Potential future IMI Call topics

About this document

The following topics are under consideration for inclusion in future IMI Calls for proposals in the longer term. The discussions on these topics are still in their early stages. For this reason, the topics may change considerably and they will probably not be ready for inclusion in an IMI Call for proposals for several months. Furthermore, as the discussions advance, it is likely that some topics will be added to this list while others will be dropped. In any case, we hope that this list will give potential applicants a useful glimpse into what is under development in the longer term, and provide additional time to enhance their network. We will update this list whenever we have updates on the status of the topics.

Document last updated: December 2019

All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.

Neurodegeneration and other neuroscience priorities

Rare neurodegenerative and neurocognitive diseases clinical platform development

The main scope of this topic will be to develop a clinical platform for rare neurodegenerative and neurocognitive diseases (RND), ready to test new therapies in a streamlined and efficient way, delivering more effective, targeted interventions that can slow or stop RND. Additionally, the research on a rare neurological disorder will be used to get insights into more complex diseases with similar genetic linkage.

Complement in neurodegenerative diseases

The main interest is around building knowledge on the druggable targets in the complement system, as neuroinflammation is widely implicated in a wide range of chronic neurodegenerative conditions, but much about the specific role of complement remains to be defined. The project will build up on the significant advances in genetic and biomarker domains made for Alzheimer's disease (AD), focusing on delivering a profile of the status of complement activity in Parkinson's disease (PD), Huntington disease (HD), amyotrophic lateral sclerosis (ALS) (or possibly subtypes of these), with corresponding suggestions of what novel therapeutic approaches/ targets could be most effective.

Expected impact:

- Foster the collaboration of the main stakeholders that are academic researchers, patients and patient advocacy groups, industry and regulatory bodies as well as reimbursement agencies to build up innovative trial methodologies appropriate for the rarity of the diseases
- Leverage the growing pipeline of therapeutic RND approaches developed by European pharma industry
- Develop the knowledge of the role of complement in PD, ALS, HD and other neurodegenerative diseases, using the technical foundations established in AD
- Apply innovative approaches in the research methodologies that will be performed (system biology analysis; complete patient biomarkers' profiling; in vivo testing of tool compounds/ antibodies in specific animal models)

Infection control including vaccines

Expansion of the AMR accelerator platform. There is still a critical need for new antibiotics. The objective is to build on the Antimicrobial Resistance (AMR) Accelerator Programme launched in 2018. The aim is to expand activities and accelerate scientific discoveries in antimicrobial resistance (AMR) and to progress a pipeline of potential therapeutic, biologic and preventive medicines & procedures. This may include host pathogen interaction (e.g. anti-virulence targets), host directed and immune therapies, alternative approaches (e.g. novel delivery systems), in silico tools (big data, machine learning, artificial intelligence (AI)) for optimizing use of available data (Clinical Trials, pharmacokinetics/pharmacodynamics (PK/PD), physiologically based pharmacokinetic (PBPK), Imaging, non-clinical safety studies). The solutions should help preventing recurrent infections, improve quality and longevity of life and reduce significantly the use of antibiotics.

Development of innovative personalized diagnostics and patient-guided therapies for the management of sepsis-induced immune suppression

The proposed topic is addressing sepsis, a global health priority being targeted by many countries and the World Health Organization (WHO). If not recognized early and managed promptly, sepsis can lead to septic shock, multiple organ failure and serious consequences including death. There are approximately 30 million sepsis patients per year worldwide. The primary aim of this topic is to develop diagnostic tools for characterizing sepsis or injury-induced immunosuppression in order to target personalized management and therapeutic solutions for improving outcomes and decreasing the occurrence of secondary healthcare-associated infections (HAI). The main objectives will be to reduce mortality and decrease secondary HAI through diagnostic and therapeutic approaches including (i) implementation of an immune-based personalized diagnostic test to clearly identify sepsis patients in an immune-suppressed state and (ii) introduction of innovative immuno-modulators in order to restore immune homeostasis. The project generated from the topic will also aim to demonstrate the medical and economic value and benefits of this approach to improve patient outcomes (organ dysfunction, disability, mortality, etc.), decrease infectious HAI complications, and reduce healthcare costs.

Modelling the impact of monoclonal antibodies and vaccines on the reduction of antimicrobial resistance

Monoclonal antibodies (mAb) and vaccines can reduce antimicrobial resistance (AMR) but quantifying their impact is methodologically challenging. This topic has the main objective to quantify the burden of disease and health care costs caused by AMR and the impact of the monoclonal antibodies and vaccines, to prepare the ground for cost-effectiveness modelling to select the best intervention strategy which could reduce such a burden. A systematic review of the literature should clarify the initial structure of the model, the potential parameters and the gaps that will be filled by a retrospective review of relevant hospital databases throughout Europe and globally Finally, while many data are currently available, the selection of data, their curation and processing should be handled through mathematical modelling to test the effect of mAb and/or vaccination strategies.

Expected impact:

▪ A pipeline of promising new agents for tackling gram -ve antibiotic-resistant bacterial infections,
▪ New diagnostics and therapeutic solutions to improve patient outcomes, decrease infectious complications, and reduce healthcare costs for secondary healthcare-associated infections.
▪ Determine where mAbs and vaccines will be most useful from health economic and disease burden perspective and with the highest chance of reducing antibiotic consumption and emergence of resistant isolates
▪ Increase the amount of scientific and value-added information on the potential role of vaccines and mAbs in reducing AMR

Big data, digital health, clinical trials and regulatory research

Data lakes

Many pharma and life sciences companies are currently creating data lakes to bring together internal data to apply analytics and create insights. However, these data often need to be complemented with other data sources. Most health data are generated outside the life sciences, e.g. electronic health records, claims, biobanks etc. In addition, control over health data is starting to shift towards the patient; initiatives and healthcare technology companies already signalling a future where the patient will be in control of data and can decide how and with who to share. To improve our ability to combine data from multiple sources and maximize insights generation from these data, we need a common approach to enable quick and efficient connectivity of data to use for diverse purposes. A fundamental requirement for this to work is to make data findable, accessible, interoperable and reusable (the underlying concepts are known as the FAIR principles). Therefore, the main objectives of this topic are: to create (1) a common set of tooling for managing and FAIRifying data lakes, i.e. the agreement or development of a common and potentially open source toolset, (2) agreement on the necessary key ontologies and standards and (3) to create a market place for datasets or individual-level data to further enhance data fluidity. With a successful implementation, users would be able to find, access and use data which data owner decides to share, and leverage them for different purposes. Data owners could do this at the individual level, e.g. a personal health record, the company level e.g. datasets from the company data lake, or an industry or even global level, e.g. data from an industry collaboration.

Personalised endpoints

Personalised medicine has been a focus for the medical field and healthcare systems for many years. The goal is to achieve optimal clinical outcome by providing the right treatment at the right dose and right time to the right person. The hope is that precision medicine will lead to fewer side effects, fewer non-effective treatments and lesser burden on the patients, as well as reduce cost and burden on healthcare. This topic aims to explore ways of implementing personalised healthcare through personalised endpoints. To this end the topic will support activities leveraging information technology, machine learning analysis to create defined patient profiles, not only defined by their medical characteristics but also by their choices and preferred outcomes.

Returning clinical trial data to patients

The sharing and secondary use of data collected in a clinical study (interventional and non-interventional) with study participants is still uncommon and rules for sharing not well harmonized within the EU. The objective is to explore the main reasons for this, including the complexities in setting up the infrastructure, processes and a common data format to enable it and the concerns around protecting the integrity of the study, study participants' privacy and confidentiality, maintaining the study blind, and supporting further research projects. This topic would be also a topic for patient and for patient organisations. In addition, the topic support activities for building and move to the next step the results of the Do-IT initiative. The topic intends to tackle the aspect of returning clinical trial data to patient in the following scenarios: Scenario 1 is after the participant leaves the trial (either after screen failure or after unblinding/ the end); Scenario 2 could be during the trial (but not while blinded or for specific data).

Expected impact:

- Patient centric data collection and data re-use
- A coherent and transparent framework to address data privacy and personal integrity issues inherent in the use of health records.
- Allow patients to tailor their care and truly achieve personalised medicine.
- Better patients stratification
- Better adherence to treatment and reduction of off-label use.
- Integration of digital health approaches in clinical practice to enable predictive and precision medicine
- Development and maintenance of standardized, robust and state-of-the-art data management
- Development of new ways to source, manage process, and analyse data in compliance with ethical, General Data Protection Regulation (GDPR) and security standards

Oncology

Real-world clinical implementation of liquid biopsy

Liquid biopsy is a promising concept for patient selection and disease monitoring in drug development and in clinical practice. However, as of today, few clinical studies used liquid biopsies to systematically and prospectively identify eligible patients for clinical studies, therapy selection, therapy monitoring or detection of first signs of efficacy. The overall objective of the topic is to support real-world clinical implementation of liquid biopsies in solid tumour indications. The goal is to evaluate whether liquid biopsies can become a clinical standard that cost-effectively and safely accelerates clinical trial enrolment, as well as therapy decisions, thereby enabling earlier changes to therapy as compared to "response evaluation criteria in solid tumors" (RECIST) in order to tackle emerging treatment resistance and spare patients from overtreatment and burden of invasively collected tumour samples. This should contribute to prolonging progression-free survival and potentially overall survival of cancer patients.

Microbiome

Since a number of years, alterations in the microbiome have been associated with the pathology of many human disorders such as inflammatory, neuro-degenerative, metabolic and infectious diseases, nutritional deficits and cancer. The fundamental basic question is whether the observed "microbiome dysbiosis" is causal for disease initiation and its progression or is the consequence of a co-adaptation of the microbes to the disease microenvironment. Increasing evidence from experiments using pre-clinical disease models suggest that many pathologies a potential significant link between the human host response to changes in the microbiome and disease occurrence or severity. Some recent studies have been able to find specific interactions between microbial generated bioactive molecules (i.e. metabolites, bacterial cellular components, etc.) and human host receptors in known disease pathways which might be amenable for therapeutic intervention. In particular for cancer, recent studies indicated a significant correlation of the composition of the gut flora and the efficacy of cancer immunotherapy. This topic will address some key gaps that need to be addressed for translation of microbiome science into true therapeutic opportunities: 1) the lack of well-controlled clinical studies that convincingly demonstrate how/that microbiome manipulation could potentially resolve certain disease phenotypes, at least partially, in humans. 2) the need for definitive exploratory medicine studies which link preclinical hypotheses about human host – microbiota disease interactions with clinical outcomes in disease subject cohorts.3) Finally, due to the overall potential impact of the microbiome on human health and disease a cross-diseases approach should be strived for. To this end the topic will support activities for the understanding of microbiome causality by pursuing studies in volunteers at high-risk for developing immune mediated diseases

Expected impact:

- Improved monitoring of disease progress
- Improved selection of patients and inclusion in appropriate clinical trials
- Improved quality of life by preventing in-appropriate medication
- Better knowledge on tumour resistance mechanisms
- Improved understanding of the translational potential of patient-derived tumor models as indicators for the patient situation
- Increased knowledge on the interaction between human organism and microbiota in health and disease
- Access to data for functional studies and further opportunities to identify novel targets and drug combinations that delay or prevent the emergence of drug resistance in cancer
- Development of gold standards for the analysis of single-cell sequencing data
- Improve the quality of care through better evidence of benefits and patient outcomes and support reimbursement decisions.

Translational safety

Pharmacodynamic drug-drug interaction predictive testing by learning algorithms to enhance safety

Clinical development usually addresses drug-drug interactions (DDI) from a metabolism standpoint based on in vitro and sometimes in silico information, and ultimately sporadically during late stage clinical trials or even after marketing authorization, i.e. when patients are confronted by polypharmacy. This topic will support activities addressing challenges related to safety issues pertaining to DDI that do not only concern pharmacokinetic, i.e. metabolic (mainly hepatically expressed enzymes) or permeability-related (e.g. efflux transporters such as P-glycoprotein) pathways, but also occur when drugs have opposing functional effects (reduced efficacy issues) and more importantly when drugs have additive or synergetic functional activities in physiological pathways.

Digital vivarium

In vivo monitoring of animals in current preclinical studies is done mostly by cage side observation from the husbandry personal. This does not allow detailed monitoring of some phases of the day such as sleeping pattern. Hence the limited ability of this monitoring to translate some findings across species including humans. Digital monitoring technologies provide a great opportunity to develop new methods to monitor the cage environment; monitor the animals for a number of biomarkers (motion, heart rate, temperature, sleep patterns) through observation or wearables and implants; and to develop software to analyse the data and detect abnormalities in some of these functions/parameters. The objective of this topic is to develop those monitoring tools of the future (cages, wearable devices for large animals, sensors) to enhance monitoring of the animal and to detect drug-induced changes that current methods do not allow to observe in animals so far and generate data suitable for use in preclinical toxicological studies. A further aim is a contribution to the 3Rs, reduction, refinement and replacement in the translational safety preclinical field.

Expected impact:

- Improved preclinical models of toxicity
- Decrease the risk presented to patients by drug drug interactions (DDI)
- Reduce dependence on animal models - refinement of pre-clinical safety studies
- Increase developability of candidate drugs

Facilitating rare disease therapies (including advanced therapy medical products) reaching patients in Europe

Clinical outcomes assessments for rare diseases

Regulatory agencies have signalled the importance of including clinical outcomes assessments (COA's) as part of drug development. This is particularly relevant to rare diseases where challenges in advancing and obtaining approval for new therapies include 1) the heterogeneity in clinical disease severity and progression in small populations; 2) the very slowly progressive nature of many rare disease; and 3) the lack of well-defined or established clinical and biomarker endpoints; (4) small populations calling for adapted development and advanced statistical and methods. In the interest of better and faster development of medicinal products for rare diseases, this topic will support activities for a consolidated and coordinated efforts towards creating and validating fit-for-purpose COA's by multiple stakeholders (including regulatory agencies). To create a first blueprint for example in a rare neuromuscular disease could be of value. The COA's should include patient reported outcomes (PRO), observer reported outcomes (ObsRo), clinician-reported outcomes (ClinRo), as well as performance-outcomes (PerfO). Coordinated and cooperative participation in COA development efforts and instrument validation with input from patient organizations, clinicians, academic medical centres, industry, regulators, and payers would underscore the importance of a comprehensive public-private partnership approach as well as create avenues to accelerate drug development and approvals

Defragmenting and shortening the path to rare disease diagnosis by using genetic screening and digital technologies

Treatment of Rare Diseases is significantly hampered by delayed diagnosis and this topic will focus on diagnosis for the following reasons. Many rare diseases are degenerative, Therefore early diagnosis is key. In

addition, rare diseases are characterized by a broad diversity of disorders and symptoms that vary not only from disease to disease, but also from patient to patient suffering from the same disease (syndrome). Those symptoms can also and often be very common. Altogether, this leads to a lengthy and burdensome path to diagnosis that has been stated to take on average 8 years and often complicated with misdiagnosis and ineffective treatments, creating a heavy human and societal cost. The topic aims to address the diagnosis gap and, in particular, explore **(a)** the potential for New-born genetic screening for rare diseases. Criteria will be defined to select the gene[s] for the panel as initial use-cases to exemplify the concept and **(b)** Empowering the patient/physician duo with an artificial intelligence/phenotypic database to increase the understanding of disease, develop diagnostic and disease algorithms and identify biomarkers in pre-clinical & early stage of disease.

Expected impact:

- Early detection and Shorter path to diagnosis for Rare Disease Patients
- Early intervention (when available), follow-up, genetic counselling (such as family planning)
- Improved clinical and patient oriented outcomes
- Patient empowerment for smarter referral
- Reduced healthcare inefficiencies
- Enable natural history projects and provide better epidemiological data
- Cost savings for the Healthcare System
- Better and faster development of medicinal products for rare diseases
- Consolidated and coordinated efforts towards creating and validating fit-for-purpose COA's by multiple stakeholders (including regulatory agencies)
- Create avenues to accelerate drug development and approvals
- Advancing COA's in rare disease (for example neuromuscular) could be an important model for subsequent efforts in other rare diseases

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

In 2020, IMI may launch a new restricted Call, similar to IMI2 - Call 19 which was launched in 2019. The final decision on whether or not to launch a restricted Call will be taken, indicatively, in Q1/2 of 2020, after an analysis of the outcome of IMI2 - Call 19.