

IMI2 Scientific Committee Work Plan and Agenda for 2019 – Executive Summary

The IMI2 Scientific Committee (SC) is an advisory body to the IMI2 JU and in particular the Governing Board (GB). Its mandate consists in providing advice on scientific questions and related issues in regards to the IMI2 programme.

At the last meeting the SC discussed its strategy and work plan for 2019, which will possibly last until beginning of 2020. There was general consent that SC actions should have prospective character rather than consist in retrospective analysis. Due to the ending of IMI2 JU the SC especially felt that any topics addressed and recommendations issued during the next 1.5 years of its mandate should also be of general value, i.e. not restricted to the IMI2 JU PPP in their applicability. The SC, therefore, decided to present its current work plan to the GB to seek approval in respect to the utility of the work.

In the last term the SC addressed important topics that were mainly intended to strengthen the structure and impact of the IMI2 programme. The SC issued opinion papers on the topics that were found to be of high relevance. These statements were published on the IMI website:

- IMI Scientific Committee position on IMI-funded digital innovation and data integration in discovery of novel medicines (January 2018)
- Sustainability solutions are important criteria determining project quality and output in IMI (June 2018)
- IMI Scientific Committee recommendations regarding public private partnership funding – what makes a topic ultimately suitable for this kind of funding model? (February 2019)

Additionally, the SC developed a paper summarizing recommendations for a new public private partnership programme in the new framework programme in Horizon Europe. The recommendations were already presented to the GB on April 5th, 2019 and the paper was adopted on April 26th, 2019 at the SC meeting.

With these initiatives the SC has attempted to support innovative research and exchange among the IMI2 stakeholders by highlighting weaknesses and important trends. With its previous actions the SC further aimed at ensuring that the high investments into IMI2 projects are reflected in project outputs and impact and that sustainability solutions are sought when assets are found worthwhile to be maintained.

Based on the SC recommendations in regards to sustainability the IMI2 programme office has developed an action plan to implement the suggestions made by the SC. The action plan was presented at the last SC meeting and there was broad consent that the IMI2 programme office is doing an excellent job in the implementation of measures to enforce sustainability of assets where necessary. This includes guidance for topic writers and applicants on the

identification of assets requiring sustainability and the development of concepts for sustainability, including an overview on relevant infrastructures available in the EU.

In view of these very positive developments and the potential impact of the SC actions the SC held a strategic discussion to identify further areas where the SC could provide support to the IMI2 programme in the remaining 1.5 years of its term. Overall, the SC members agreed that additionally to structural issues there is a need to provide more input on the research program and the science performed in IMI2, including a gap analysis based on the IMI2 strategic research agenda.

As a result of the discussion the committee decided to distinguish A). issues related to the governance and structure of IMI2 from B). topics focussing on the research performed in IMI2.

Within these categories the SC identified five topics that were prioritized to form a work plan:

A. Tentative topics related to the IMI2 programme structure and governance

- a. Data infrastructure and integration
- b. Involvement of regulators and regulatory science
- c. Equitable access

B. Tentative topics related to the research programme

- a. Recommendations for research on rare diseases within a PPP
- b. Repurposing of drugs

An abstract summary of these topics is provided below. Further proposals such as “adverse events” were de-prioritised at this time point but may be picked up later.

The SC further welcomed that the IMI2 programme office is working on gaining better visibility of the actual outcomes and impact of terminated projects in IMI1 and IMI2. It was further discussed that the latest plans for patient expert engagement presented at the SC meeting are considered as excellent, in particular since patient engagement is viewed as a central element in a PPP in health care and this issue had been discussed in many occasions in the SC meetings. The SC further discussed that a dedicated plan for engagement of physicians and physician associations is needed but felt that support from the SRG would be more efficient, while the SC is not in the position to oversee this process.

Brussels, May 30th, 2019

On behalf of the IMI2 Scientific Committee

Prof. Dr. Isabelle Bekeredjian-Ding, Chair

Prof. Dr. Dolores Cahill, Vice Chair

Abstract summaries of the SC “hot topics” for the work plan:

A- Tentative topics related to the IMI2 programme structure and governance

a. Data infrastructure and integration

Biomedicine is by now a data rich science. IMI and IMI2 have largely contributed to the production of data and to the development of data generation technologies. Additionally, IMI has supported a small number of key projects dedicated to explore technical solutions for data handling, data labelling (metadata and FAIRification) as well as to the integration of biomedical data.

The on-going developments in OMICS (large scale sequencing, single cell sequencing, organoids, metabolomics, high-throughput screening, etc), medical and personal devices, natural language processing (NLP) on medical documentation, medical imaging, and other technologies, will make even more obvious the pressing need of dealing with biomedical data in a systematic and sustainable manner.

It is important to state that in this area the interest of society, public research, pharma and IT companies align well. All of them need access to clean, well-organised, connected, reproducible and reachable data, and all of them are interested in the development of technologies that will enable the exploitation of these data on firm legal and ethical basis. In this context, the IMI and in the potential future public-private partnerships seem to be the appropriate vehicle to develop the infrastructures to make possible to all the stakeholders to benefit from the data in the framework of the appropriate level of data access and security.

Fortunately, Europe have already invested in the construction of biomedical and compute infrastructures that now offer the perfect basis for the construction of an “European Biomedical Data Infrastructure -or Infrastructures”, bridging the current gap in the use of biomedical data by industry and society.

Finally, this consistent “European Biomedical Data Infrastructure” will be an essential pillar for the development of the new wave of artificial intelligence/machine learnings (AI/ML) medical assistants, that will open for Europe the doors of the Medicine of the Future.

b. Involvement of regulators and regulatory science

Early involvement of regulators is recommended in IMI2 projects because translation and implementation often require regulatory feedback and approval. Thus, engagement of regulators is strongly encouraged in IMI2. Regulators can contribute as researchers in development and testing of new methodology or they can engage in their role as regulators and policy makers, e.g. in the evaluation of the specific public health needs, by providing regulatory advice, in identifying implementation hurdles at an early stage, or in the development of new regulatory solutions as well as in supporting global harmonisation of

regulatory procedures. Despite these opportunities the IMI2 Scientific Committee (SC) has observed three major issues in regard to regulatory involvement: 1.) consortia are often hesitant to engage with regulators, which may be due to inexperience, 2.) there is reluctance of regulators to participate in IMI2, which is often based on the perception that there might be a conflict of interest, and 3.) when new regulatory concepts are required project consortia often limit themselves to dissemination of information to regulators but restrain from implementing “regulatory research” for providing scientific evidence that could justify the change. The SC plans to develop a discussion paper on how to improve regulatory participation in IMI2 projects.

c. Equitable access

Despite benefiting from public investment and incentives, pharmaceutical companies often launch their new products with so high prices that are not affordable for lower income EU member states. As equitable patient access considerations are not mandated or not even addressed in IMI2 call texts, the current public private partnership widens the health gap between health between rich and poor EU countries.

The situation is further complicated by disproportional allocation of IMI2 research funds to EU-15 versus the EU-13 countries, which means that clinical hypotheses are less likely tested in lower income member states. No EU-13 countries are associated with above the average IMI2 funding per million population, which indicates inequity in the current grant allocation system on historical basis rather than inefficiency of EU-13 research centres in the application process.

IMI2 should reconsider two dimensions of equity in future calls, including 1) more equitable access to IMI2 research funds across EU member states and 2) more equitable patient access to medical innovation accelerated by public-private partnership.

B - Tentative topics related to the research programme

a- Recommendations for research on rare diseases within a PPP

IMI2 includes in its objectives the fight against rare diseases and several ambitious projects have already been launched. EFPIA members already demonstrated their major involvement in rare diseases as well as a lot of European SMEs and academic groups, not to mention the natural involvement of large patients representative groups and the stimulating role of the regulators. The landscape has considerably improved during the last years with the launch of large European initiatives (ECRIN, European Joint Programme on Rare Diseases, Eurordis, European Reference Centers, etc.). Thus, there is an opportunity to foster a better and faster development of medicinal products for Rare and Ultra Rare Diseases in Europe. At the precompetitive level, based on PPP and combining high-level approaches versus applied pilot initiatives, IMI2 should be able to propose innovative strategies related to target screening, preclinical models, natural history, evaluation criteria including patient reported outcome measures (PROMs) and real world evidence. Finally,

decision tools should improve the predictability and probability of success and allow early market access as well as fair pricing.

The professionalisation of patient organisations and single patient experts has evolved drastically, thanks to educational programs such as the EUORDIS summer- and winter-school and the EUPATI patient expert training course. The growing pool of well-educated patient representatives and professional patient organisation are a valuable asset to Rare Disease research projects. Especially in Rare Disease where a lot is still unknown, patient involvement is necessary to complete the picture of a rare disease, to understand patients unmet needs and to conduct research in a patient friendly and patient centered way.

b. Repurposing of drugs

Pharmaceutical R&D of new molecules is costly, the average innovation process of new medicines costs more than 2.5 billion USD, when sunk costs of unsuccessful development projects are also taken into account (DiMasi JA, Grabowski HG, Hansen RA. *Journal of Health Economics* 2016;47:20-33.). Repurposed and repositioned (or value added) medicines may generate important clinical benefit in new (2nd) medicinal indications while on patent and after they go off-patent. Also, new strategies in precision medicine for individualised therapies involve going through libraries of existing drugs to find new use of drugs or drug combinations in individual patients or sub-groups of patients. In addition, epidemiology is increasingly used as a viable byway to detect signals of effectiveness for repurposing agents by using a combination of prescription and health registers to investigate whether agents with a prior preclinical or theoretical evidence base may have beneficial effects when applied in previously not tested indications. The development costs of repurposing or documenting new indications for existing medicines is significantly less compared to development of new medicines. However, third-party payers may not acknowledge the value proposition of repurposed (value added) medicines, as after patent expiry their objective is to facilitate savings in health care budgets through generic price erosion. As it is difficult to justify premium price for the added value, the return on investment for drug repurposing is questionable. The IMI2 Scientific Committee advocates strategic discussions on how to improve the business model for value added medicines, and potential IMI calls to facilitate research in this field and advance drug repurposing strategies for both on-patent and off-patent medicines.