; the final EFPIA funding report has not been accepted for any of the projects. However EFPIA in-kind contributions were already reported and accepted and amounted to EUR 385.2 million and total EU funding was already accepted for an amount to EUR 411.2 million according to Annual Activity Report 2016.

IMI JU Knowledge Management and IP Policy

The IMI JU Knowledge Management and IP Policy was based on the following documents: IMI IP Policy (2007),[22] IMI IP Guidance Note (2010),[23] and the IP Policy in IMI JU actions

[22] IMI Intellectual Property Policy, 2007
[23] IMI IP Policy Guidance Notes for IMI Applicants and Participants, November 2010

(2008)[24] all available at: http://www.imi.europa.eu/content/intellectual-property-policy, and the Grant Agreement (last modified in December, 2013) available at:

http://www.imi.europa.eu/content/documents#grant_agreement.[25]

The guiding principles for the IMI IP Policy ensure that it is:[26]

- aligned with IMI objectives as a public-private partnership;
- adapted to specific research needs and challenges;
- enabling broad participation of:
  - private and public entities in IMI projects (academic institutions; small biopharmaceutical companies; large biopharmaceutical companies); and of
  - patients' organisations and regulatory agencies;
- promoting knowledge creation, together with its disclosure and exploitation;
- achieving fair allocation of rights;
- rewarding innovation;
- providing flexibility for participants to establish the most appropriate agreements serving the project objectives.

The guiding principles for dissemination are:

- the obligation to disseminate the foreground; and
- to disseminate as soon as reasonably practicable, but no later than one year after project expiry or termination.

The material subject to dissemination was described in detail in the Grant Agreement. IMI IP and Dissemination Policy were designed as one flexible policy to serve multiple interests. The process aimed to enhance bringing medicines to market by providing incentives for participation, freedom to access, compensation for background, dissemination of information thereby supporting European biopharmaceutical industry.

IMI has made an effort to discuss, clarify and guide its project applicants and beneficiaries as well as other stakeholder groups through the IPR issues.

One issue when negotiating the IP was the extra level of complexity brought by the large consortia. When the project was closer to the interest of the larger pharma companies, the agreement became very elaborate and technical in a way which was difficult for academic partners or SMEs to comprehend.

Most academic partners acknowledged that the IMI projects in which they had been collaborating were successful. Nevertheless, some partners indicated that the discussions concerning IP issues took too long before the project start, significantly delaying the projects. In at least one case, the IP negotiations had been taken so long, that the project ended before the partner was able to deliver the work package, as this part of the project was dependent on the results from other work packages.

7.1.2.5 Inclusiveness of the best European players

The information reported in section 6 indicated that more than half of the academic participants in IMI JU projects were affiliated to the best universities and research institutions. Similarly, more than half of the European companies that participated to IMI JU projects ranked among the best companies (in terms of R&D investments) in Europe and the world top 100 companies.

IMI projects have brought together all types of stakeholders. In IMI JU, however, mid-cap companies could not receive funding, while in many cases these companies still depend very much on external funding. As discussed above this has now been addressed in IMI2 JU.

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[24] www.imi.europa.eu/sites/default/files/uploads/documents/ipr-helpdesk-doc-on-imi-ipr-policy_en.pdf
[25] IMI JU Model Grant Agreement Annex II – General Conditions, Part C, IMI-GB-DEC-2013-3
[26] www.imi.europa.eu/sites/default/files/uploads/documents/Intellectual%20Property/GuidanceNote_Draft3-1_10Nov2010.pdf

To ensure that the best academic groups or best SMEs contributed to innovation in certain fields, input from these types of stakeholders should also be taken up in the design of call topics. This has been addressed in IMI2 JU and the opportunities to contribute to topic development or even topic suggestion have significantly improved with a wider consultation process that involves a wide range of (putative) stakeholders.

An issue that was a matter of debate since the very beginning of IMI JU and that is still preventing some of the major European institutes from broad participation in IMI projects was how the IP policy was handled by the JU. Although, it was clear that much can be negotiated before starting an IMI project, the fact that no exclusive rights can be guaranteed on side ground results, jeopardised the exploitation of those results as venture capital providers demand exclusive rights. It was argued that since the Bayh Dole Act in the US,[27] academia obtained a credible tech transfer position to translate more scientific results into innovative applications for society. This has proven instrumental to setup the large numbers of start-up 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 both from academia and SMEs from participating in IMI JU projects, especially those potential partners that may be expected to deliver the most important results or have the highest ambitions and strongest tech transfer activities.

The IMI Website in its IP section highlights projects such as European Lead Factory (ELF) and eTox as some of the best practices of IMI IP policy in action, in particular the ELF IP regulations have actually prevented leading life science organisations from participating in this consortium. There are examples of research institutions that are running their own smaller version of partnership programs for hit-to-lead development activities on key discoveries. This issue, although acceptable to EFPIA companies and perhaps not critical to IMI JU functioning, may have resulted in the absence of some of European leading research groups and most innovative SMEs in IMI projects.

7.2 Efficiency

This section deals with how efficiently the IMI JU mission and strategy have been implemented to achieve the main objectives. It first analyses the clarity 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 IMI JU as outlined in the Council Regulation and what the effect of the change was from operating under different programming periods under FP7 and Horizon 2020 while the IMI JU projects all started in FP7 and most are still continuing. 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 score of the robustness of the monitoring and control systems within IMI JU as a whole and in individual projects and project participants. Under the modalities of IMI 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.

7.2.1 Joint Undertaking mission and governance

7.2.1.1 Roles of the different governing and advisory bodies

In general, the roles of the different governing bodies in IMI JU appeared to be clear and well defined. The single decision making body of the IMI JU was the Governing Board (GB). The day-to-day management of the IMI JU was the responsibility of the Executive Director supported by his IMI JU Executive Office staff. The third governing body was the Scientific Committee (SC), although it had no decision making or executive functions but did have an advisory role in the area of research agenda and scientific priorities. Two additional advisory bodies were the States Representative Group (SRG) and the Stakeholders' Forum.

The IMI JU Governance structure depicted in figure 1 in section 3.1.3 was taken from existing IMI documents. However, the expert group questions whether this figure reflects

[27] 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.

reality with respect to the level of decision making. The figure suggests that the Scientific Committee has the same decision-making power as the Governing Board, while it is clear from the legal documents that the Scientific Committee has been merely an advisory body with marginal or no influence on the Governing Board, next to the two external advisory bodies: the IMI States representative Group and the Stakeholders Forum. In addition, the arrows suggest there was interaction and communication between the different bodies. In fact, there were interactions between the IMI Executive Office and the different advisory bodies, but not between these bodies. This was reported in several interviews, including the representatives of the governing and advisory bodies of IMI JU, that the advisory groups were not familiar with each other nor of the scope of activities carried out by each of them. These interviews also suggested that neither of these bodies had significant influence on the activities of the IMI JU and its operations. Their roles, as voiced by their respective representatives have been outlined below.

Role of the Governing Board

The Governing Board (GB) was the IMI JU main decision making body. The GB comprised two members with different goals and modes of operations, i.e. EFPIA and the EC, which rendered the decision making processes difficult. The IMI Executive director as well as the Commission and GB members are accountable for reporting to the European Parliament (EP), which expects evidence of bringing benefits to society and patients as well as of evidence of 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 goals are clearly different and often created tension and difficult negotiations to align interests.

Role of the Executive Director

The IMI JU Executive Director, supported by the Executive Office, was strictly an executive body with little to no decision making power about the overall structure and strategy of the IMI JU. All important elements of the IMI JU operations had to be approved by the GB. More details on the IMI Executive Office operational efficiency is discussed in section 7.2.3 of this document.

The IMI scientific officers were involved in the logistics but did not contribute directly to the selection of project proposals, which was not in their mandate. Projects were assigned as much as possible to align with the expertise and background of the officers. One of the tasks of the IMI scientific officers was to select expert evaluators from the EMI expert database.

Role of the SC

The main role of the SC was to give strategic science-based recommendations to the IMI JU GB and Executive Office and to advise the GB on the continued relevance of the Strategic Research Agenda and the scientific priorities that formed the basis for the specific IMI Call Topics. It was the EFPIA members that design the calls with different rounds of discussion with several EFPIA companies willing to contribute in-kind to the research on a given call topic. The call topic proposals in IMI JU have been made available to the SC and SRG for comments and advice. However, from the available documentation and the interviews it was unclear how the GB deals with recommendations of the SC and whether the SC has sufficient feedback from the GB. While the chair of the SC was quite satisfied with the communication between the SC, the GB and Executive Office, other SC members were not aware whether advice they provide was taken into account.

Role of the SRG

The SRG disseminated information from the IMI JU to its national and regional stakeholders, and advocated the need to take account of important national or regional trends with respect to the IMI goals and work programmes. The SRG was consulted by the IMI JU on the work programme and specific call topics to avoid duplication of efforts when similar projects were ongoing in other programmes.

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 Executive Office and IMI current and potential beneficiaries. It was also an important promotional event demonstrating the main achievements of IMI JU and promoting the ongoing activities under IMI2 JU.

7.2.1.2 Effect of the overlap of IMI JU and IMI2

The overlap of IMI JU and IMI2 JU projects, given the changes in the main objectives, governance structure and the legal framework has created considerable challenges for the IMI JU Executive Office as well as for the GB assisted by its advisory bodies to realise this mission. This has been confirmed by some of the interviewed representatives of the IMI JU Executive Office, who indicated that operationally it was difficult to work under the two different frameworks.

The mission of IMI JU, launched in 2008, was *"to support the development of efficient and safe medicines for patients across Europe by removing research bottlenecks in the drug development process and by increasing investment in the biopharmaceutical sector in Europe."*[28] The mission of IMI2 JU has been reformulated 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."* and is pending the approval of the GB at the time of writing of this report.

In IMI JU it was specified that the goal was to "significantly improve the efficiency and effectiveness of the drug development process with the long-term aim for the pharmaceutical sector to produce more effective and safer innovative medicines".[29]

Some of the interviewees from various IMI JU bodies reported that the differences between IMI JU and IMI2 JU processes and other instruments of the relevant framework programme (FP7 or Horizon 2020) was an ongoing source of confusion.

IMI2 JU, launched in July of 2014, included goals "to develop next generation vaccines, medicines and treatments, such as new antibiotics."[30] Six specific objectives were defined to reach these ambitious goals. As these objectives were quite different from IMI JU, a discontinuity was introduced in the ways to monitor progress towards meeting the goals and objectives of both phases of the JU.

As a consequence, especially because most of the IMI JU projects were still ongoing at the time of writing this report, the IMI Executive Office staff members were navigating through two different frameworks both strategically and operationally. It has not helped that IMI JU has failed to produce measurable and SMART KPIs that would provide metrics to convincingly demonstrate the progress to achieve its goals and objectives as well as the socio-economic impacts of both phases of the JU.

7.2.1.3 Robustness of monitoring and control systems

The robustness of monitoring and control system in IMI JU can be analysed from three perspectives according to the expert group:

i) progress monitoring: a KPI system to monitor progress in the program as a whole and within individual projects;
ii) processes monitoring: means to assure efficiency of the processes and procedures in IMI JU with respect to calls for proposals, time to grant, spending efficiency etc.;
iii) monitoring and control of eligibility and compliance of all IMI JU activities, including individual projects.

Progress monitoring

The monitoring of progress repeatedly received criticism during the previous two interim evaluations as the KPIs were considered insufficiently robust. In the early stages of IMI JU implementation, the metrics involved primarily scientific metrics such as publications with impact factors, citations, patents as well as metrics on collaboration and level of interactions between various IMI JU project participants.

[28] IMI Annual Activity Report, 2010
[29] www.imi.europa.eu/content/history
[30] www.imi.europa.eu/content/imi-2

The First IMI JU Interim report identified this weakness in its executive summary and set of recommendations: [31]

> "The lack of identified and used key performance indicators by the IMI JU risks making the output of the whole initiative diffuse."
>
> Recommendation 7: Develop monitoring and evaluation processes.
>
> "There is a need to develop sound monitoring and evaluation processes, to generate the indicators and evidence needed to strengthen IMI's capabilities for monitoring of projects and taking strategic decisions. The results should be measured regularly and accountability for results should be ensured."

The experts performing the second IMI JU interim evaluation were unsatisfied with the progress in defining and implementing a robust KPI system, as evident from the following statements: [32]

> *"Recommendation 2: Alongside the existing KPIs, aggregated KPIs need to be developed and measured in order to quantitatively demonstrate the IMI impacts and socio-economic benefits."*
>
> Whilst KPIs have been developed, they have focused primarily on scientific output. The socio-economic potential has not been sufficiently well captured. The fact that IMI has helped to create over 1500 direct new jobs, for example, is commendable and more metrics of that kind need to be in place.
>
> The evidence and opinions of the stakeholders support the conclusion that the definition and way of presenting the KPIs does not sufficiently encompass the value proposition of IMI. The scientific metrics (publications, networks of academics, etc.) have been collected and are quite convincing (…). These indicators, however, do not address the downstream macro-economic impacts or the general IMI objectives. The expert group is aware that it is difficult to calculate a return on investment (ROI) from R&D in simple terms. Nonetheless, a convincing long-term strategy and system are needed to better evaluate the overall IMI impact on the biopharma industry in Europe, on the healthcare system and on the European economy. The newly proposed set of KPIs does not yet appear to address this issue.
>
> During the next period, the development and monitoring of a set of KPIs to provide greater impact assessment will need the GB's sustained attention."

In 2013, following the second interim evaluation there were a few qualitative KPIs added to the 2011 monitoring framework (such as "the extent to which IMI projects cover the value chain of drug development" or "validated standards, measurements, methodologies, models, simulation technologies, tools and platforms successfully integrated in the R&D process")[33] that were difficult to measure and could not be easily aggregated. There was no reference or solid baseline for measuring progress.

Following the launch of IMI2 JU, the above set of KPIs was revised to be better linked to the main policy objectives of IMI JU (established under Council Regulation 73/2008 of 20 December 2007) and IMI2 JU (replacing and succeeding IMI JU and established through Council Regulation 557/2014 of 6 May 2014) and focus on performance in the following key strategic areas of the Joint Undertaking's activities, namely:

(1) the coverage of the research portfolio, i.e. adequate implementation of the annual scientific priorities;
(2) the degree of progress of IMI projects in delivering pre-set results and achieving targeted research;
(3) performance;
(4) the impact of the IMI programme on the regulatory framework as well as EU competitiveness;

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[31] www.imi.europa.eu/sites/default/files/uploads/documents/Governance/FirstInterimEvaluationOfIMI2011.pdf
[32] www.imi.europa.eu/sites/default/files/uploads/documents/Governance/2ndInterimEvaluationIMI.pdf
[33] www.imi.europa.eu/sites/default/files/uploads/documents/AAR2013.pdf

(5) the level of collaboration and SME participation so far;
(6) the level of involvement of patients groups;
(7) the extent of communication and awareness of IMI among all target groups; and
(8) the overall efficiency, budget execution and the level of awareness of the IMI Executive Office.[34]

The above KPIs were still subject to the same criticism. The KPIs are insufficient to measure the socio-economic impact and industry competitiveness, although they do provide some measures of openness/ stakeholder involvement, process efficiency and scientific/ project output (although in many instances still based on qualitative examples).

During this final evaluation of IMI JU, several stakeholders were interviewed and asked about this issue. A new Performance Measurement Framework - under discussion for approval by the GB at the time of the evaluation - was presented by Pierre Meulien. This framework was built according to coherent intervention logic. However, the expert group identified serious flaws in the proposed framework and invited the IMI Executive Office and Governing Board members to rework the framework. The expert group unanimously agreed that **the proposed framework was not relying on SMART (Specific, Measurable, Achievable, Relevant and Time phased) KPIs**. The expert group concluded that it was **unlikely that the proposed framework will significantly improve the performance assessment process**.

More specifically, the expert group indicated that the KPIs have not been and were still not sufficiently aligned with the stated objectives of IMI JU and outlined that every key objective of IMI JU should be reflected by a simple measurable KPI. A number of the proposed KPIs addressed a mixture of examples and numbers and were more qualitative indicators with no target for what should be achieved.

The expert group recognised that, despite repeated recommendations and criticism from the various expert evaluator groups, the development and testing of an accountable Performance Measurement Framework including SMART KPIs has been delayed under IMI JU and that no baseline metrics have been identified even after the repeated recommendation in the different independent expert reviews.

The lack of baseline metrics was seen as a major gap. The expert group believed that baseline metrics, in some, or even in most cases, could still be retrospectively integrated and used.

The expert group found it particularly difficult to analyse the socio-economic impact of IMI based on the Performance Measurement Framework presented. The inclusion of baseline metrics would have improved the ability of the IMI JU Executive Office and review panels to analyse progress. The last socio-economic impact report prepared for IMI JU could have been used to identify relevant SMART- KPIs.

Within the Innovative Medicines Initiative Logic Model and Performance Framework 2016 document published on the IMI website, the IMI 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.

Yet it has so far failed to provide a set of SMART KPIs to measure these outcomes.

Process monitoring

When monitoring the efficiency of the functioning of the IMI JU Executive Office, the data it provided indicated that IMI Executive 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 IMI JU activities and projects seemed to include adequate controls to assure eligibility of costs as well as efficient budget use and limit fraud. The monitoring system identified thus far only one case of scientific fraud. The funding for that partner was stopped after an audit launched by IMI Executive Office, which confirmed the efficiency of the process monitoring system.

[34] www.imi.europa.eu/sites/default/files/uploads/documents/Governance/IMI_AAR2015.pdf

Furthermore, it was brought to the attention of the expert group that there seems to be a difference in obligations between EFPIA members and the beneficiaries under IMI JU. In IMI JU there was no regulation in place to prevent that a company withdrawing 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 IMI JU recognised this as a system deficiency. There was no mechanism in place to enforce the industry commitment made at the start of a project. In practice, in cases of industry member early withdrawals there were negotiations within the consortium and with EFPIA to find a solution. Companies not fulfilling their commitments cannot be penalised, but EFPIA functioned as a broker to find an equitable commitment among existing or new consortium members. EFPIA, as representing member in the GB did not appear to have an enforcement system in place for their members.

There were few of such cases, but the 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. It should be noted, however, that the in-kind budget in IMI JU needs to match at programme level; differences at the project level are acceptable. The expert group assessed that IMI JU had no mechanisms in the programme available to address the risk of unbalanced contributions and ensure that the in-kind (industrial) contributions match the public cash contribution. It was clear to the expert group that there are different systems of risk management on the public and the private side of the partnership.

Progress monitoring and use of funding

As part of the control system, expert audits addressing beneficiaries and EFPIA partners were organised. There was a two-level control first focussing on cost claims of eligible costs and then a second level of *ex-post* control, which can lead to adjustments. This procedure was also followed for the in-kind part of the budget. 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, it was mentioned that EFPIA companies under IMI JU have been reluctant to disclose detailed cost break-downs per project, in particular the personnel costs, 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 SRG have been insisting on increasing transparency of the calculation rules and composition of in-kind contributions by pharma companies and is part of a discussion that was continued under IMI2 JU.[35],[36]

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, IMI JU should enable a similar analysis as for the other Horizon 2020 programmes, with detailed breakdown analysis of participants.

As outlined in more detail below, it should be noted that the in-kind budget needs to match the EU contribution at programme level, while differences at the project level are acceptable. Although before the topic launch and during projects implementation the in-kind commitments are thoroughly monitored, there were no legal/financial mechanisms available to guarantee that the industrial commitments of in-kind contributions were made. According to an IMI executive official pharmaceutical companies that would not fulfil their commitments would still be eligible to participate in future projects. It should be noted that possible IMI JU deficits of the in-kind budget cannot be transferred to IMI2 JU.

Monitoring of the progress at project level has not yet resulted in the premature termination of an IMI project. Nevertheless, sometimes it was necessary to reorient parts of the project along the way. Continuous steering and adapting when appropriate was both possible and

[35] www.spiegel.de/international/europe/imi-in-eu-project-citizens-count-corporations-cash-in-a-1025550.html
[36] http://sciencebusiness.net/news/77013/Reprieve-for-under-fire-EU-pharma-partnership-after-Parliament-vote

advisable. IMI projects have been designed as large-scale research networks and infrastructure platforms with multiple, interdependent deliverables. Stopping a project would therefore mean a bigger loss. An annual analysis of the outputs linked to the budget spent and combined with an evaluation of the deliverables and resources would have been a good practice as a final project report can only give an overview of final deliverables, but does not include any other form of analysis.

A solid performance measuring system should have made it more straightforward to objectively measure progress and correlate with the budgets allocated.

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;
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 IMI.

Direct funding to academia and SMEs coming from the European Union followed the same rules of eligibility and control as other programmes under the framework programme.

In line with the legal basis, the in-kind contribution must match EU funding for the whole IMI JU programme, but not at the level of each project. Strict controls and the electronic tools/database were in place, although this did not include an enforcement mechanism to ensure the final matching of private and public budgets at programme level. At project level both overspending and underspending of in-kind contributions were reported.

In the opinion of a senior level member of the IMI Executive Office if the gap between the in-kind commitment and the public funded part were reasonable, "it would be politically acceptable when IMI JU had delivered good, high-impact results". A significant gap in in-kind industry contribution and the public cash funding could however be interpreted as a failure of the IMI programme in the context of private funding leverage and industry investment in R&D in Europe. In reality, the funding gap between industry contribution and EC contribution remained low for total project costs in all running and completed IMI projects as of the end of 2016. There was a difference, calculated as (EFPIA-EC)/(EFPIA+EC), of 0.7% in committed costs and a difference of -3.3% in accepted costs.[37] Overall, these differences appear to be low and within acceptable limits.

Analysis of in-kind contributions showed **high variability of the in-kind contributions among the EFPIA companies**. There was no correlation seen between the in-kind contribution of the EFPIA companies and their ranking according to R&D expenditure (Figure 8). In some cases smaller EFPIA members have provided significantly higher in-kind contributions to IMI projects than their larger counterparts. There were also large discrepancies among similar size R&D leaders. A more detailed analysis is made in section 7.3 EU Added Value.

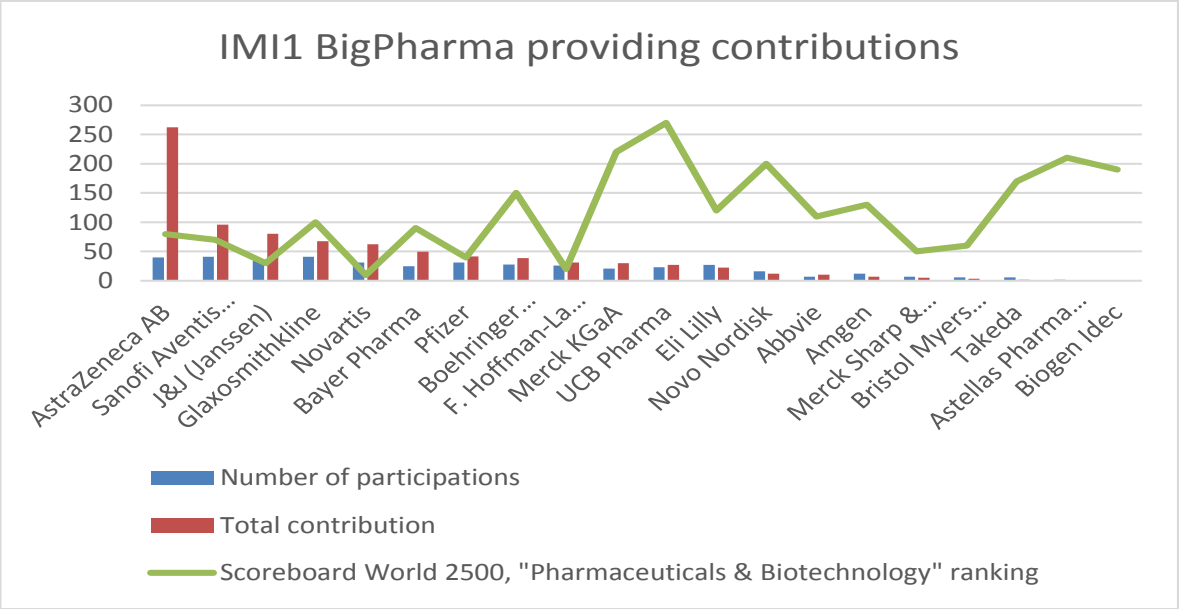
Possibly **these differences result from various levels of alignment of corporate strategies with IMI priorities and the PPP model**. An important aspect is that IMI projects have to fit the core business of the company and the company's philosophy embracing public-private partnerships as a means to gain competitive advantage or reduce cost of bringing new therapies to market.

There was also a clear difference observed between EU-based and non-EU based EFPIA companies in terms of the level of in-kind contribution. The total contribution to IMI JU by EU headquartered companies was over EUR 653 million while for non-EU headquartered companies it was only approximately EUR 300 million. However if European (i.e. including Switzerland & Iceland) vs. non-European companies have been considered, this gap widened to EUR 756 million vs. EUR 196 million. Per European participant the average contribution was EUR 28 million versus EUR 15 million for companies with headquarters outside of Europe.

[37] IMI2 JU Annual Activity Report 2016

Under IMI JU 10% of the in-kind contributions were eligible from costs incurred outside of the EU. While attracting global companies to have activities in Europe was a major goal of the joint undertaking, this however reduced the possible leveraging power to support the investments in the EU and associated countries by 10%.

Figure 8: In-kind contributions vs. rank in R&D spending



It was clear from Figure 8 that there were substantial differences among the EFPIA companies in IMI JU participation and engagement. AstraZeneca was a clear leader, while companies that were top ranked in the Scoreboard World 2500 such as GSK, Sanofi, Novartis, Pfizer or Roche contributed almost an order of magnitude less. Members such as Boehringer Ingelheim, or UCB Pharma contributed very high relative to their lower ranking. There was no correlation between the rank in R&D spending and in-kind contribution to IMI JU. In fact some of the global leaders such as Novartis, Pfizer on Merck (MSD) have invested relatively low budgets in IMI JU projects when compared with their World R&D scoreboard ranking (top 5).

Some companies like AstraZeneca spent significantly more of their annual R&D programme in IMI JU type of projects than for example Hoffman-La Roche. Table 3 gives an overview of the in-kind budget allocated to IMI projects by the main pharmaceutical companies in relation to their annual R&D budget.

Table 3: The annual R&D budget of selected EFPIA companies in relation to their in-kind contributions to IMI JU (scoreboard 2015)

EFPIA company	R&D expenditure (2015) million EUR	In-kind contribution committed to the entire IMI JU duration million EUR	% R&D budget 2015, versus in-kind contribution committed to the entire IMI JU duration	% of the total IMI JU in-kind budget from industries
F. Hoffman-La Roche	8640	31	0.4%	3.3%
J&J	8300	80	1.0%	8.4%
Novartis	9000	63	0.7%	6.6%
Sanofi	5250	95	1.8%	10.1%
GSK	4210	68	1.6%	7.1%
AstraZeneca	5120	262	9.0%	27.5%

Examples of impacts of IMI JU projects on companies R&D can be found in Annex 9.

It should be noted that the companies' R&D budgets cover a broader spectrum of research and development than the IMI projects, which focussed primarily on precompetitive research. Nevertheless, when comparing the R&D investments of the pharma companies with their total IMI JU in-kind contributions, it was clear that **the R&D investments in IMI**

projects of the pharmaceutical companies, with few exceptions were relatively small. These data raised questions about the actual significance and impact of IMI on the competitiveness of the European pharmaceutical industry.

However, the level of in-kind contribution from the industry may have reached its maximum as it needs to be matched by the EU contribution. As the latter was secured in the Council Regulation, and already took a significant part of the budget of the Health theme in FP7, in the current constellation the in-kind contribution from EFPIA members could not have been increased. Other mechanisms to achieve a stronger leveraging effect may have to be considered.

Some of the interviewed IMI beneficiaries and other stakeholders advocated milestone-based payments. According to IMI rules this would in principle be possible, but it could not be a standard procedure and would need to be on a case-by-case approach as in some cases significant investments were needed 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. It could have improved the flexibility and lead to faster progress and overall improvement of projects. This may be considered in later programmes.

In terms of efficiency an obvious question was whether the objectives of IMI JU could have been achieved with lower costs from the public budget and using the regular calls and instruments of the framework programme. The main argument against this premise was that IMI JU produced a considerable leverage of private funds, which could not have been achieved under the regular framework instruments.

Overall at this stage of IMI JU, the expert group believed that the total IMI JU funding of the combined EU cash and industry in-kind contribution was sufficient to achieve its ambitious objectives as set out in the regulation establishing the IMI JU PPP and the *ex-ante* impact assessment.

7.2.1.5 Communications and dissemination strategies

Communication and dissemination of the IMI JU was based on the IMI Communication Strategy document that was created and approved in 2015, which was after IMI JU had ended. As the document was only finalised and approved by the Governing Board after the last IMI JU calls for proposals were launched, the strategy is really more relevant for IMI2 than for IMI JU. It should be noted that the strategy was updated annually and the last update took place in January 2017, but the document is not publically available.

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. Communication is an important area which is referred to several times in further sections of the report.

The 2016 Annual Activity Report of the IMI JU detailed the communication activities that have been realised through several communication channels and targeted a wide range of IMI stakeholder groups. Various channels were used to address internal (inside the IMI consortia) and external target groups, including IMI stakeholders from research organisations, SMEs, patient organisations, regulators as well as the general public, politicians, Member State representatives. These channels include: events, such as international conferences, stakeholder fora, webinars, meetings, information sessions, workshops, roundtables, debates. Also scientific peer reviewed publications, electronic newsletters, other on-line materials, printed articles and information brochures were an important communications channel. Furthermore also the website and social media, such as Facebook, Twitter and LinkedIn, as well as traditional media channels like news, newspaper and periodical articles, or movie clips were used to provide information.

According to the IMI Communication Strategy document, the IMI 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 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.

According to the results of the IMI JU Beneficiary Survey, which should be interpreted with caution as a result of low response rates, the following communication channels of IMI 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).

In terms of communication and dissemination efficiency to the general public, the perception evident from the public consultation, which should be treated with equal caution for the same reason as the beneficiaries' survey, was that there is some room for improvement. Only 42-43% 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 that the IMI JU website provided easy and effective access to knowledge generated by the projects funded under IMI JU. Although the most recent public consultation focused primarily on the current IMI2 JU, the IMI JU website is designed to communicate both on IMI JU and IMI2 JU results.

It was reported by several interviewees there was room for improvement with respect to communication and knowledge dissemination, which may also improve the sustainability of outcome of IMI projects. Not only the IMI JU Executive Office has a role here, also project coordinators should be involved more and preferentially as part of the project from the start. The main objective of the communication strategy should not only focus on increasing the awareness of IMI JU, but should also highlight the attractiveness and European added value of the initiative so as to attract more stakeholders to participate in IMI JU projects.

Although also only relevant for IMI2 JU, 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.

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.

Monitoring will further address the levels of patient interest in IMI, as measured by involvement in committees and panels, visits to patient pages of the website, interest in social media, and attendance at events.

As the monitoring under IMI JU lacked a solid performance assessment methodology that measures scientific output in the form of publications, and also gives insights in socio-economic impacts realised, the varying perception on IMI JU is difficult to contradict.

There was a need for broader communication on the results and outcomes of IMI research activities to build further on these outcomes and to take away the continuing concerns about the lack of transparency of IMI activities. Indeed, access to IMI project outcomes for entities outside of the relevant consortia was by several interviewed stakeholders and expert group members reported to be difficult. There was a need for a built-in system that ensures platform accessibility to the entire community of academic centres and industry. Access policy should be clear at the project level as well as at the IMI JU level. This does not necessarily mean access for free, but open access on fair and reasonable terms. Such access policy should be part of the communication and knowledge dissemination strategy.

In conclusion, although the communication strategy, tools and channels to raise awareness have improved and appear to be logical and well thought through, reasonable and extensive, they mainly are of importance for IMI2 JU and their implementation (i.e. website tools, clarity and content) leave room for improvement. In addition, the monitoring of the effectiveness and impact of the communication strategy could be further enhanced by broader communication and ensuring broad access to results and outcomes of IMI JU projects.

The IMI JU Executive Office has a most important task to increase awareness of the positive outputs of IMI projects. This should be also an important responsibility of project coordinators to better communicate the project results using different fora as part.

7.2.2 Operational effectiveness

In general, the GB and the IMI JU Executive Office have taken significant efforts to achieve the objectives. The meetings, webinars and help desk were very well appreciated by stakeholders. The interactions of the GB and the IMI Executive Office with the SRG have improved significantly over time with respect to reporting on statistics and outcomes of the ongoing projects.

There were comments however from one of the SC members that sometimes 'artificial consortia' were formed, because of too much focus on gender and geographical balance. In addition, the expert group heard an opinion that it was perhaps more efficient and productive to rely on existing consortia that have been proven to work effectively and efficiently rather than forming new ones. The expert group disagreed with such an approach and found no evidence in the data that would support consortia to be formed with the main objective of reaching the correct geographical or gender balance. In fact, the data show that there was very little geographical balance among IMI JU beneficiaries with almost 60% participation and funding concentrated in four (UK, Netherlands, France and Germany) of the 27 Member States. Lack of openness to new consortia and beneficiaries would not only prevent IMI JU from welcoming new opportunities and breakthrough ideas generated outside of the established networks, but also destroy true competition – the key element of innovation.

7.2.2.1 Satisfaction of beneficiaries with the service of the JU

The project coordinators survey, although very limited in terms of the numbers of respondents (34), who were over-represented by industry (>60% of responders were from industry contributing in-kind) and therefore not providing an overall view of any statistical significance, gives some indication about the level of satisfaction of IMI JU beneficiaries.

The positive comments and responses concerned primarily direct channels of communication with the IMI JU Executive Office (discussed in detail in the previous subsection). The majority of responders were generally satisfied or very satisfied.

The interactions with, competency, willingness to help and efficiency of direct interactions with the IMI JU Executive Office was also viewed very positively (in general 74 to 94% of the responders were satisfied with the various forms of interactions and the efficiency of the IMI JU Executive Office). There were some comments that the direct collaboration with the scientific officers has improved over time of IMI JU functioning and that it is much more efficient than getting feedback from financial or legal departments of IMI JU. There were also comments about 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 by the responders with reserved optimism (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 IMI JU was much more reserved or even negative.

For instance, only 35% of the responders strongly agreed that the evaluation process was clear and transparent, 32% "slightly agreed" with this statement, while over 20% questioned its transparency and openness. There were additional comments about "the role and potential control rights of EFPIA partners in two-stage proposals not exactly clear" from SME beneficiaries.

There were mixed feelings among the beneficiaries with 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 consider they did not receive clear explanation for their application not being selected for funding, with additional comments about the timing of the proposal submission deadlines (immediately after the new year's / holiday break or after the summer vacation).

During the interviews several stakeholders expressed concerns on different aspects of IMI efficiency, but the main critical voices pertained to:

- Lack of accountability by EFPIA companies for the commitments made and for transparent cost allocations as well as no consequences for defaulting industry partners;
- Top-down approach for call topic design making the calls too narrow and prescriptive, on the one hand not leaving much room for creative ideas coming from outside EFPIA on the other often preventing SMEs from participating; furthermore a few (including unsuccessful) applicants suggested that by publication of the topic, the winning consortium was often already informally formed and only in very limited cases the outcome of the competitive call process had proven otherwise, raising concerns about the transparency and openness of the process;
- Slow decision making processes in very large consortia and IP / access rules generally weakening or destroying the ability to raise private funding for progression of most innovative assets discouraging the best research institutions in Europe as well as IP-based asset driven SMEs from participating.

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

There was consensus that this was much improved since IMI2 implemented the Strategic Governance Groups or SGGs to address this issue. In some cases the interest to further support outcomes from IMI projects may be limited as it depends mainly on further support by the companies involved, and frequently face the lack of such. In other cases, such as the European Lead Factory, regulatory and financial hurdles limit the possible in-kind contributions by the industry.

This finding fuelled the perception among some non-EFPIA participants that EFPIA companies were mainly interested in collaborating in IMI projects to influence the regulatory process and therefore were less interested in sustaining outcomes from the projects once finalised.

7.2.2.2 Visibility of the EU as partner in IMI JU

The EU was generally perceived as an important partner in the IMI JU PPP. From the public consultation survey (although focused on IMI2 JU, some general opinions are equally valid for IMI JU) 70% of the responders 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 responders 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 IMI 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 IMI JU is commonly viewed as an EU programme and that the EC is one of the founding members of the IMI JU. In all communications both logos of the founding members of the joint undertaking are clearly visible.

7.2.3 Operational efficiency

7.2.3.1 Efficiency of the management

According to the IMI JU Executive Office representatives, the staffing of the Executive Office was suboptimal, especially because the number of projects to manage was constantly increasing. Furthermore, since late 2014 there was an overlap with IMI2 JU, which created many inconsistencies and confusions. There appeared to be a significant imbalance with more financial and administrative staff members and relatively low number of scientific staff, especially with the heavy work load assigned to the latter. The IMI project handling was identified to be both time consuming and complex.

According to the data provided by the IMI Executive Office at the end of 2016 it employed 41 staff engaged in operational (26.8 FTEs, including 8.3 project officer FTEs) and horizontal activities (14.2 FTEs). The total salaries of these employees added up to EUR 4.8 million. The nine IMI scientific officers were responsible for managing 84 projects which, by the end of 2016 included 25 IMI2 JU. This volume translated to approximately seven projects per person or 10.1 projects per FTE. This seemed to be 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 and selection of independent experts, but did not contribute to the selection of project proposals.

Based on the 2016 IMI Annual Activity Report,38 total operational expenditures amounted to approximately EUR 175.2 million while total costs of running the IMI Executive Office amounted to approximately EUR 8.15 million for administration, which therefore represented just over 4.45% of the total EU operational expenditure (reflecting the cumulative project funding for 2016) or 2.2% of the total EU (cash) and EFPIA (in-kind) contributions. These numbers indicated an acceptable, although considerable cost for running the IMI JU programmes (for comparison, a typical cost of running a EUR 100 million venture fund was in the order of 2-2.5% per annum). *Ex-post* control efficiency of the projects and expenditures audited appeared to be fairly high with audit coverage of 22.14% achieved for an estimated expense of 0.96% of the total operational budget and 1.38% of the total operational payments in 2016.

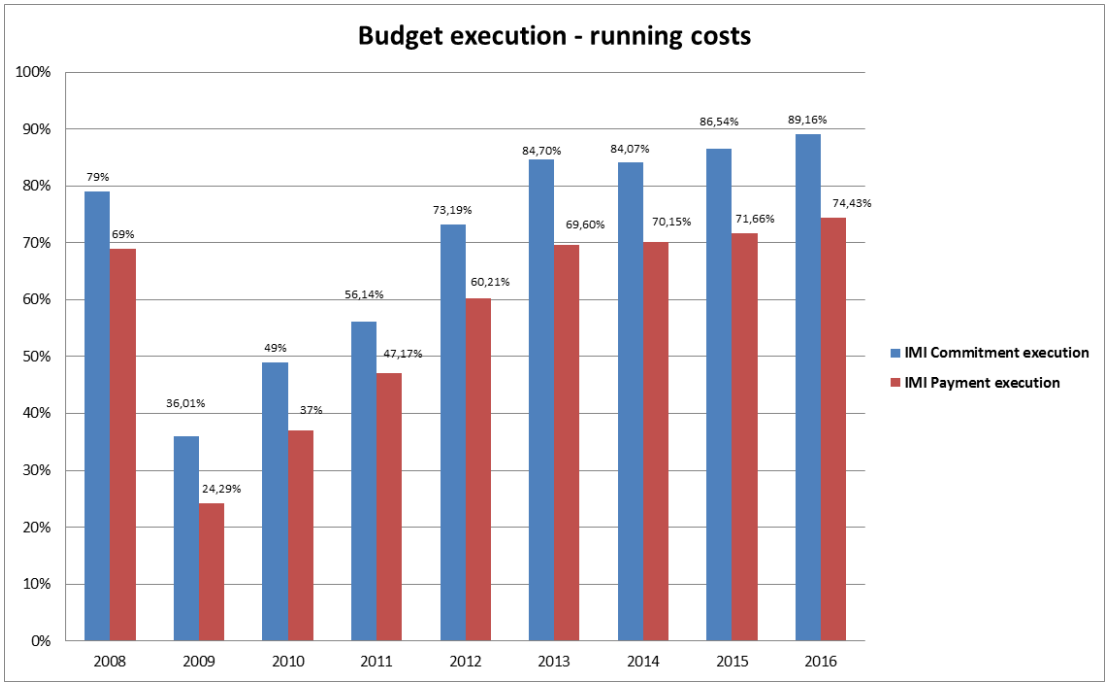
The expert group concluded that the IMI JU is operated and managed very well, although attention should be given not to impose a too heavy workload on the scientific officers, given the continuously increasing number of projects.

7.2.3.2 Budget execution

The numbers seemed to indicate that IMI Executive Office staff was meeting and sometimes exceeding its targets. Budget execution has been relatively efficient as evident from figure 9.

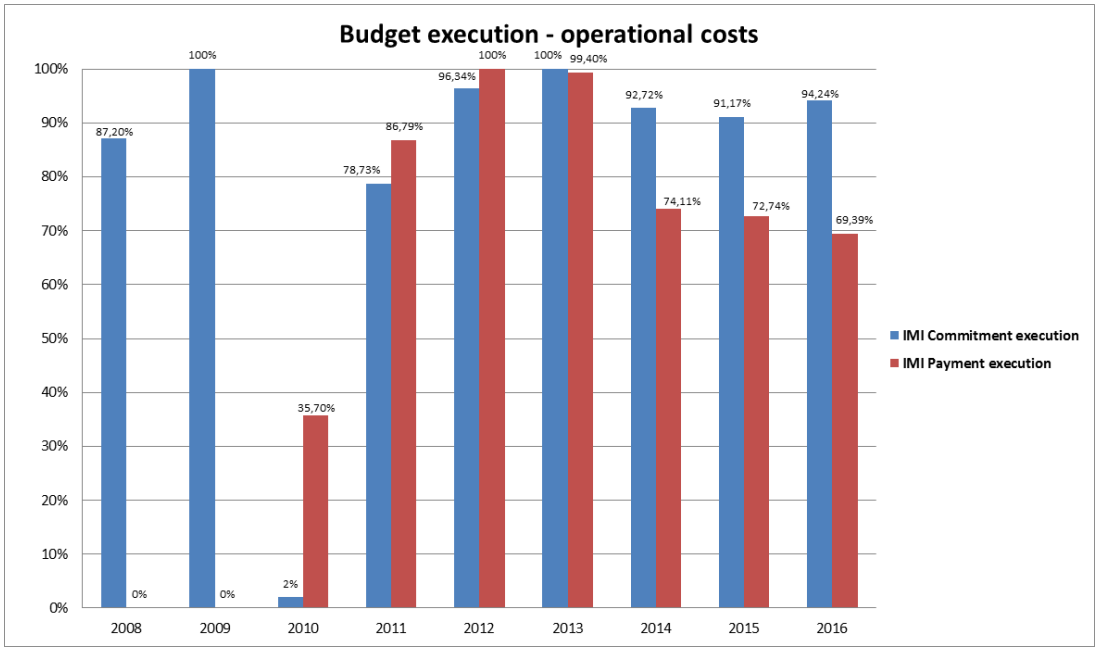
Figure 9: Budget Execution: a) Running and b) Operational costs

a)



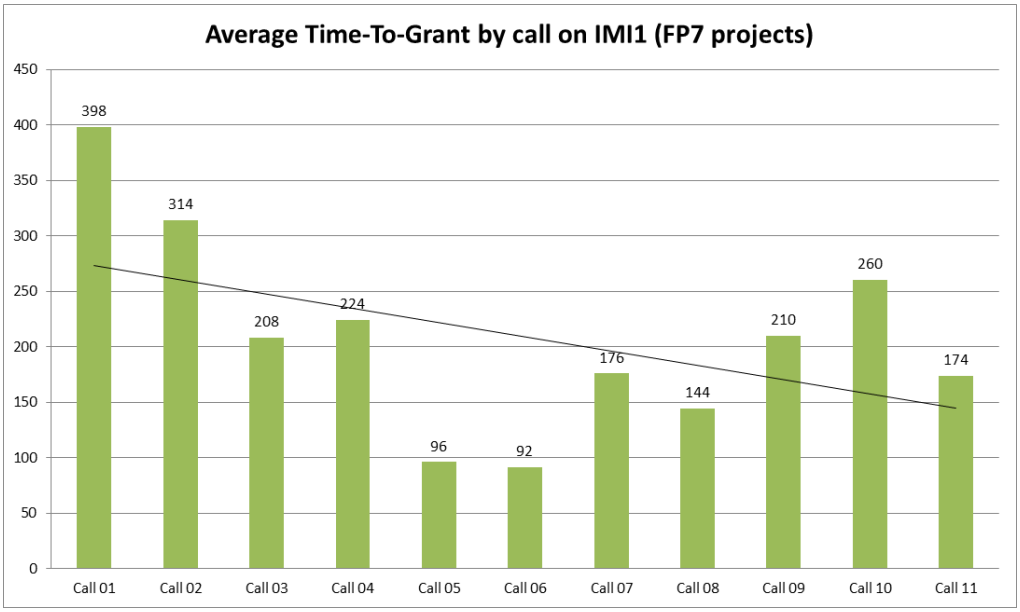
[38] Not yet published on the IMI Website. Made available to the expert group by the IMI Executive Office.

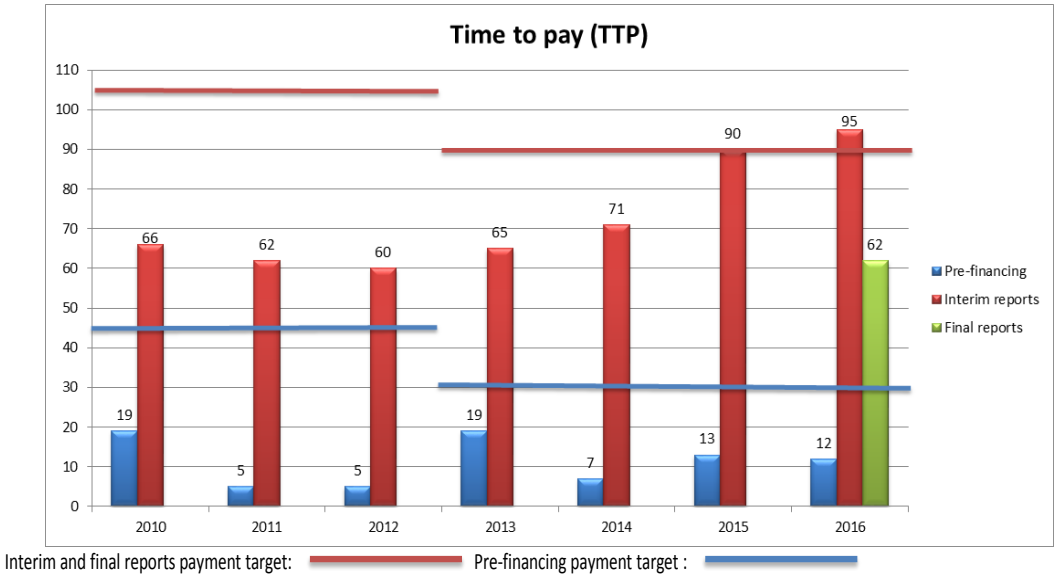
b)



Time to grant in IMI JU for the first two calls took more than one year and almost a year, respectively. This improved to well below the 290 day target set and this trend continued to decrease as evident from figure 10 below. Similarly, the time to pay has generally been below the set targets. However, in recent years the time to pay upper ceiling for interim reports had been exceeded. This was some cause of concern; especially for the small SMEs times to pay exceeding 90 days could create a liquidity problem.

Figure 10: Time to grant (top figure) and time to pay (bottom figure) vs. targets.





In conclusion, the expert group considers the operational efficiency including the efficiency of management and budget execution as satisfactory for IMI JU and generally below the limiting thresholds of time to pay and time to grant. Overall satisfaction with the IMI JU's services of the surveyed beneficiaries has been higher than 88%: 65% of responders being satisfied (and 23% very satisfied).

7.3 Relevance

In this section the expert group was asked to analyse and conclude whether the rationale to establish an IMI JU were valid and sufficient to justify the creation and existence of the public-private partnership.

As outlined in section 3.2 describing the baseline, there was an urgency felt to launch an initiative to strengthen the European pharmaceutical industry and increase its competitive position.

According to the Council Regulation establishing the IMI JU, the general objectives were to create conditions to increase investments in the European biopharmaceutical sector. To strengthen the competitive position of European pharma industry, 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 was meant to provide socioeconomic benefits for European citizens, contribute to the health of European citizens, increase the competitiveness of Europe and help to establish Europe as the most attractive place for biopharmaceutical research and development.

To achieve its objectives, IMI JU aimed to foster collaboration between all stakeholders such as industry, public authorities (including regulators), organisations of patients, academia, and clinical centres. IMI JU has established itself since its start in 2008 as a pioneer of open collaboration. Many academic research institutions benefited from the introduction of IMI JU. IMI JU also improved cooperation with the European Medicines Agency (EMA) and other national medicines agencies.

The pharma representatives at IMI agreed on the very positive results of IMI JU, as **for the first time competing companies were collaborating in precompetitive research.** They commonly decided on call topics that address questions a single company cannot answer by itself. IMI JU was considered a unique initiative that has not met its counterpart elsewhere in the world. The success of these collaborations is evident from the different projects that have successfully been running or still are continuing and from the in-kind contributions that have been spent according to the commitments made when designing the projects.

However, it is still unclear whether the establishment of IMI JU has actually achieved the ultimate goal of securing and improving the competitiveness of the European pharmaceutical industry and made Europe more attractive for investment in biopharmaceutical research. A representative of the IMI JU Executive Office pointed out that there were no guarantees that the IMI projects will eventually lead to the development of therapies or new medicines in Europe even though most actors in the IMI projects were European based companies or companies that have activities in Europe.

IMI projects have established resources and facilities to boost drug discovery in Europe and have developed new tools for research and advanced research in important areas like dementia, diabetes, and medicines safety. These tools will probably help to reduce the use of animals in research, and to reduce the time of development of new medicines. IMI projects have also helped to improve procedures for monitoring the benefits and risks of medicines once they are on the market.

However, **there were no examples to date of IMI bringing new, safer and more effective therapies or products to patients or that the time to develop such new applications had been shortened**. Given the average timelines of bringing new medicines to the market and the average running time of an IMI JU project this may not come as a surprise, but the added value of the IMI JU for patients or society in general was therefore hard to demonstrate in this evaluation report. By the end of 2016 only 21 out of 59 projects had reached the end of their IMI funding cycle; it was perhaps too early to bring a definitive appreciation on the role of IMI on boosting the competitiveness of European pharmaceutical industry.

It was believed by IMI representatives that if IMI JU had not existed, there would be other joint ventures securing in cash financing for pharmaceutical companies and SMEs. As it was suggested by those same representatives that IMI JU was envied elsewhere, it could have been expected that the model would have been replicated in other parts of the world. This, however, did not happen so far, perhaps because other joint venture models may be simpler than the IMI JU framework.

Through the IMI JU programme, the pharmaceutical industry was committing EUR 1 billion, which was matching an equal budget from the FP7 Cooperation programme addressing Health, for collaborative research in Europe. Although compared with other EU-funding sources this was a relatively significant investment, **the private budgetary commitment concerns in-kind contributions and represented only a low percentage of their total R&D expenditure even though under IMI JU the focus was on precompetitive research** and thus not covering the entire scope of research and development.

A success, but at the same time a limitation of the IMI JU, was linked to its status of a public-private partnership between EFPIA and the EC. As the representative of the pharmaceutical industry and particularly of 'big pharma', EFPIA - and consequently IMI JU - was not well adapted to attract SMEs, which are essential to increase health innovation in Europe. For the same reason, EFPIA cannot be the only pilot to address the question of the future in medicine. Already at the time the IMI JU was launched, it was clear that innovation for the patient did not only concern the development of novel drugs but also of diagnostic tests (including genomics, transcriptomics,…), the use of imaging, robotics, connected objects, impacting data management sector, all of which were not within the remit of EFPIA.

It also proved difficult for biotech SMEs that are developing new products to get public funding in IMI, as this type of companies have limited activities in the pre-competitive space. It can be questioned whether the focus on precompetitive space for funding was still the best way to proceed. On the other hand, assets created by IMI projects may still be beneficial for SMEs. One of the interviewees indicated that SMEs were too defensive to share platforms and tools for the development of advanced therapies.

The lack of a performance monitoring system made it hard to assess whether the goals of increasing competitiveness of the European pharma industry were within reach as this was the main argument to start the public-private partnership. If the European pharmaceutical sector was not increasing its activities and investment in Europe it can be questioned whether the goals to shorten the time of drug development could be achieved in another way, such as through stronger promotion of European SME involvement that can be considered to be the engine of European economy.

In this respect it may be concluded that the creation of an initiative such as IMI JU was justified, while the targets put forward were open-ended and not ambitious enough. The expert group was also not convinced that the framework conditions were always the best suited to achieve those goals. Socioeconomic indicators that demonstrate an effect of the establishment of IMI JU are lacking. The fact that SMEs and academia find it sometimes difficult to participate in IMI JU projects, for different reasons that were described above, indicate that framework conditions may be improved so as to create a more stimulating environment in which all partners can participate. The risk of excluding important actors from SMEs, midcap companies or academia should be minimised and comments from those partners should be taken at heart.

The results that IMI JU projects have delivered, confirm 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 have helped to address some of the biggest challenges in health research. The scientific excellence and results of IMI projects, as reflected in publications, were significant specifically in the context of precompetitive research. Given the specificities of this area, only a limited number of publications were found in the TOP 20 journals ranked by impact as described in section 7.1.1.

7.4 Coherence

In this section the expert group set out to analyse whether the IMI JU programme was coherent within FP7 and with other EU policies and interventions. In addition the expert group will assess to what extent IMI JU was coherent with other programmes that have similar objectives, whether the initiatives were complementary, created synergies or were overlapping.

The Seventh Framework Programme for Research (FP7), the Competitiveness and Innovation Programme, the European Research Agenda and the Innovation Union policy established that collaboration can maximise the contribution of R&D to achieving smart, sustainable growth in Europe. The main goals of FP7 are outlined in box 5.

The expert group received input from different stakeholders and members of the various IMI bodies on their views on coherence and complementarity in the various FP7 initiatives, and in addition relied on published documents and annual reports.

Box 5 Objectives of FP7*

The Framework Programmes for Research have two main strategic objectives:

- to strengthen the scientific and technological base of European industry;
- to encourage its international competitiveness, while promoting research that supports EU policies.

FP7 is 7th Framework Programme for Research and Technological Development, which ran for seven years from 2007 until 2013 with a total budget of over EUR 50 billion that reflects the high priority of research in Europe.

Indeed, FP7 is a key tool to respond to Europe's needs in terms of jobs and competitiveness, and to maintain leadership in the global knowledge economy.

This money is (for the most part) spent on grants to research actors all over Europe and beyond, in order to co-finance research, technological development and demonstration projects. Grants are determined on the basis of calls for proposals and a peer review process, which are highly competitive.

In order to complement national research programmes, activities funded from FP7 must have a "European added value". One key aspect of the European added value is the transnationality of many actions: research projects are carried out by consortia which include participants from different European (and other) countries; fellowships in FP7 require mobility over national borders. Indeed, many research challenges (e.g. fusion research, etc.), are so complex that they can only be addressed at European level.

* http://ec.europa.eu/research/fp7/understanding/fp7inbrief/what-is_en.html

7.4.1 Strengthening the scientific and technological base of European industry

Although the ToR indicated that alignment or duplication with other EU programmes needs to be assessed to explore synergies and complementarity, the information available did not allow to do this analysis, but could possibly be produced by the European Commission's services.

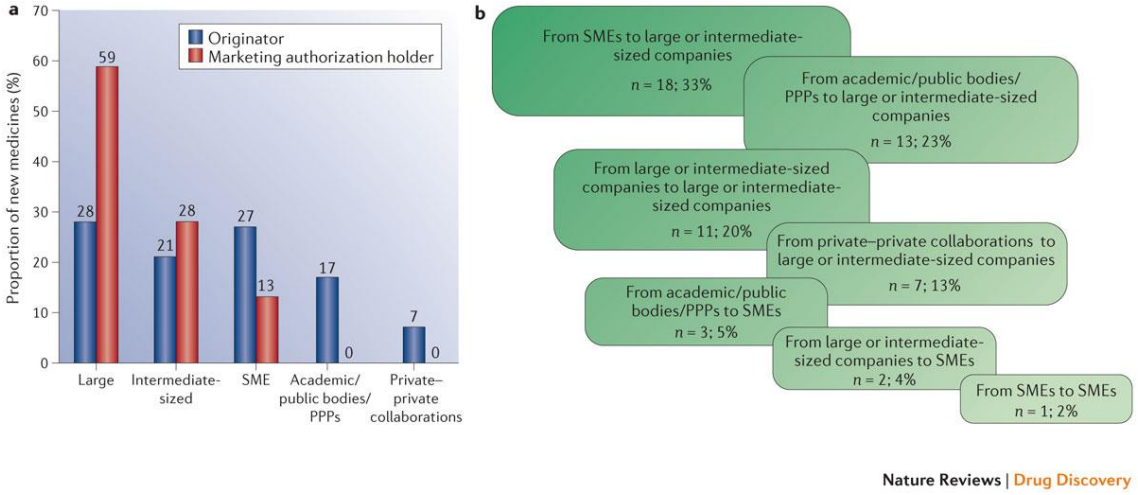
In line with the objectives of FP 7, IMI JU should have contributed to strengthen the scientific and technological base of European industry.

Another main goal in line with FP7 was that IMI JU should have encouraged the European international competitiveness while promoting research that supports EU policies. If correct

that European pharmaceutical industry proved to be more resilient against crisis as described above, and that pre-IMI disinvestment was switched to new investments in European biomedical research in pharmaceutical companies, IMI-JU would have made a main achievement to meet the FP7 objectives. However, these statements were not often documented in an objective way.

To analyse whether IMI JU contributed to increasing the competitiveness of European pharmaceutical industry, the situation in Europe in the field of drug development and especially where developments occur, should be taken into account. Therefore, the IMI JU framework and the consortia should include all those who support the development of medicines in Europe (figure 11).

Figure 11: Origin of new medicines in the European Union (2010-2012)[39]



a| Originator and the marketing authorisation holder for all 94 approved products evaluated, divided according to organization type;

b| Direction of product transfers between organisation types during development; the size of the lozenges is representative of the proportion of transfers. PPP, public–private partnership; SME, small or medium-sized enterprise.

According to figure 11, for the period 2010-2012, SMEs were the source of 27% of new medicines in Europe. Therefore, it was considered that the objective of "Promoting the involvement of small and medium-sized enterprises (SME) in its activities" was consistent with the objectives of "Strengthening the scientific and technological base of European industry and fostering its international competitiveness, while promoting research that supports EU policies". At this point, it is important to note that the participation of SMEs in IMI JU has represented only 15.96% of the 1203 EU-funded participations. These SMEs accounted for 13.25% of total EU funding for IMI JU. Figure 11 also indicated that 17% of the new drugs in the period studied, had their origin in academia, public bodies or public-private partnerships. Private-private collaborations were at the origin of 7% of the new medicines. The participation level of academia and other research organisations in IMI JU corresponded to 54.4% of the total and 83.5% of the total public budget.

The participation of SMEs and the return on investment in the projects funded through IMI JU, together with the quality of achievements should be compared with similar projects funded by FP7.

Although it was hard to compare projects, some examples indicated that IMI JU projects have a much larger budget, but not necessarily more ground-breaking outputs. Box 6 illustrated two projects with related AMR goals, funded in IMI JU and by FP7.

[39] Reprinted by permission from Macmillan Publishers Ltd: Nature Reviews Drug Discovery 13:92-93, Lincker *et al*., advance online publication, 31 January 2014 (doi: 10.1038/sj /nrd4232)

Box 6 Two projects addressing methods to detect bacterial infections

RAPP-ID is an IMI JU project that aims to provide an integrated solution that addresses the technological challenges to enhance clinical decision-making and improve the quality of care and clinical outcomes for the people of Europe and worldwide.

The project will develop a point-of-care-testing (POCT) for rapid detection of bacteria, tuberculosis bacteria, fungi, as well as viruses and patient's markers of infection by combining novel specific probes, novel methods of sample preparation, and demonstrated ultra-high sensitive detection methods in hospital patients in less than 2 hours and for outpatients in less than 30 minutes. The platforms will also determine resistance to the most commonly used antibiotics.

The research will focus on the pathogens and markers of infection involved in blood infections, lower respiratory tract infections, including community-acquired pneumonia and ventilator-associated pneumonia and in tuberculosis.

The Horizon Prize for Better Use of Antibiotics was installed by the European Commission to develop various methods of detection and differentiation of a bacterial infection.

The EUR 1 million Horizon Prize awarded a project that developed a finger prick test that can diagnose in less than ten minutes a bacterial infection and identify if a patient can be treated safely without antibiotics. The easy-to-use test is expected to be available for patients by 2018. It has been developed by Minicare HNL in a combined research effort or P&M Venge AB from Sweden and PHILIPS Electronics from the Netherlands.

For the Better Use of Antibiotics Prize, two other finalists were in close competition, presenting innovative patient-focused technologies.

7.4.2 Promoting research that supports EU policies

One of the general goals within the FP7 was to address the grand societal challenges. As half of the IMI JU budget came from the framework programme, these goals were also evaluated by the expert group. To specifically address the societal challenges, the Joint Programming Initiatives (JPIs) were installed to pool national resources and coordinate efforts. The JPIs on Neurodegenerative Diseases (JPND) and on AntiMicrobial Resistance (JPIAMR) were the two relevant JPIs of which the topics were also addressed in IMI JU. To reduce fragmentation and integrate the efforts to address the societal challenges, it was expected that the different public funded initiatives were aligned.

However, according to JPND representative there was limited interest from IMI counterparts to join forces. Moreover, it was indicated by JPND representatives that the work of JPND on standardisation protocols in biomarker generation[40] has been ignored by IMI partners and in some IMI JU projects similar goals seemed to be set. JPND regretted that there was no dialogue or collaboration with the actors of the relevant IMI projects in the field of neurodegenerative diseases to interact and learn from each other, although according to JPND representatives efforts were made to set up such a dialogue.

There were nine projects under IMI JU that addressed antimicrobial resistance and the development of new antibiotics. The Joint Programming Initiative AntiMicrobial Resistance (JPIAMR) addressed the same challenge, but the programme focussed more on the earlier research and on different aspects and hence was more complementary than overlapping. There was a good dialogue between JPIAMR and the relevant IMI projects on AMR and a representative of JPIAMR participated in the SGG on AMR to identify possible collaborations and align initiatives. Figure 12 gives an overview of where IMI projects relative to AMR projects funded by other sources are located in the value chain.

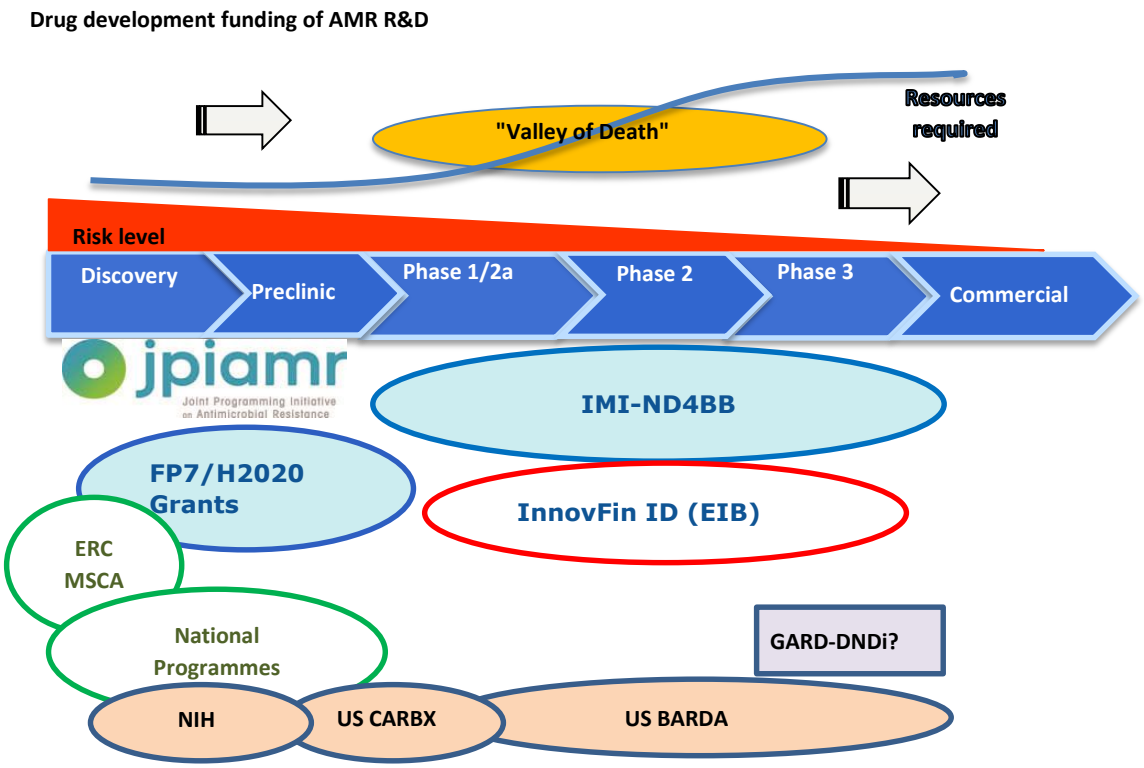
Furthermore, duplication of AMR related work by the JU and the JPI was actively prevented by the "EC-JPI AMR-EPFIA-IMI" group that was set up for this purpose. In this context three

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

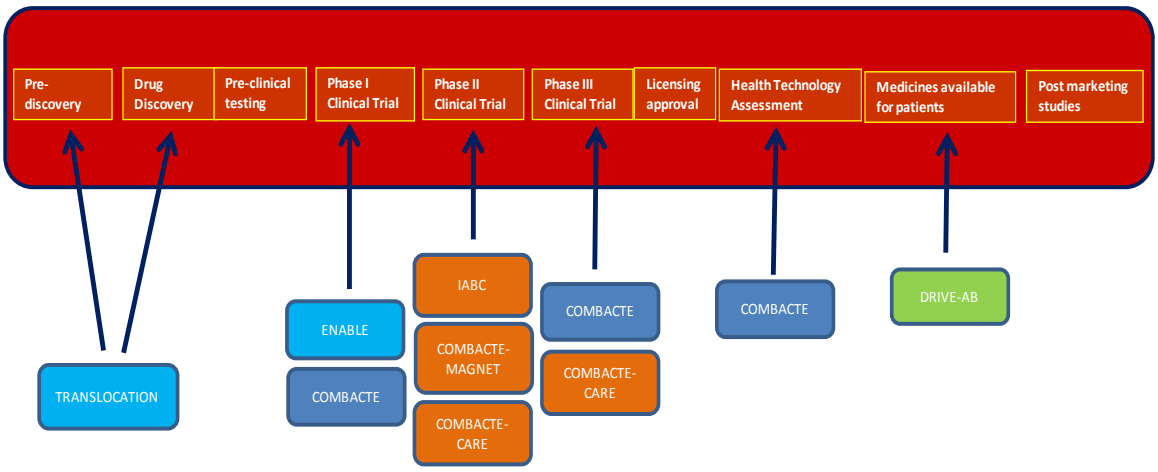
workshops were organised: one in 2014 in Brussels, followed by one in 2016 in Stockholm and one in early 2017 in Paris. Nevertheless, contacts could have been more intense to stimulate interactions and to build on, for example the mapping information gathered by JPIAMR, especially as the threat of AMR could only be addressed properly by a holistic approach that integrates academia, healthcare professionals, regulators, and industry and fragmentation between different initiatives such as under IMI and JPIAMR will not improve the current threat.

Figure 12: Overview of IMI projects addressing antibiotic resistance (b) relative to AMR projects funded from other sources in the value chain (a)

Part a



Part b



Representatives of IMI JU and from both JPND and JPIAMR agreed that collaborations with both JPIs could be improved. According to a GB member the difference between IMI projects and JPI projects was the size as reflected in the budgets and the number of consortia participants. The IMI projects were much larger and can thus bring a **structuring effect**, whereas JPI projects were more focussed on single issues with smaller budgets.

In contrast JPI representatives found the IMI projects too much top-down determined by industry, allowing very little flexibility and creativity. The fear was that such projects were less likely to lead to general true innovation, on top of the fact that results of IMI projects may not become publicly accessible. 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.

An EFPIA representative advocated increasing the complementarity of IMI JU and the FP7. IMI was meant to improve drug development, whereas the framework programme had other objectives; 'Silo's' still existed and it was felt that these could be broken down by increasing collaborations.

In general it was believed by several interviewees that **there should be stronger emphasis to integrate results from different projects, not only from projects under IMI, but also projects funded through the FP7**. This should reduce fragmentation and help avoid duplication, while by stronger integration, new added values may be created. A member of the SC agreed with this vision and advocated for better coordination with FP7 projects and build on synergies. One idea that was put forward was to give a follow up of FP7 projects in IMI or vice versa. This would need better coordination.

Another common comment was that **the results of the different IMI projects were not known outside of the consortia and results were only accessible to partners within a certain consortium**. Also the interaction between the different consortia should increase and results should be accessible to all stakeholders in the field, also from outside the IMI community.

The expert group also tried to address the coherence with the Health Programme under the Directorate-General for Health and Food Safety (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. Broadening the SRG with representatives from regions may help to align with regional strategies and policies. Although this is also part of the responsibilities of SRG representatives, it is not always appropriate for national representatives to represent private initiatives and sometimes difficult to achieve. 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. Under IMI JU such alignment with national or regional policies or strategies was very limited.

Synergies with international initiatives were also rather limited. There were several international initiatives that are similar to IMI JU, although IMI JU was more ambitious in scale and scope than all other initiatives such as C-Path, the Global Health Innovation Technology Fund (GHIT) or the NIH's Accelerating Medicines Partnership (AMP).

In February 2015, the US House of Representatives issued a white paper on the "21st Century Cures initiative". Launched by the House's Energy and Commerce Committee, it studied what steps can be taken to accelerate the discovery, development and delivery of cures. It was recognised that what was missing in the USA was a public-private partnership that would bring together the various stakeholders and would need to be "modelled after the Innovative Medicines Initiative".[41]

The organisation that was most similar in its mission to IMI JU was the USA based **Critical Path Institute (C-Path[42])** set up by the FDA in 2004/5. C-Path specifically referred to IMI

[41] https://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/files/114/FINAL%20Cures%20Discussion%20Document%20White%20Paper.pdf
[42] https://c-path.org

in its Mission Statement. IMI JU had a very constructive collaboration with C-Path, illustrated by the annual joint meetings of which the third one will be organised in 2017.

Nevertheless, C-Path's funding model was 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 came 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 collaboration between C-Path and IMI JU encouraged the FDA and EMA to collaborate as well, which would increase the probability that both agencies made similar decisions when authorising medicines.

Table 4 gives an overview of the most relevant international initiatives with similar goals to IMI JU. It was clear that IMI JU had the largest budget and broadest scope. More detailed information on the respective initiatives (other than C-Path) is given in Annex 10.

With the data the expert group had available, it was not possible to compare the outcomes of the projects funded by the different international initiatives. In some cases, this was because IMI consortia were young. In other cases, because despite being mature consortia, the results of R&D needed 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.

Table 4: Comparison of different international initiatives.

	START YEAR	BUDGET GOALS	BENEFICIARIES	HEALTH TARGETS	FINANCING PARTNERS	LOCATED
Innovative Medicines Initiative	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	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	2004/5	15M$/ year	Industry; academy; regulatory agencies;	Alzheimer; accelerate clinical research; Parkinson's; tuberculosis; paediatric trials, multiple sclerosis; regulatory science, etc.	1/3 FDA; 1/3 Industry; 1/3 Charities	USA
Global Health Innovation Technology Fund	2017	96M$ 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)	2014	230M$/ 5 years	Scientists from NIH and Industry	Alzheimer; Type 2 Diabetes; Rheumatoid Arthritis and Lupus;	NIH; FDA; Biopharma industries; non-profit organizations	USA
Combating Antibiotic Resistant Bacteria X	2016	350M$/ 5 years	Product developers from any country	Antibacterial products, not just therapeutics.	US government; Wellcome trust UK; AMR centre UK;	USA

7.5 EU Added Value

The EU added value relates to changes that can reasonably be attributed to an EU intervention rather than other factors. The added value of the IMI JU can be evaluated by comparing the objectives assigned by the Council Regulation for the implementation of IMI in 2008 and the results achieved by the end 2016 to get a more precise midterm overview as most of the IMI JU projects are yet to finish.

The quantitative assessment of the added value of such an ambitious programme was complicated for several reasons. First, although there was no doubt that the IMI programme had produced a reasonable level of results it was difficult to compare these results with those obtained in other biomedical research programmes of FP7, because **no baseline nor specific key performance indicators to measure the cost to benefit ratio of the different projects have been agreed**.

Second, **the time constants of the pharmaceutical industry were much longer than those of other industries**, such as e.g. the IT industry; the average time for research evidence to reach clinical practice is 17 years. It was thus difficult to assess the outcome of a programme within only six or seven years considering all the results obtained by the end of 2016.

By the end of 2016, 21 projects had reached the end of the IMI JU funding cycle, of which at the time of evaluation, only six were finalised and discussed in closeout meetings. Other closeout meetings were scheduled in 2017 after the completion of this IMI JU final evaluation report. Another 38 projects were still running, some of which will end only in 2020 and 2021. Therefore, at this point the current evaluation of the added value can only be but partial.

The third reason why the quantitative assessment of the added value was complicated, was because **the IMI JU focus was on pre-competitive research**, which has an outcome more towards increasing capability rather than product delivery. It was more difficult to evaluate pre- or non-competitive research activities than activities that lead directly to the approval of a medicine or a vaccine. If the activities were measured in terms of the quality or number of publications, number of patents, etc., the added value must also be evaluated in comparison with other programmes of FP7 aimed at least indirectly at the same goals.

Finally, a fourth reason illustrating that establishing the added value was not straightforward was that **some of the 59 projects arising from IMI JU, focused on specific health issues** such as neurological diseases, diabetes, infection, metabolism, lung disease or oncology. **Other projects focused on broader challenges in drug development**, like drug and vaccine safety, use of stem cells for drug discovery or sustainability of chemical drug production and also **another category of projects address education and training issues**. The added value of these three categories of projects must be evaluated with different specific indicators.

In spite of these limitations, some conclusions could be drawn. The analysis identified the added value reached through the increase in the participation of academia in precompetitive research projects, the creation of specialised research networks and facilities, the effect on employment in life sciences, on commercialisation of project results, on attracting SMEs, patient organisations, and regulatory agencies. The analysis identified some early societal impacts but most importantly focused on whether the overarching goal of strengthening the European pharmaceutical industry was within reach. It should be noted that the analysis focused on changes "that can reasonably be attributed to an EU intervention rather than on other factors".

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

IMI JU projects currently involve **845 academic teams and over 7 000 researchers** working in different disciplines across Europe and beyond. These numbers represented an indisputable success given that academic researchers usually prefer or are not encouraged to participate in applied research projects in collaboration with industry for reasons such as different focal interests, the importance of top publications, career issues. IMI JU as a public private partnership made a bridge between academia and industry, although many calls in FP7 also encouraged such type of collaboration.

IMI JU claimed that it has established a reputation of scientific excellence and was recognised as a global leader in open innovation in health research and medicines development. A key question was whether the best universities and research organisations were involved in IMI.

Thirteen universities participating in IMI JU were in the Top 50, 27 were in the Top 100 and 65 in the Top 200 (benchmarking to the U-Multirank). A number of universities had several

participations in IMI projects. More than 50% of all participations and EU contribution was for universities ranked amongst the 200 first universities. Altogether, this can be considered a **fairly good result for a specialised programme not dedicated to basic research**.

Table 5 lists **the research organisations that were most involved in IMI JU**. It was noticeable that these organisations were also the **leaders in Europe**. Inserm was the first most innovative biomedical research organisation in Europe and the second in the world after the US department of Health and Human services (Thomson Reuters, 2016). IMI was thus successful in attracting researchers who were used to apply to more fundamental calls in FP7 on diabetes, neurodegenerative diseases, oncology, and infectious diseases. **However, all these organisations had their own technology transfer structure** organised as a department or a private company and had a good success in translating the results of their labs into start-up companies.

It was also possible to combine basic research and translation into added value for society without participating in IMI-funded projects. VIB, the Flemish Institute for Biotechnology in Belgium, was a good example. They participated in only one IMI project, but they have 37 ERC grants, 588 employees in VIB start-ups with 1016 industrial collaborations and 42 products or diagnostic tests in development.

Table 5: Research organisations most involved in IMI JU

Research organisations	IMI contribution (million EUR)
INSERM	12.2
Max-Planck Gesellschaft	11.1
Fraunhofer Gesellschaft	7.7
Helmholtz Association	6.4
CNRS	6.1

It was commonly accepted that most of the innovations were the unpredicted results of excellent fundamental and curiosity-driven research. This has been well understood by the pharmaceutical industry. The complexity of life processes, e.g. the redundancy and interrelationships of metabolic and cellular pathways, has clearly appeared after (or in spite of) the success of human genome sequencing. Industry considered that it was becoming more and more difficult to discover innovative drugs from their own research. They have thus established collaborations with the best academic teams around the world, independently of IMI JU. The question was, therefore, to understand if the scientists engaged in IMI were among the best in Europe.

The researchers in IMI projects come from academia, industry and SMEs, and, as IMI JU claimed, they must be the innovators who carry, circulate and apply knowledge, and who used the knowledge infrastructure, both for creating and absorbing innovations. With such a formulation it would be unfair to simply compare their publications or their H-index with those who apply for an ERC grant.

By the end of 2016, IMI JU generated **2690 publications published in more than 796 journals, with 56% published in top 10 % impact ranked journals**, including in Lancet Neurology, Science Translational Medicine, Nature (and other Nature journals e.g. Nature Genetics, Nature Medicine, and Nature Neuroscience), Science, and the Journal of the American Medical Association (JAMA).

The average journal impact factor for IMI research is 5.968 and the field-normalised citation impact for all IMI papers is 2.03, comparable with the UK Medical Research Council (2.08), and almost twice the 1.14 for the EU (the baseline being 1 for the world). Although these results are good, it would be presumptuous to claim that it corresponded to "World-class science and increased levels of R&D excellence". While the IMI Executive Office rightly points out that classic bibliometrics were not well suited to measure and incentivise collaborations - which was a key aspect that consortia were leveraging - it has not provided other performance indices that could replace them.

Next to increasing the collaboration with academia, **the establishment of vast research networks, including 480 EFPIA teams was probably one of the highest added values of IMI JU**. Examples illustrating of long term networks in specialised fields can be found in Annex 11.

Some early societal impacts have been reported.

- IMI education and training projects are working to increase European knowledge capital for the whole life-cycle of medicines research, from basic science through clinical development to pharmacovigilance.
- Some 685 trainees have followed PharmaTrain courses, with over 28% from pharmaceutical companies. 58 students are following EU2P's flexible and fully e-learning programme, with access to 160 different topics. More than 320 students have participated in 20 new SafeSciMET courses in drug safety sciences courses. Information on more than 6 000 courses is available through EMTRAIN's 'On-course' online course portal.
- IMI's education and training projects launched their new pan-European LifeTrain framework for continuing professional development in the biomedical sciences. The framework will enable biomedical professionals to work collaboratively across disciplines and national boundaries.
- EUPATI is a patient-led initiative that aims to develop the first European Patients' Academy on Therapeutic Innovation, providing training courses, educational material and an online public library to empower patients to engage effectively in becoming true partners in pharmaceutical R&D. The project has developed a network of more than 1000 members from 53 countries with a wide mix of healthcare professionals, patients, caregivers, PR/communications specialists, industry and academic representatives.

The involvement of six patient associations in the latter project has been criticised, because some interpreted it as a way to train patient groups to lobby the regulatory agencies for faster approval of new medications (see below). Discussions with representatives of patient associations have shown that they were aware of such a risk. EMA has been a partner in a number of projects, but the agency limits such participations to very specific cases. EMA also agreed to contribute and to participate in the SC .

7.5.2 Added value through creating significant opportunities for recruitment and employment in life sciences and related R&D

The IMI Executive Office indicated that there were now 2,272 full-time jobs employing and developing highly-skilled personnel directly associated with IMI projects. Every job directly associated with life science R&D had a leveraging effect of creating further jobs indirectly elsewhere in the economy. According to studies for the UK one R&D job was associated with between 3 and 5.7 jobs in the economy as a whole. Extrapolating this suggests around 13,000 jobs within the European economic area may have been created from IMI. However, so far there was **no indicator available to demonstrate that IMI JU induced an additional leveraging effect, beyond the expected industry matching contribution**.

7.5.3 Added value effect of the programme on pharma companies

EFPIA illustrated the added value of IMI JU by reporting on 6 companies that integrated IMI results into the companies R&D practice, which may have increased the ability to upscale or start new types of activities or development programmes. However, it remains hard to appreciate since there was no basis to compare with other FP7 programmes.

Table 6, summarising information from EFPIA, aimed to illustrate in which domains IMI JU could realise impact across the value chain. It refers to projects which were not necessarily described in the examples provided by companies.

Table 6: Impact domains from IMI JU across the whole value chain

Discovery:	• Identification of new hits and leads (screening centre with proprietary compounds). • First human Beta cell line for diabetes research.
Early development:	• Regulatory qualified safety biomarkers. • In silico predictive models (based on bioinformatics and chemo-informatics). • Identification of novel epigenetic mechanisms and early biomarkers for non-genotoxic carcinogenesis. • Normalised and structured data of about 8,000 legacy GLP toxicology reports from 13 Pharma companies, and about 100 predictive algorithms (in one project alone, E-Tox).
Late development:	• Definition of regulatory endpoints, e.g.; for autism, sarcopenia, asthma, pain. • Development of antibiotics (new compounds, new formulations). • Development of Ebola vaccines and diagnostics (clinical trials, manufacturing, diagnostics, deployment). • Clinical trial infrastructure and fast-fail cohorts (paediatrics, antimicrobial resistance, autism).
Patient access:	• Defining and measuring outcomes relevant for and aligned between patients, payers, regulators (BD4BO). • Applicability of adaptive models based on real world evidence (Adapt Smart). • Integration of patient voice in benefit risk evaluations (PREFER). • Definition of evidentiary standards for pragmatic trials (GETREAL). • Methodological standards in Pharmacovigilance (PROTECT).

7.5.4 Added value towards bringing results closer to the market

By the end of 2016, only 21 projects out of 59 had reached the end of their IMI funding cycle. Nevertheless, the IMI executive office reported on important project outputs from both IMI JU and IMI2 JU, including:

- 33 patents by end of 2016 (including 32 from IMI1 projects);[43]
- 1.18 patent applications per €10 million cost accepted and reimbursed by IMI JU in 2016;[44]
- 43% of the finished IMI1 projects having created spin-offs by end 2016;[45]
- 6 trademarks; [45]
- 3 licensing deals;
- 33 results implementation by industry;
- 17 sustainability plans;
- 7 commercialisations, by autumn 2015;.and
- 2768 full-time jobs created by end 2016.[45]

These results were significant but should be evaluated in relation to those obtained by the various and numerous technology transfer offices in Europe, of major research organisations or universities, such as Inserm Transfert, the Helmholtz association, VIB, Cambridge University, or Karolinska Institute. In the 2014, the European Patent Office ranking for "Pharmaceuticals" ranked Inserm Transfert 5th after Novartis, Sanofi, Merck &Co and Boehringer Ingelheim and above Hoffman La Roche which is number 6.

[43] Annex 5 of Annual Activity Report 2016 available at: http://www.imi.europa.eu/content/documents
[44] Annex 8 of Annual Activity Report 2016 available at: http://www.imi.europa.eu/content/documents
[45] Report on "IMI's added value" available at: http://www.imi.europa.eu/sites/default/files/uploads/documents/Publications/IMI_SocioeconomicImpact_Autumn2015.pdf

Although the IMI Executive Office provided examples of IMI projects that brought results more rapidly to the market, the lack of specific KPIs prevents from any comparative and quantitative appreciation of the IMI added value of these potentially important achievements. Examples provided by the IMI Executive Office can be found in Annex 12.

7.5.5 Added value through collaborations with regulatory agencies

Under IMI JU, **nine regulators have participated** on 21 occasions in 10 projects out of the 59 IMI JU projects (16.95%). National regulatory agencies for medicines and EMA were generally represented either as partners or advisors and participated only in a few consortia. Better cooperation with regulatory authorities meant faster progress in developing effective new treatments for patients. IMI projects have developed close and productive relationships with the European Medicines Agency (EMA) and other national regulatory agencies for medicines were in close consultation with IMI projects. **A number of projects** (e.g. EU-AIMS, SAFE-T) **have already received EMA qualification advice of novel methodologies for medicine development to maximise potential impacts of project results on regulatory practices**.

EMA provided the expert group with several examples of projects they have seen for qualification or scientific advice with respect to the qualification process that aimed at innovative methods and tools for drug development. These include: EU-AIMS, SAFE-T, PROACTIVE, EUROPAIN, SPRINT-T, EPEAD, PRISM, MARCAR, eTOX, STEMBANCC, ADVANCE and ORBITO.

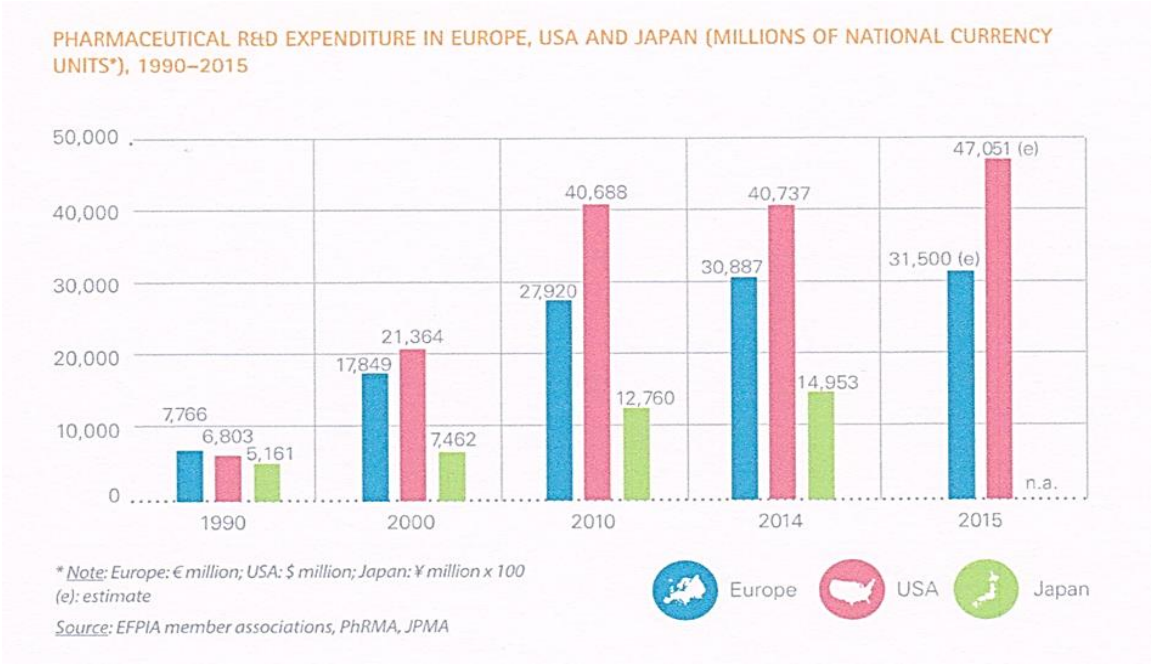
IMI played a positive role according to EMA because it broke down the silos between academy, industry and patients, compared to other EU funding mechanisms. It facilitated the dialogue between EMA and the pharmaceutical companies, it helped staff members from EMA and others to be trained in pharmacovigilance; several workshops between EMA, FDA, EC DG Research, academics, and industry were organised.

7.5.6 Added value of IMI on the growth and competitiveness of the pharmaceutical industry

The added value on economic growth and competitiveness which was the major goal for which IMI JU was installed, was considered. In particular the European pharmaceutical industry performance compared with the US was scrutinised. The US is the largest market for pharmaceuticals (including biopharmaceuticals), accounting for around 35% of the global market. The US is also the world leader in biopharmaceutical research and development (R&D). According to the Pharmaceutical Research and Manufacturers Association (PhRMA), US firms conduct the majority of the world's research and development in pharmaceuticals and hold the intellectual property rights on most new medicines. The biopharmaceutical pipeline also has over 7,000 new medicines currently in development around the world with approximately 3,500 compounds currently being studied in the US - more than any other region around the world.

According to EFPIA the expenditure by the pharmaceutical industry in 21 EU countries has increased from EUR 22.7 billion in 2009 to about EUR 25 billion in 2014 (figure 13). This figure needs to be put in context however. Indeed, **the R&D expenditure increased by 12.8% between 2010 and 2015 in Europe, while in the same period the increase was 15.6% in the US. The effect of IMI JU to increase the research efforts was not clear**.

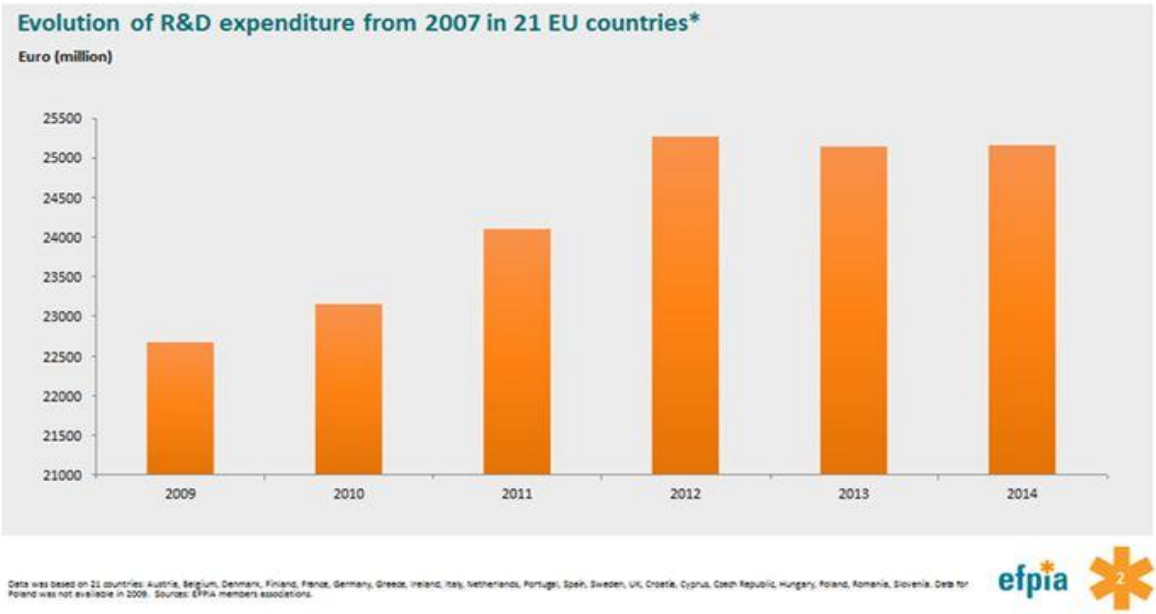
Figure 13: Pharmaceutical expenditure in Europe, USA and Japan (millions of national currency units) 1990-2015 (source: EFPIA)



However, as emphasised earlier in this report, IMI only funds precompetitive research. Furthermore, the overall IMI annual (in-kind) contribution of the EU pharma companies was very small compared with the total R&D budgets of these companies, amounting to about EUR 25 billion. This makes it hard to argue that IMI JU provided an incentive for European pharma industry research.

EFPIA showed that the expenditure in R&D in 21 EU countries has increased from 2009 to 2012, but seemed to have reached a maximum then as there was a slight decrease from 2012 to 2014 (figure 14).

Figure 14: Evolution of R&D expenditure from 2007 in 21 EU countries (source: EFPIA)



During the same period the evolution of R&D expenditure was slightly higher in the US (15.6%) than in Europe (12.8%).

EFPIA also claimed that employment in the pharmaceutical industry has proven to be more resilient (+3%) than in many other sectors in the EU, such as furniture (-4%), electronics and computer, and electric equipment (-4%), while similar to motor vehicles (+4%).

The economic added value per employee in the pharmaceutical sector was higher than in comparable industries. The gross value added per employee between 2011 and 2014 was stable at EUR 150 000 compared to about EUR 100 000 for chemicals and EUR 75 000 for motor vehicles. These data showed the importance of the pharmaceutical industry in Europe, but **did not give an indication of the role of IMI in the competitiveness of the European pharma industry**.

As for the European added value the main question was whether IMI objectives could have been attained at national level. Given that that only a few EU countries have a real international pharmaceutical industry, sole national actions taken in these countries, most likely would have been largely insufficient to boost competitiveness significantly.

7.5.7 Leverage effect

Two types of leverage can be defined in IMI JU. The built-in **mandatory leverage**, which is demanded by the regulation establishing the IMI JU – as 50% EFPIA in-kind contribution, and **additional leverage** that is stimulated from the industry and external sources, on top of the mandatory leverage.

The proportion of the total EFPIA in-kind accepted versus the total EU funding accepted is 0.94 (EUR 385.2 million/ EUR 411.2 million, according to Annual Activity Report 2016).

As no aggregated data were available on the amount of additional leveraged funding and no default mechanisms were in place to ensure such leverage, these may negatively impact the overall objectives of IMI JU. The additional leveraging effect was in the IMI JU *ad hoc* and on a project-per-project basis.

Annex 13 provides examples of leveraged funding and continued funding aimed at assuring project sustainability.

IMI JU has brought examples of 15 consortia that attracted follow-on or leveraged funding, from private and/or public sources as a result of an initial IMI grant.

Twelve projects leveraged additional in-kind contribution from industry, patient foundations and national governments.

- ULTRA-DD attracted EUR 1.5 million from several patient organizations.
- EMIF MET attracted EUR 50K from Novo Nordisk Foundation.
- GETREAL has secured a further EUR 1 million from EFPIA companies to support sustainability activities.
- EUCLID allowed to identify (after screening the European Lead Factory) a set of compounds which interferes with a new target. It could be used to reverse metabolic complications in type 2 diabetes. A Swedish spin-out company was created.

This finding showed that IMI Public Private Partnership was able to facilitate the development of coherent long term strategic investments in health from research to industry with the help of charities and ministries. Since these results concern only precompetitive research it was difficult to appreciate whether they will really contribute to EU policies of health, biopharmaceutical research, life sciences research and above all to economic growth.

7.6 Lessons learned from the previous evaluations

The previous external evaluations covered the operation of the IMI JU, from 2008 to 2013. The expert group examined the follow-up and implementation of these recommendations and assessed the extent to which the identified shortcomings in implementation have been addressed to date in the implementation modalities of Horizon 2020.

The Court of Auditors (CoA) provided a yearly assessment of the accounts of the IMI JU. The audit approach taken by the CoA comprises analytical audit procedures, testing of transactions at the level of the Joint Undertaking and an assessment of key controls of the supervisory and control systems. The report from the CoA and the opinion of the European Parliament are the key pillars of the JU's discharge procedure, which was separate from the European Commission discharge. It was the JU responsibility to follow up the recommendations made by the CoA and/or the European Parliament.

The previous evaluation provided the following recommendations.

- Recommendation 1: IMI needs to finalise and implement an articulated communication strategy with clear and measurable goals and objectives, addressing both the key stakeholders and a wider audience.

The communication strategy has been developed and thought through, but some points remain to be improved (see as outlined in section 7.2.1).

- Recommendation 2: Alongside the existing KPIs, aggregated KPIs need to be developed and measured in order to quantitatively demonstrate the IMI impacts and socio-economic benefits.

As outlined in section 7.2.1.3, a SMART accountable KPI framework has not fully been realised and needs further improving. The expert group specified this requirement in a note sent to the GB prior to their discussion on 14 March 2017 on the proposed new Performance Measurement Framework that had been presented to the expert group.

- Recommendation 3: IMI should make an additional effort to increase engagement from a wider range of industry stakeholders.

This recommendation was taken up when installing IMI2 JU, in which the effort to increase participation of other industry sectors has been thorough. In addition, IMI JU has put substantial effort to increase the participation of SMEs. Nevertheless, the success of the efforts was not overwhelming. It seems that certain framework conditions to improve the participation were not totally met.

IMI JU succeeded in reaching out to patient organisations and to regulatory agencies that are essential for safety and timely access to medicines for patients.

- Recommendation 4: The IMI Executive Office should seek further ways of reducing bureaucracy and ensure that it has the optimal organisational structure for the tasks ahead.

The IMI Executive Office has put substantial effort to reduce bureaucracy and installed an optimal organisational structure. Nevertheless, IMI JU is subject to the EC framework conditions and hence not totally responsible for the bureaucratic pressure. As for its internal organisational structure, the staff may need to grow further as pressure on the staff can be significant, but IMI JU Executive Office proved to have improved its work significantly as demonstrated by the shortened the time to grant or to pay.

- Recommendation 5: IMI should seek to maximise the potential of its advisory bodies to gain support for the remaining calls and other activities at all levels.

This recommendation seems to have improved under IMI2 JU, but may still be improved further. Several testimonies indicated that it is unclear how call topics are being defined, and how input can be delivered or how input is taken on board. There is still a lack of adequate communication between the EFPIA partners that hold the pen and stakeholders that may also defined research needs in the remit of IMI JU. Furthermore, there is insufficient communication between the different advisory bodies, in contrast to the suggestion created from the governance representation (fig 1). The advisory groups could also have played a more significant role in communicating the findings and outcome of IMI projects. This role was never emphasised by IMI JU.

- Recommendation 6: IMI needs to plan for and design new and more flexible funding mechanisms to ensure the sustainability of current and future projects, where appropriate.

The point to ensure sustainability of project results or outcome was mentioned several times by several stakeholders and seems to remain an important need. Under IMI JU sustainability of project outcomes and results was not an objective from the start. However, the installation of closeout meetings when concluding IMI JU projects and in IMI2 JU of thematic Strategic Governance Groups, combined with the uptake of sustainability issues while designing projects, are measures that are likely to support sustainability of project outcomes and results and to make those accessible to build on in future projects when appropriate.

8. CONCLUSIONS

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

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

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

To get answers on these five aspects it was necessary to understand the initiative. IMI JU was created to support the European pharmaceutical industry and has as specific objectives to improve the efficiency and effectiveness of the drug development process to produce more effective and safer innovative medicines. The socio-economic situation justified the development of such a public private partnership.

To achieve these goals the founding partners each provided EUR 1 billion. The running costs of Executive Office were shared by both partners and were around 4% of the total costs for the full period of IMI. Research projects were financed in cash by the public partner, while the EFPIA partners provided an equal budget in kind.

To achieve the objectives a strategic research agenda was developed that formed the basis for an annual work programme that defines topics to address. Calls for 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 Executive 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 input and for open dialogue which did not seem to exist.

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

Although not included in the onset of IMI JU projects, many have advocated that important outputs should be sustained to build on further. There were only a limited number of examples of project outputs that were sustained. This may suggest a lack of interest or only a low priority for pharma industry (EFPIA).

Related to this perception of a lack of transparency and communication was the frustration vented about how the SRA and call topics were being developed. This was found to be 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 objectives set.

The objectives of IMI JU were also in line with the objectives of FP7 to strengthen the scientific and technological base of European industry and to encourage international competitiveness. However, the SME inclusion in IMI projects could have been higher. Especially when compared with the average participation of SMEs in FP7, in which the target for SME participation was set to 20% of the budget, this has not been reached in IMI JU where the EU contribution for SMEs was only around 13%, whereas for the FP7 Health theme (excluding IMI) this reached almost 18%.

For SMEs, but also for some academic stakeholders participation in IMI JU projects was not straightforward. The governance of the large IMI consortia was considered time consuming and complex. In addition, the negotiations on intellectual property were found to be very challenging, as the focus on precompetitive research from pharmaceutical companies was most likely core business for an SME and they may prefer not to share the background IP. 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 are often not adequately equipped to negotiate IP rights in the setting of the IMI pharmaceutical companies.

In IMI JU, mid-cap companies and companies from other sectors than pharmaceutical were not eligible for EU funding. This was a clear missed opportunity which has been corrected when setting up IMI2 JU.

One of the main achievements 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 the leading industry partner from an ongoing project, even though EFPIA negotiated to find solutions. Although this did not happen often, when it did occur 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 imposes significant extra effort as work packages need to be rewritten and parts of work need to be taken over by others and adaptations to a potential new partner have to be made.

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

From a geographical point of view, it was clear that IMI JU was generally not present in EU-13 countries. Some countries were outperforming significantly when compared with others. The absence of large biopharmaceutical companies and strong bio-pharmaceutical research in EU-13 countries may be an explanation why there is limited collaboration between academics and big pharma companies by tradition and may be linked to the low participation level in IMI JU.

The coherence of IMI JU with the objectives in FP7 could have been improved not only through specific actions targeting to broader geographical spreading, but also through aligning better with other initiatives such as developed by the Joint Programming Initiatives, some of which addressing the same societal challenge as covered in the SRA of IMI JU. Closer interaction and collaboration may enhance innovation in these areas.

The added value of the IMI JU was more challenging to evaluate, in particular because the initiative did not succeed in setting up an accountable performance measuring system using SMART KPIs. The annual reporting and current KPI system under development were not aligned with the impact assessment goals and success criteria at the origin of IMI JU.

The IMI Executive Office indicated that project outputs include new spin-off creations, trademarks, licensing deals, results implemented by industry, sustainability plans, commercialisations, and patent applications. However, by the end of 2016, only 21 projects out of 59 have reached the end of their IMI funding cycle. Furthermore, IMI JU also led to over 2000 direct jobs created, which leverage the creation of other jobs elsewhere in the economy. Next to that IMI projects also created a significant scientific output as evident from the scientific publications. So far however, there were no examples of IMI bringing new, safer and more effective therapies or products to patients or that the time to develop such new applications has been shortened. The results also must be evaluated in relation to those obtained by the various and numerous technology transfer offices in Europe and other financing programmes and in relation to the available budget.

It would be a major success if IMI JU could have a demonstrable effect on making Europe more attractive for investing in biopharmaceutical R&D. Although compared with other EU-funding sources IMI JU mobilised significant private investment, which were 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 were in general always relatively small and cannot be correlated to the overall company R&D budgets. Even though under IMI JU the focus was on precompetitive research and thus did not cover the entire scope of research and development. The level of in-kind contribution was however limited by the fact that this needed to be matched by the EU budget, which was specified in the Council Regulation to a maximum of one billion Euros.

There was also still insufficient transparency on how the in-kind contributions were calculated. Although IMI representatives often mentioned that IMI 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 also be questioned when the investments from outside Europe were taken into account in the calculations of in-kind made investments, even though these were global companies. The headquarter location should not be the determining factor to assign the in-kind contribution, but rather the location where the actual activities were supported.

In conclusion, the expert group agreed that **the reasons to create a public private partnership to strengthen the European pharma industry were valid and the goals were justified** at the time when IMI JU programme was launched. Whether the right framework conditions were set

to achieve these goals, is not clear. Quantifiable indicators to demonstrate a socioeconomic benefit were lacking, which made it more difficult to evaluate the potential impact of the programme. If the European pharmaceutical sector is not increasing its activities and investment in Europe it can be questioned whether the goals to shorten the time of drug development could have been achieved using different mechanisms such as the stronger promotion of European SME involvement as a way to stimulate the European competitiveness. Nevertheless, IMI JU also realised a number of very promising results in line with the objectives of the programme.

It was clear that a long-term strategy is required before the joint undertaking may realise a demonstrable effect supporting the competitiveness of the European pharmaceutical industry. Currently, IMI and EFPIA representatives were unable to identify socio-economic benefits from IMI JU and claimed that more time was needed before health indicators will indicate a change. It was therefore perhaps too early to bring a definitive appreciation on the role of IMI JU on boosting the competitiveness of European pharmaceutical industry.

9. ANNEXES

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9.1 Annex 1: Experts short biographies

Name of experts	Nationality and Gender	Short biography
André Syrota	French Male	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). 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. 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).
Kathleen D'Hondt	Belgium Female	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. 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).
Katherine Payne	UK Female	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).
Belen Crespo	Spain Female	Director of the Spanish Agency of Medicines and Medical Products Member of EMA Management Board 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. 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.
Marcin Szumowski	Poland Male	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.

9.2 Annex 2: 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

9.3 Annex 3: 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

9.4 Annex 4: 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 than 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 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?

9.5 Annex 5: 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	C*ountries* in EU before the accession of ten candidate *countries* on 1 May 2004	Countries which joined EU after 2004
Austria	Austria	
Italy	Italy	
Belgium	Belgium	
Latvia		Latvia
Bulgaria		Bulgaria
Lithuania		Lithuania
Croatia		Croatia (from 1st July 2013)
Luxembourg	Luxembourg	
Cyprus		Cyprus
Malta		Malta
Czech Republic		Czech Republic
Netherlands	Netherlands	
Denmark	Denmark	
Poland		Poland
Estonia		Estonia
Portugal	Portugal	
Finland	Finland	
Romania		Romania
France	France	
Slovakia		Slovakia
Germany	Germany	
Slovenia		Slovenia
Greece	Greece	
Spain	Spain	
Hungary		Hungary
Sweden	Sweden	
Ireland	Ireland	
United Kingdom	United Kingdom	

Associated Countries

Legal entities from Associated Countries can participate under the same conditions as legal entities from the Member States. Association to FP7 takes place through the conclusion of an International Agreement. As of 31 December 2013, the following countries were associated to FP7:

Albania
Bosnia and Herzegovina
Faroe Islands
Iceland
Israel
Lichtenstein
Moldova
Montenegro
Norway
The former Yugoslav Republic of Macedonia
Serbia
Switzerland
Turkey

9.6 Annex 6: List of IMI JU projects

Project Acronym	Number of partici-pants	Types of participants	EFPIA contribu-tion (EUR)	IMI JU contribu-tion (EUR)	Project website
ABIRISK	40	9 EFPIA; 3 SMEs; 25 academic/ research; 2 other; 1 patient organisation	9,450,211	18,170,217	www.abirisk.eu
ADVANCE	29	7 EFPIA; 3 SMEs; 11 academic/ research; 8 other	5,017,353	4,999,811	www.advance-vaccines.eu
AETIONOMY	20	4 EFPIA; 2 SMEs; 13 academic/ research; 1 patient organisation	8,021,460	7,993,234	www.aetionomy.eu
APPROACH	26	3 EFPIA; 4 SMEs; 16 academic/ research; 2 others; 1 patient organisation;	7,499,999	7,500,000	www.approachproject.eu
BioVacSafe	24	4 EFPIA; 3 SMEs; 17 academic/ research	7,999,683	17,425,664	www.biovacsafe.eu
BTCure	39	9 EFPIA; 5 SMEs; 23 academic/ research; 2 others	15,616,595	17,362,872	www.btcure.eu
CANCER-ID	32	6 EFPIA; 6 SMEs; 18 academic/ research; 2 other	7,565,692	6,620,000	www.cancer-id.eu
CHEM21	21	6 EFPIA; 5 SMEs; 10 academic/ research	13,871,772	9,829,638	www.chem21.eu
COMBACTE-CARE	21	3 EFPIA; 15 academic/ research; 3 other	59,317,760	23,871,500	www.combacte.com/combacte-care
COMBACTE-MAGNET	40	5 EFPIA; 2 SMEs; 27 academic/ research; 6 other	91,662,413	75,340,000	www.combacte.com/About-us/COMBACTE-MAGNET
COMBACTE-NET	41	5 EFPIA; 1 SMEs; 33 academic/ research; 2 other	90,055,721	109,433,010	www.combacte.com/combacte-net
COMPACT	22	7 EFPIA; 1 SMEs; 14 academic/ research	18,217,735	10,184,909	www.compact-research.org
DDMoRe	29	11 EFPIA; 6 SMEs; 12 academic/ research	10,616,336	10,399,426	www.ddmore.eu

DIRECT	28	5 EFPIA; 22 academic/ research; 1 other	18,816,527	21,388,643	www.direct-diabetes.org
DRIVE-AB	23	7 EFPIA; 1 SME; 14 academic/ research; 1 other	3,105,250	6,299,987	www.drive-ab.eu
EBiSC	32	9 EFPIA; 6 SMEs; 17 academic/ research	8,778,546	21,840,379	www.ebisc.org
EHR4CR	37	10 EFPIA; 5 SMEs; 21 academic/ research; 1 other	7,555,883	7,194,044	www.ehr4cr.eu
ELF	36	7 EFPIA; 14 SMEs; 15 academic/ research	91,337,070	79,999,157	www.europeanleadfactory.eu
EMIF	65	10 EFPIA; 10 SMEs; 43 academic/ research; 2 patient organisations	24,354,503	24,356,849	www.emif.eu
EMTRAIN	30	16 EFPIA; 12 academic/ research; 2 other	3,664,510	4,324,999	www.emtrain.eu
ENABLE	41	4 EFPIA; 16 SMEs; 19 academic/ research; 2 other	22,952,360	58,900,000	www.nd4bb-enable.eu
EPAD	36	13 EFPIA; 16 academic/ research; 2 other; 1 patient organisation;	30,204,986	25,880,000	www.ep-ad.org
eTOX	32	13 EFPIA; 5 SMEs; 13 academic/ research; 1 other	10,157,590	6,910,018	www.e-tox.net
eTRIKS	17	10 EFPIA; 1 SME; 5 academic/ research; 1 other	10,336,178	10,309,818	www.etriks.org
Eu2P	25	15 EFPIA; 7 academic/ research; 3 other	4,019,661	3,708,225	www.eu2p.org
EU-AIMS	29	7 EFPIA; 6 SMEs; 15 academic/ research; 1 patient organisation	9,773,543	20,490,981	www.eu-aims.eu
EUPATI	36	21 EFPIA; 4 academic/ research; 4 other; 7 patient organisation;	5,701,178	5,250,000	www.patientsacademy.eu
EUROPAIN	27	12 EFPIA; 2 SMEs; 12 academic/ research; 1 other	11,165,740	6,229,343	www.imieuropain.org

FLUCOP	22	6 EFPIA; 12 academic/ research; 2 other	6,100,208	6,100,000	www.flucop.eu
GETREAL	30	15 EFPIA; 1 SME; 8 academic/ research; 5 other; 1 patient organisation;	6,910,397	8,000,000	www.imi-getreal.eu
iABC	24	2 EFPIA; 17 academic/ research; 5 other	25,550,025	24,331,609	www.iabcproject.com
IMIDIA	21	8 EFPIA; 1 SME; 12 academic/ research	16,940,659	8,060,760	www.imidia.org
iPiE	25	12 EFPIA; 3 SMEs; 7 academic/ research; 3 other	5,698,230	3,000,000	www.i-pie.org
K4DD	21	7 EFPIA; 3 SMEs; 11 academic/ research	9,831,318	8,286,930	www.k4dd.eu
MARCAR	12	5 EFPIA; 1 SMEs; 6 academic/ research	5,155,604	6,049,578	www.imi-marcar.eu
MIP-DILI	29	12 EFPIA; 5 SMEs; 11 academic/ research; 1 other	12,648,466	15,335,538	www.mip-dili.eu
NEWMEDS	21	11 EFPIA; 3 SMEs; 7 academic/ research	13,789,412	8,986,216	www.newmeds-europe.com
Onco Track	23	8 EFPIA; 5 SMEs; 10 academic/ research	11,201,557	16,757,282	www.oncotrack.eu
Open PHACTS	35	10 EFPIA; 5 SMEs; 16 academic/ research; 4 other	6,412,905	11,466,433	www.openphacts.org
ORBITO	29	13 EFPIA; 3 SMEs; 10 academic/ research; 3 other	12,360,856	8,975,392	www.orbitoproject.eu
Pharma-Cog	42	12 EFPIA; 5 SMEs; 22 academic/ Reseach; 1 other; 2 patient organisation;	11,690,333	9,658,388	www.pharmacog.eu
Pharmatrain	50	15 EFPIA; 29 academic/ research; 6 other	3,489,181	3,510,300	www.pharmatrain.eu
PRECISESADS	30	5 EFPIA; 2 SMEs; 20 academic/ research; 3 other	9,890,865	9,999,323	www.precisesads.eu
Predect	21	9 EFPIA; 3 SMEs; 9 academic/ research	9,661,201	8,756,641	www.predect.eu

PreDiCT-TB	20	3 EFPIA; 2 SMEs; 15 academic/ research	9,296,106	14,778,855	www.predict-tb.eu
PRO-active	20	8 EFPIA; 1 SME; 9 academic/ research; 2 patient organisations	7,221,617	6,767,597	www.proactivecopd.com
PROTECT	38	14 EFPIA; 2 SMEs; 15 academic/ research; 6 other; 1 patient organisation;	10,864,491	11,009,715	www.imi-protect.eu
Quic-Concept	24	8 EFPIA; 1 SME; 15 academic/ research	6,809,606	7,000,000	www.quic-concept.eu
RAPP-ID	21	5 EFPIA; 4 SMEs; 12 academic/ research	6,379,048	6,828,438	www.rapp-id.eu
SafeSciMET	33	15 EFPIA; 18 academic/ research	18,326,521	13,901,971	www.safescimet.eu
SAFE-T	26	12 EFPIA; 4 SMEs; 10 academic/ research	3,607,540	2,374,904	www.imi-safe-t.eu
SPRINTT	26	5 EFPIA; 4 SMEs; 15 academic/ research; 2 other	23,454,392	23,999,439	www.mysprintt.eu
STEMBANCC	38	11 EFPIA; 3 SMEs; 23 academic/ research; 1 other	20,761,386	26,000,000	www.stembancc.org
SUMMIT	27	6 EFPIA; 19 academic/ research; 1 other	15,252,050	14,654,559	www.imi-summit.eu
TRANSLOCATION	28	5 EFPIA; 7 SMEs; 15 academic/ research; 1 other	8,135,833	15,984,202	www.nd4bb.eu
U-BIOPRED	47	12 EFPIA; 24 academic/ research; 3 other; 5 patient organisation;	14,574,652	9,935,501	www.ubiopred.eu
ULTRA-DD	10	4 EFPIA; 4 academic/ research; 2 other	21,664,981	21,200,000	www.ultra-dd.org
WEB-RADR	19	8 EFPIA; 2 SMEs; 6 academic/ research; 2 other; 1 patient organisation;	2,754,044	2,270,000	www.web-radr.eu
ZAPI	21	3 EFPIA; 5 SMEs; 12 academic/ research; 1 other	9,875,000	9,538,688	www.zapi-imi.eu

9.7 Annex 7: Examples of important results from IMI JU projects with SMEs relevance

Endocells, a French-based SME in the IMI diabetes project IMIDIA, developed the first ever human beta cell lines to be cultured in the lab that behave naturally. Their innovative technology has been fast-tracked because of collaboration with pharma partners. They now have a commercial product, a market for their cell line and their customer base is increased.

Chemotargets, based in Spain in the eTOX project on medicines safety, has a project-independent licencing agreement for use of their modelling approaches with one of the large pharma companies as a result of participating in the IMI project.

ICDD, another French SME, is working on protein profiling of Alzheimer's disease patients. Thanks to its participation in an IMI project, it has been able to access animal models, blood samples from patients across Europe and clinical data from multi-site European studies, tools that are normally beyond the reach of small companies.

Taros Chemicals, based in Germany, is a key player in IMI's European Lead Factory project. The project is developing a major new pan-European platform for drug discovery which comprises a large compound collection and associated screening centre.

Firalis, from France, participates in the IMI project SAFE-T, and credits its participation in an IMI project for being able to increase from 6 to 50 employees.

EBISC participant, **Roslin Cells Ltd**, has initiated a new spin out in UK named Roslin Cell Sciences Ltd.

Open PHACTS has created a sustainable pay-to-use platform that links up diverse drug discovery databases, through the **spin-off Open PHACTS Foundation**.

Cellular Phenomics & Oncology from Berlin, is a spin-off from cancer project ONCOTRACK to conduct the biological and pharmacological testing of new cancer therapeutics and diagnostics in preclinical models.

Education and training project Pharmatrain has created the **PharmaTrain Federation** to manage and continue developing project 'assets' created during the IMI-funding phase.

9.8 Annex 8: Examples of IMI JU projects in which patient organisations participated

U-BIOPRED is working on treatments for severe asthma through a dedicated patient input platform where patients provide advice on ethical, scientific, and communication issues. **PROactive** is developing methods to incorporate the impact of chronic obstructive pulmonary disease (COPD) on patients' daily lives into drug development.

Patient organisation Alzheimer Europe is an active partner in the IMI projects **Pharma-Cog, AETIONOMY, EMIF and EPAD**.

EU-AIMS for new treatments for autism has received USD 1M from the US-based patient advocacy group Autism Speaks.

Diabetes patient organisation JDRF has contributed to IMI's **IMIDIA** and **SUMMIT** projects.

EUPATI is a patient-led initiative that developed European Patients' Academy on therapeutic innovation, with training courses, educational material and an online public library, empowering patients to engage more effectively in the development and approval of new treatments.

9.9 Annex 9: Non-exhaustive list of examples of impact of IMI JU outputs on companies R&D, as provided by EFPIA

Novartis (fifth IMI JU contributor with 6.6% of IMI JU in-kind contributions - EUR 63 million)

- MARCAR
  - Access through MARCAR to extensive EFPIA and academic partner carcinogenesis study tissue biobanks and associated phenotypic and molecular profiling databases has enabled Novartis to enhance mode of action-based carcinogenicity assessments for development products whilst leveraging maximum value from legacy animal-based preclinical toxicology studies.
    - Furthermore, membership of the MARCAR consortium enabled Novartis scientists to gain external recognition as leaders in field of derisking drug-induced carcinogenicity.
- eTOX
  - Novartis will now benefit of the bespoke eTOX system (eTOXsys®) containing normalised and structured data of about 8,000 legacy GLP toxicology reports from 13 Pharma companies, and about a 100 predictive algorithms. Thanks to the eTOX experience and connections established during this consortium, PCS is now launching a data-driven and scalable strategy to address *in silico* predictive safety in which eTOXsys® will be a central part, at low risk and with a higher chance of success.
- Safe-T
  - Several novel biomarkers of drug-induced liver, kidney, and vascular injury, to be used for clinical safety monitoring. could be supported by EMA and FDA. Several of these biomarkers have now been used in multiple internal Novartis studies.

Sanofi (second IMI JU contributor with 10.1% of IMI JU in-kind contributions - EUR 96 million)

- IMIDIA
  - Access to deeply validated human beta-cell line for portfolio projects and as tool for the functional validation of candidate genes
    - Comprehensive understanding of human islet function reveals knowledge driven human target candidate identification
    - 2 follow-up collaborations initiated
- SAFE-T
  - Safety biomarkers implemented in preclinical studies
- European Lead Factory
  - 12 internal screens performed on Sanofi targets
  - Internal follow-up chemistry performed
- eTOX
  - eTOX databases fully used for request for in-silico toxicology group and regulatory questions from development projects
- PROTECT
  - New methods applied in Sanofi for the assessment of Benefit/Risk in the context of absence of association for any product on the market
- OrbiTo
  - Already applied on Sanofi compounds, optimization of decision trees for in vivo models to test for API/formulation studies
- COMPACT
  - Methods support development of 2 compounds
- PRECISESADS
  - Clinical data generated to be integrated in the development of compound

Boehringer Ingelheim (eighth IMI JU contributor with 4.1% of IMI JU in-kind contributions – EUR 39 million)

- OncoTrack
  - Biomarker signatures internalized into Boehringer Ingelheim R&D processes
  - Patient derived xenograft models used in-house
- PREDECT
  - 3D multicellular organoid-like models used in-house
  - Animal models under evaluation for in-house use
- SAFE-T
  - Safety biomarkers likely to be implemented in future preclinical and clinical studies (pending need)
- SUMMIT
  - Outcomes of the SUMMIT animal intervention studies have provided important insights with regard to an animal model used by Boehringer Ingelheim
  - A disease model developed in the SUMMIT project is under evaluation for in-house use
  - Biomarkers under development may be incorporated into Boehringer Ingerlheim's R&D (results pending)
- U-BIOPRED
  - In-house evaluation of the U-BIOPRED data set is informing NTC and biomarker discovery internally

UCB Pharma (eleventh IMI JU contributor with 2.8% of IMI JU in-kind contributions – EUR 27 million)

- European Lead Factory
  - Access to a large and diverse chemical library that has provided hits for multiple projects
  - 8 target screens have been selected so far
  - 4 programs have had post QHL work; 1 program was stopped before QHL (portfolio decision); 3 programs have screens in progress

Bayer (sixth IMI JU contributor with 5.2% of IMI JU in-kind contributions – EUR 49 million)

- SAFE-T
  - Liver, kidney and CV safety biomarker validated with relevance for own development programs
- OncoTrack
  - Novel modelling approach with potential value for other indications
  - New animal models for profiling of development compounds, applied for first development compounds
- EU Lead Factory
  - Access to a unique screening library to otherwise unattainable hits
  - 15 screens performed and 9 further progressed into our portfolio
- eTOX
  - Search and simulation tools becoming integral part of the lead compound evaluation process and prioritization of most promising candidates
- EHR4CR
  - EHR data standards and IT infrastructure allowing to run feasibility tests with clinical trial protocols against high quality clinical centers, allowing faster recruiting and avoiding some protocol amendments
  - Harmonized clinical trial center network still under development but with high potential for faster trial execution

- CHEM21
    - Flow chemistry approach developed which is now scaled-up within our company
- EUPATI
    - Access to high-quality training material in 10 languages, used for external and internal R&D training activities
    - EU guidance for patient involvement in R&D giving us a better framework for our own code of practice
    - Access to a broad patient organisation network
- EBISC
    - Immediate access to innovative technologies, saving ca. 2 year of time in comparison to independent in-house development

Novo Nordisk (seventeenth IMI JU contributor with 1.3% of IMI JU in-kind contributions – EUR 12 million)

- IMIDIA
    - Development and validation of the first human beta cell line (EndoC) has allowed Novo Nordisk to licence the EndoC cells to be used in new beta-cell standard assays for its internal research.
    - StemBANCC and EBiSC have been utilised for disease modelling and drug discovery resulting in improved in vitro cellular models for accelerated and more precise drug discovery and safety assessment.
    - DDMoRe has provided with models for Glucose Profile Predictions.
- ABIRISK has been instrumental for Translational Safety in building and internal immunogenicity prediction platform including human and murine T-cell assays and a humanized mouse model.
- EUPATI**:** The involvement in establishing the programmes for education and empowerment of patients has given Novo Nordisk the opportunity to direct engage with a range of patient group stakeholders and patient experts in R&D.

9.10 Annex 10: Other initiatives comparable to IMI JU (other than C-Path)

The Global Health Innovation Technology Fund (GHIT)[46]

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 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)[47]

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.

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

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46 https://ghitfund.org/en/

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

Combating Antibiotic Resistant Bacteria Initiative (CARB-X)[48]

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.

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

9.11 Annex 11: Examples of long term networks in specialised fields

New Drugs 4 Bad Bugs: this programme represents an unprecedented partnership between industry, academia and biotech organisations to combat antibiotic resistance in Europe by tackling the scientific, regulatory, and business challenges that are hampering the development of new antibiotics.

Ebola+ platform: the platform contributes to efforts to tackle a wide range of challenges in Ebola research, including vaccines development, clinical trials, storage and transport, as well as diagnostics. Even in the short term, the benefits to the local community of the 'EBOVAC-Salone' trial are important. New facilities had to be built to run the study, including the first emergency room at the local district hospital, and a vaccine storage facility. In addition, the project provides both jobs and training for local healthcare workers, who will also gain valuable experience by working on the trial.

EU-AIMS: This project has set up a clinical research network in autism which currently consists of 75 sites spread across 37 European countries and covering nearly 15 000 patient visits per year.

COMBACTE: under this project, a pan-European clinical trial hospital network - CLIN-Net - was set up, with more than 300 clinical sites in 37 countries to conduct high-quality clinical studies, to find new antimicrobials against resistant bacterial pathogens.

PROTECT: established the open access European drug consumption database of 45 298 adverse drug reactions for 654 medicines using data for 17 European countries.

9.12 Annex 12: Examples of IMI JU projects that brought results more rapidly to the market

- SUMMIT, an IMI diabetes project, has developed a breakthrough technique for a non-invasive ultrasound-based method which has wider applications for other types of patients.
- CHEM21 is working to reduce the environmental impact of drug development and manufacture. Sanofi is now exploring how to industrialise CHEM21's process for producing an anti-fungal treatment.
- SafeSciMET has now commercialised 20 drug safety sciences courses as well as an accredited advanced MSc degree in Drug Safety Sciences.
- U-BIOPRED has commercialised a provocative chemical agent developed by the project to be used as a tool for studying severe asthma.
- EUROPAIN consortium SME, Neuroscience Technologies, based in Spain, has opened an affiliate in UK and have commercialised biomarkers discovered during the project.
- BioVacSafe SME Immunoarray has commercialised an ichip® antibody technology providing molecular diagnostics for measuring specific antibodies. The test has been launched in a commercial setting in the US.
- EU-AIMS SME partner Noldus Information has commercialised new tools to test behaviours in mouse models for autism.

9.13 Annex 13: Examples of leveraged funding and continued funding aimed at assuring project sustainability

IMI JU project acronym	Leverage
APPROACH	During project implementation the consortium has attracted one additional EFPIA partner who will contribute additional in-kind.
DDMORE	During project implementation the consortium has established a foundation for the sustainability of project resources and first partner Servier will contribute €100,000/year.
EBISK	During project implementation the consortium Biogen is providing additional funding to subsidize new cell lines. CHDI has contributed €264,000 Euro for new lines.
EUCLID	Public programme owners have attracted further funding to follow-up on results of their screens by European Lead Factory. The researcher, Dr Margit Mahlapuu from the University of Gothenburg, has identified a new target which could be used to reverse metabolic complications in type 2 diabetes. With the help of the EUCLID project, she screened the European Lead Factory library of the then 320 000 industry compounds and identified a set of selective and potent small molecules which interfere with this target. She went on to create a spin-out company, ScandiCure, whose aim is to further develop these molecules into a first-in-class anti-diabetic drug. The company already secured an investment from GU Ventures AB, an investment company and an incubator owned by the Swedish state.
EMIF MET	During project implementation the consortium has attracted €500,000 from Novo Nordisk Foundation, and €10,000 from German Diabetes Association to help bridge the funding gap (75% rate of reimbursement of research costs).
EPAD	Roche Diagnostics has provided an additional in-kind investment into the project. In addition, Edo Richard and Maartje Schermer from WP8 (RUMC) have obtained a new grant from the Dutch Organisation for Health Research and Development to delve deeper in some ethical and conceptual issues around early diagnosis in dementia, as already studied in the context of the project.
EU-AIMS	During project implementation the consortium has attracted additional funding from Autism Speaks (€ 582,420) to sponsor a research assistant and a post-doctoral student and research consumables. Autism Speaks also contributes their personnel to conduct research activities with direct cost amounting to €17,580.
GETREAL	GetReal has secured a further €1M over two years from EFPIA companies to support sustainability activities.
K4DD	K4DD partners were granted computational time for PRACE (Partnership for Advanced Computing), enabling faster and more eleborate analysis of the K4DD results.
OncoTRACK	Archiving of OncoTrack data after completion of the project will be supported by funds from the government of Luxembourg, supporting the ELIXIR hub at the University of Luxembourg.
RAPP-ID	Researchers from RAPP-ID were awarded follow on grants: the ROUTINE project (FP7) aimed toward the development of urinary track infections diagnostics; the ND4ID project (H2020) is a Marie Curie Initial Training Network grant to develop unique educationprogramme focused on technological aspects of diagnostics development.
ULTRA-DD	During project implementation the consortium has attracted additional funding (€1.5 million for the next two years) from several patient organisations, including Myeloma UK and The Brain Tumour Charity to sponsor postdoctoral researchers whose scientific outputs will contribute directly to the ULTRA-DD project. The project has also secured additional €10,000 from Bayer pharma.
IMIDIA	During the project lifetime the consortium has secured additional funding ($600,000) from JDRF to support expansion of research activities in T1 diabetes.
SUMMIT	During the project lifetime the consortium has secured additional funding ($438,361) from JDRF to support integrating SUMMIT's diabetic kidney disease genetics efforts.
PHARMACOG	During the project lifetime the consortium has secured additional funding from Spanish Ministry of Economy and Competitiveness (IDIBAPS), who provided 4-year funded PhD student that worked in the project.

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The Council Regulation (EU) No 557/2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking stipulates in Art.19(2) that the interim evaluation referred to in Article 11(1) shall also include a final evaluation of the IMI Joint Undertaking as initially established under Council Regulation (EC) No 73/2008. The final evaluation of IMI JU shall be conducted by 30 June 2017, by the Commission with the assistance of independent experts.

The current final evaluation of the operation of the IMI JU covers the period from its establishment in 2008 to 31 December 2016. Its main objective is to assess the performance of the IMI JU and its progress towards the objectives set out in Council Regulation (EC) No 73/2008.

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 an interim report of the IMI2 JU, published under EUR 17527 EN.

Studies and reports

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