Topic: Digital endpoints in neurodegenerative and immune-mediated diseases

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.

Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages

Part of IMI2 JU Digital Transformation of Clinical Trial Endpoints programme

Introduction to the IMI2 JU Programme on Digital Transformation of Clinical Trial Endpoints and problem statement

The development of novel treatments requires reliable and sensitive measurements of patients' clinical conditions and, when possible, functional capacity in daily living. The current clinical assessments, based on subjective clinical scoring systems, are characterised by low sensitivity, high variability, low sampling frequency (i.e. monthly assessments) and, in some case, insufficient detection of the patient's actual needs. The consequences of these limitations for the development of novel treatments are significant, leading to increased probability of failed clinical trials, higher costs and excessive complexity in study management, often increasing patient burden for no real benefit.

The recent invention and diffusion of affordable digital technologies is offering the possibility to detect and monitor the progression of clinical conditions and their impact on daily living activities in patients in a cost-effective manner. The advantages for this digital transformation are impressive and have been well-reviewed in several articles. However, while more and more medical devices are receiving regulatory approval as diagnostic supports, very few digital procedures (that require a combination of particular digital devices, performance on tasks, passive data collection and algorithmic data extraction) have gained a qualification to be used as a clinical trial endpoint. If qualified, these endpoints could also allow for the possibility to rapidly scale-up to a very large number of patients, thereby driving a change in how clinical trials are implemented.

In this programme, we propose to identify, profile and validate digital devices, platforms and procedures based on mobile or residential technology for remote assessment of health-related parameters that could effectively substitute for the currently used clinical endpoints and functional outcomes required for obtaining regulatory approval and facilitate health technology assessment (HTA) relevance for novel treatments.

Need and opportunity for public-private collaborative research

Several pharmaceutical companies are exploring ways to apply digital technology to clinical development programmes and in post-marketing authorisation assessments of drug efficacy, tolerability and safety. One key aspect of this progress is the regulatory recognition of such endpoints, which requires proper validation. To achieve this objective, a wide variety of expertise across a number of stakeholders is needed:

- clinical trial expertise from pharmaceutical companies;
- patient advocacy groups to ensure the technologies developed are aligned with patients' needs;

- small and medium-sized enterprises (SMEs), larger technology companies and academic groups with expertise in digital devices, digital device implementation, digital data collection and analysis, including artificial intelligence (AI) approaches;
- academic groups with an in-depth clinical understanding of patients' conditions;
- regulators to advise on the requirements for validation.

By working together to jointly tackle this problem using an interdisciplinary, precompetitive and transparent approach, solutions can be developed that should align with the main regulatory requirements as well as with the societal goals of addressing the key health challenges recognised by the World Health Organisation (WHO) and other institutions. A critical point of the programme will also be the openness towards the contribution from other programmes running in Europe, USA or in other part of the world.

Overall objectives of the programme

The key objectives of the programme are:

- to identify appropriate digital devices & platforms for the transformation of the standard clinical and functional endpoints into digital endpoints;
- to experimentally test the validity of the proposed digital endpoints in clinical trials, with the final aim to select a few endpoints and progress them to obtain qualification from regulatory agencies;
- to progress towards the validation of digital procedures to profile activities of daily living (ADL) / disabilities/ health related quality of life (HRQOL) measures whose ecological validity is recognised by patients and payers.

Structure of the programme

The programme is divided in three main activities:

- selection & implementation of digital platforms, devices, procedures and other technology, data processing, simulation and modelling to optimise the digital endpoint transformation process;
- initial focus on delivering the digital transformation for a specific group of patients with progressive disorders affecting movements and activities of daily living with therapeutic unmet needs described in the first topic of this programme, i.e., with neurodegenerative movement disorders (NMD) and immune mediated inflammatory disorders (IMID);
- design of a clinical & regulatory plan, with appropriate data analysis leading to a scientific validation for the proposed digital endpoint and consequent progression of the most promising solutions into a regulatory path for qualification, including assessment on how policy-makers, HTA bodies and payers can take into account the proposed digital endpoints in their decision process.
- The validation plan for digital endpoints and outcomes measures should be aligned with Clinical Trials Transformation Initiative (CTTI) guidelines (https://www.ctti-clinicaltrials.org/files/detailedsteps.pdf).

Data management platform, digital sensors & procedures

An efficient generic data management digital platform that has already been partially developed for health care use will be selected as part of topic 1. This platform should allow the use of different standardised datasets, the plug in of several devices and data-streams, be flexible and easy to adapt for use in clinical trials.

The projects will focus on the latest advances in biosensors and mobile technologies to develop and validate novel clinical and real world endpoints while building on work that is already being done in this area. Therefore, it is critical that the platform has the possibility to integrate already standardized data. For example, in the first topic of this programme, it is likely that within the next 2-3 years a digital

transformation of motor sign measurements currently delivered by UPDRS-3[1] will be available [1]. Therefore, this first topic will focus on developing the non-motor sign and symptoms, of relevance for activities of daily living (ADL), i.e., those captured by UPDRS-2.

This platform will be made publicly available for other future digital transformation topics and elsewhere, while the specific IP for all plug-in for proprietary technologies and solutions will be protected.

Future topics in the programme will focus on other indications and where possible use the platform already implemented for the first topic of this programme, if successful. However, these future topics may also select other platforms and technologies to suit their particular objectives.

Collaboration agreements

To maximise the overall impact of the programme, and ensure synergies and learnings are fully shared, the projects in the programme will be expected to sign collaboration agreements with each other. The collaboration agreements should allow for the sharing of the technology platforms, learnings on device selection, development and the implementation during the clinical studies and any other relevant activities.

The respective options of Article 2, Article 31.6 and Article 41.4 of the IMI2 Model Grant Agreement will be applied.

Specific challenges to be addressed

Neurodegenerative movement disorders (NMD) and immune mediated inflammatory diseases (IMID) can cause considerable disability and morbidity in spite of the availability of approved treatments. Recent estimates suggest that neurodegenerative disorders are becoming one of the fastest growing costs for healthcare systems [2]. Movement disorders, in particular Parkinson's disease (PD), affect about 1.2 million European citizens, a number set to double by 2050 [3]. While rarer, the burden of Huntington's disease can be up to 5 times higher than that of PD patients [4].

The socio-economic burden of IMID is well known [5]. An estimated 2.5–3 million people in Europe are affected by inflammatory bowel disease (IBD), with a direct healthcare cost of EUR 4.6–5.6 billion per year. Recent studies have suggested that more than 2.3 million individuals are diagnosed with rheumatoid arthritis (RA) in Europe, generating annual direct and indirect costs of management of over EUR 45 billion [6].

The continuous progress in the understanding of neurodegenerative processes and immunopathology are building hope that breakthroughs will soon be made and new agents will enter clinical development in the next few years. However, most of the current clinical endpoints used in trials for neurodegenerative or autoimmune-mediated disorders are based on ‘scores’ and focus on assessing the severity of disorder-specific signs & symptoms at a given stage of the disease progression. These values may vary in degree or intensity among different patients, suggesting a relevant biologic variability, as well as in the training and capacity of the ‘rater’ in scoring the symptoms or in self-assessing the disabilities, in case of direct response of the patients. The consequences of these limitations for drug development are significant, leading to increased probability of failed trials, higher costs and excessive management complexity and lost opportunities for patients. Therefore, it is imperative to improve the efficiency of clinical trials to maximise the chances for delivering novel therapies for patients with unmet needs within the next 5-10 years.

Digital technology, in particular remote monitoring systems, if properly implemented and validated, could provide a critical help in improving measurements of efficacy by increasing sensitivity and precision, reducing variability, and enhancing their ecological validity making them closer to the actual unmet needs of patients. This project will develop a technology platform to collect and analyse sensor/generated datasets, principally high resolution passively and actively collected digital measurements, i.e. actigraphy, socialisation parameters and momentary self-reported assessments, mainly using (but not limited to) wearables and smartphone sensors and apps. The project will also

[1] Unified Parkinson's disease rating scale

seek to engage the European Medicines Agency (EMA) in providing scientific advice and give the direction for its validation and, eventually, acceptance of at least one digital endpoint to be used in future clinical trials of drug development.

Need and opportunity for public-private collaborative research

As stated in the introduction to the programme, pharmaceutical companies are exploring ways to apply digital technology to clinical development and in post-marketing authorisation assessments of drug efficacy, tolerability and safety. One key aspect of this progress is the regulatory recognition of such endpoints, which requires proper validation.

To address these challenges and deliver the digital transformation of endpoints in neurodegenerative and autoimmune mediated diseases, a range of different expertise is required to work effectively together. This includes technical expertise in device development such as that found in digital technology companies, SMEs and academic groups, as well as strong technical, statistical, analytical and data management expertise to integrate the data from the devices with existing data from academia, the pharmaceutical industry and other consortia for developing and updating the endpoint & disease models. By combining this expertise with clinical scientists (both industry and academic) and patients in a public-private partnership, the best digital technologies can be adapted and optimised to the specific features of the clinical /functional endpoints. Finally, regulatory knowledge is essential to ensure the technologies can receive regulatory validation and therefore have maximum long-term impact.

An additional critical point will also be the openness towards the contribution of data from other private-public partnerships running in Europe, USA or in other parts of the world, so to leverage all available knowledge.

Scope

Subtle impairments in accomplishing daily activities are sometimes reported among the first signs of a disorder that will progressively develop towards more severe disabilities for individuals affected with NDD and IMID. Identifying the ADLs that first or more consistently are affected by the disorders and tracing their progression using original digital solution is a key aspect of the present project. In fact, advances in micro-sensors and mobile technologies have the potential to enable seamless, continuous, objective measurements of symptoms and disabilities, providing more precise and higher frequency data collection. The early identification of impairment and the possibility to follow its worsening with precision and reliability are essential tools for assessing the effects of novel treatments that should target the disorder in its early phases. In fact, if the disorders progress beyond a certain point, the disabilities may not be reversible, justifying early interventions.

The focus of this programme is to provide an effective digital transformation of clinical endpoints for the following disease clusters.

The NMD cluster:

- Parkinson's disease (PD)
- Huntington's Disease (HD)

The IMID cluster:

- Rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE)
- Inflammatory bowel disease (IBD).

The main objectives of this project will be:

- the identification and characterisation of subtle disabilities in the activities of daily living (ADL) that worsen over time, that are either common or partially shared among the NDD and IMID hereby considered, so to represent a patient related outcome that can be used for assessing the effects of treatment in the real world and also beused for helping the comparative therapeutic impact among disorders of novel treatments;

- the identification of digital solutions that appropriately measure clinical and behavioural signs & symptoms related to ADLs that are specific for each one of the disorders mentioned below, so as to obtain better standards than the current clinical scales and that can be considered of relevance by regulatory authorities in clinical development trials for novel treatments.

In the case of PD and HD, the focus will be on a set of signs & symptoms that can be optimally measured by a selected series of sensors, devices, platforms and procedures to provide a proper correlation with scores of the UPDRS for PD and UHDRS[2] for HD (or equivalent clinical scales) that would satisfy regulatory standards. As other programmes are targeting the motor aspect of PD patients, the aim of this project is to target other ADL and behavioural aspects of the disorders that are often very early complaints from patients.

For patients with all disorders, i.e. NMD and IMID, critical ADL related to quality of life (QoL) measures will need to be prioritised within the context of the global condition as patients, so as to identify digital solutions whose precision, reliability and ecological relevance are relevant to patients, clinicians, regulators and payers

The selected ADLs should be evaluated in both NMD and IMID patients, in order to test if the use of the proposed technology is sensitive enough to assess the levels of disability across disorders, but also specific enough in identifying the underlying primary drivers (e.g. fatigue, pain, anxiety, etc.) that contribute to determining the disability in the various groups of input of both patient associations (advocacy and research foundations) and clinical experts in supporting the choice of specific ADL/disabilities to be profiled.

The project is suggested to be divided temporally in 2 parts.

Part A is an approximately 1.5-year long period for digital technology initial implementation and validation using modelling and beta-testing in a small group of patients, aimed at selecting the best technologies that establish a reasonable relationship with the targeted clinical endpoints.

Part B is an approximately 3.5-year long validation programme aimed at demonstrating that the selected digital procedures properly represent the rating scale-based clinical endpoint and ADL, and are sensitive to pharmacologic treatments. Data will be analysed with modern algorithmic approaches, engaging expertise of all consortium members also during this period.

Expected key deliverables

Part A: The first 1.5 years

- identification of the digital data management platform;
- prioritised list of sign & symptom-based clinical endpoints for NMD that are amenable for digitisation and selection of the most promising device and procedure;
- prioritised list of ADLs/disabilities/HRQOL measures amenable to original digital solutions in NMD and IMID, possibly using the same digital devices proposed for clinical endpoints;
- Public release of the adapted digital data management platform with appropriate privacy protection assurances and seamless integration to EMR systems to enable e.g. monitoring protocol compliance, for quality assurance, data integration, and ensuring data integrity;
- introduction of some existing digital solutions that have already been successfully used i.e. from the literature (anchoring dataset);
- development of novel methods to probe the ADLs or other endpoints not previously addressed in the literature (innovative dataset);
- initial test of feasibility, acceptability and utility with some volunteers;
- collection of available data from project members and external sources; initial proposal of models for the diseases (starting with PD and HD), establishment of clinical trial simulation package to

[2] Unified Huntington's Disease Rating Scale

test the expected digital technology data delivery and their impact on different clinical trial designs;

- pilot study synopsis in NMD: exploration in a small group of patients with PD and HD of the various devices for acceptability, feasibility and utility, to be possibly run in one or two clinical centres for clinical endpoints. At least two ADL/disabilities digital devices will be tested among those that have been discussed as common or partially common with IMID;
- pilot study synopsis in IMID exploration in a small group of IMID of the various devices for acceptability, feasibility and utility, to be possibly run in one or two clinical centres for clinical endpoints. At least 2 ADL/disabilities digital design will be tested among those that have been discussed as common or partially common with NMD;
- Scientific advice from the regulatory agencies, including FDA[3] and EMA[4] on the proposal for the longitudinal study in part B.

Part B: The last 3.5 years

- Longitudinal study in digital mobility and clinical outcome assessment over 2.5 years in PD, HD and IMID populations for assessing clinical endpoints and ADL/ disabilities:
  - development of clinical protocols and IRB, ethics committee approval;
  - a clinical observational part of the study to establish correlations of digital endpoint with clinical endpoints for PD and HD and for ADL/disabilities/HRQOL across both NMD and IMID patient populations;
  - the adaptive nature of the study should help to include possible changes based on the scientific advice from EMA, possibly FDA and HTA agencies based on data from the interim analysis and associated clinical trial simulation scenarios (e.g., after one year).
- Data analysis:
  - digital data management plan, including digital data format and standardisation, alignment with legal requirements, privacy aspects, storage backups and cybersecurity;
  - performance of algorithm-delivered recognition of digital endpoints and ADL/disabilities/HRQOL patterns for automatic detection;
  - assessment of the precision and sensitivity of digital endpoints vs. clinical scales and their effects on sample size and effect size in simulated clinical trials;
  - assessment of the precision and sensitivity of ADL/disability/HRQOL digital sequences to estimate ADL/HRQOL scores and their effects on sample size and effect size in simulated clinical trials across the different disease populations;
  - interim assessment after one year (or another duration) to provide a robust dataset for engaging in a second round of EMA Scientific Advice;
  - final analysis package to support a request for the qualification of the use of the novel digital endpoints via EMA scientific advice, early HTA consultation and, possibly, FDA.
- Overview and position paper as well as a series of scientific articles on digital transformation on clinical trials.
- Final public event to showcase the results of the project.

[3] Through, for example, C-Path

[4] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp&mid=WC0b01ac05800229b9

Expected impact

Digital transformation of clinical and real-world measures of ADL / quality of life measures relevant to patients and care-givers will give deeper and more detailed insights into how diseases progress and cause disabilities in patients, which, in turn, will enable development of interventions that better address these clinical deficits and disabilities.

Digital endpoints when combined with patient self-reported outcomes and other traditional clinical measures will provide a more valid and complete assessment of patient and care-giver impact of disease and their treatments.

Digital transformation of clinical and real-world endpoints will enable larger and more inclusive clinical trials and reduce patient burden thus allowing assessment of interventions in more diverse and representative populations.

Use of passive digital technologies will increase the efficiency of clinical trials, enabling faster clinical development and a reduction in the time taken to bring new therapies to patients. These technology enabled endpoints with passive data collection will make larger and longer follow-on studies to assess real world impact of therapies on patients possible, thus enabling more effective value driven health care decision making.

It is expected that, in the long run, this project will enable the development and evaluation of more effective therapies for patients thus improving outcomes for patients and reducing cost for all stakeholders.

Applicants should also demonstrate how they will impact on the competitiveness and industrial leadership of Europe by, for example, engaging suitable SMEs.

Potential synergies with existing consortia

Applicants should take into consideration, while preparing their proposal, other relevant initiatives (national, European - both research projects as well as research infrastructure initiatives - and non-European initiatives) in particular those in the pre-competitive space. Synergies and complementarities should be considered to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap and duplication of efforts and funding, but at the same time to open up a dialogue for best-practice and actual data sharing, so as to cross-fertilise the present project.

For example, other initiatives are addressing to the selected diseases, as such:

- MJFF Parkinson Disease Digital Biomarker DREAM challenge[5];
- FNIH Accelerated Medicine Partnership in PD clinical trials started in 2017[6];
- Several HD consortia are exploring the basic aspects of the disorder;
- MRC UK funded consortium: Immune-Mediated Inflammatory Disease Biobanks - UK.[7]

There is potential synergy with other IMI projects that focus on digital medicines such as **RADAR-CNS** (www.radar-cns.org) in patients affected by epilepsy, depression, multiple sclerosis, related to reuse of parts of the tech platform, sharing challenges in designing and operationalising clinical studies. Other projects are: **EMIF** (www.emif.eu), **eTRIKS** (www.etriks.org), **EHR4CR** (www.ehr4cr.eu), and the other relevant programmes, especially in regard to learnings about data management, privacy, transfer, data analysis and definition of clinical outcomes.

An additional synergy could be via interactions /collaboration with Critical Path Parkinson (CPP)[8] initiative for the regulatory approval of digital endpoints for PD and possibly HD.

5 https://www.michaeljfox.org/research/levodopa-data-challenge.html
6 https://fnih.org/what-we-do/current-research-programs/accelerating-medicines-partnership-parkinsons
7 www.imidbio.co.uk
8 https://c-path.org/programs/cpp/

Collaboration with EUnetHTA Joint Action 3 (European network for Health Technology Assessment – www.eunethta.eu/) should be considered given the technological expertise related to digital platforms with high flexibility and to ensure acceptability of the results by the HTA community.

Collaboration with ECRIN, which is a not-for-profit infrastructure supporting multinational clinical research projects in Europe will be also considered. ECRIN provides information, consulting and services to investigators and sponsors in the preparation and in the conduct of multinational clinical studies.

Finally, consideration should be given to collaborating with the CTTI project 'Developing Novel Endpoints Generated by Mobile Technology for Use in Clinical Trials' (https://www.ctti-clinicaltrials.org/projects/novel-endpoints). Such agreements would enhance the ability of various types of digital data to be captured, analysed, and shared with greater efficiency, and would be an additional boon to the field.

Industry consortium

The industry consortium is composed of the following EFPIA companies:

- Janssen (lead)
- Takeda (co-lead)
- AbbVie
- Astra Zeneca
- Biogen
- Eli Lilly
- Orion Pharma
- Pfizer
- Roche
- Sanofi
- UCB

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

- Parkinson's UK
- CHDI Foundation[9]

Expected contribution by industry participants

EPFIA companies will contribute personnel with specific competences that will either complement or add and extend to those requested of the applicants.

The EPFIA personnel competences that will complement those of the applicants are:

- expertise in regulatory activity;
- expertise in patient reported outcomes;
- expertise in relations with HTA, insurance and payers;
- expertise in patient association, legal and ethical aspects;
- expertise in digital data standardisation for regulatory application;
- expertise in patient-centric approaches working with vocational groups.

Other competences will be made available to align and extend those of the applicants:

- expertise in legal and financial and project management;
- expertise in clinical study design, biostatistics, expertise in assessment of clinical domains;

[9] Its participation is subject to formalisation of its association to IMI2 JU for the present topic.

- expertise in disease modelling and longitudinal analysis of cognition, function, biomarker and clinical data;
- expertise in functional assessments, including activities of daily living (ADL);
- expertise in digital data management and platform use, as well as device and sensor characterisation
- therapeutic area expertise along with years of digital and clinical endpoint strategy knowledge.

During the project, members of the industry consortium will contribute relevant data generated in prospective activities that are part of broader clinical studies independent from, but related to the project. Relevant data generated in such activities are deemed necessary for the project to achieve its objectives, and the introduction of the data to the project constitutes an in kind contribution which entails access rights to these project results in line with IMI2 JU IP rules. The prospective activities to generate these data subject to the above are as follows.

- Janssen's prospective data will come from primary and secondary endpoints (PnSEP) and exploratory endpoints (ExpEP): self reports and actigraphy data from an IMID (RA and/or IBD and/or SLE) clinical study with an in-kind relevant data generation value estimated at EUR 5 300 000.
- Takeda's (and the associated Oshi Health) prospective data will come from an observational trial in PD for validating various technologies and possibly also from some asset studies (baseline and/or placebo data). Also, some IBD placebo data will be shared. The in kind data generation value is estimated at EUR 2 500 000.
- Sanofi will share actigraphy data which can be used to infer sleep quality and serve as a marker of fatigue, and also PD data from prospective clinical studies with value estimated at EUR 3 000 000.
- CHDI will bring HD datasets to be reviewed for potential endpoints such as longitudinal observational, single time-point, imaging, biofluids, or data modelling results with an in-kind relevant generation value estimated at EUR 1 000 000.
- Pfizer will contribute data related to quality of life measurements with an estimated relevant generation value of EUR 125 000.
- AbbVie will provide data from Ph0 studies in PD patients having an estimated relevant generation value of EUR 800 000 as follows:
    - provide data contributions in CDISC standards once those are defined for digital;
    - provide data passively collected from a Phase 0 study to assess specific motor deficits (bradykinesia and tremor) - via a medical grade digital watch before and after treatment;
    - provide sleep data passively collected from the Phase 0 study along with measures of general activity (steps) and digital measures of cognition.
- Biogen will bring data from a validation study in the PD area.

Such activities, despite being part of broader independent clinical studies, will be integrated in the action as part of relevant work packages and deliverables. The introduction of these data is considered highly important and directly relevant for the project because they will contribute to achieving meaningful results in developing digital endpoints for the disease areas included in this topic: PD, HD and IMID.

Furthermore, some companies (such as Astra Zeneca, Orion Pharma, Eli Lilly) will also provide, as background of the action (Article 24 of the IMI2 Model Grant Agreement), historical data from other patient cohorts and use the work involved in transferring these data to the project as part of their in kind contribution.

Indicative duration of the action

The indicative duration of the action is 60 months.

Indicative budget

The indicative in-kind and financial contribution from EFPIA partners and IMI2 JU Associated Partners is EUR 21 300 000.

This contribution comprises an indicative EFPIA in-kind contribution of EUR 19 400 000 and an indicative IMI2 JU Associated Partners in kind contribution EUR 1 900 000.

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

The financial contribution from IMI2 JU is a maximum of EUR 21 000 000.

Applicant consortium

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

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium, which will join the selected applicant consortium in preparation of the full proposal for stage 2.

This may require mobilising, as appropriate, the following expertise:

- clinical and disease area experts with specific knowledge of the disorders in focus;
- clinicians and psychologists with expertise in the critical aspects of ADL and HRQOL, including psychological aspects of the assessment of the personal perceived disabilities as well as of caregivers and attending staff or physicians to corroborate the patient profile;
- clinical and statistical experts with demonstrated knowledge of the design and conduct of clinical studies;
- expertise in clinical data management, algorithmic and statistics;
- expertise in patient advocacy and engagement, privacy and ethical considerations;
- expertise in legal aspect of data privacy with particular reference to the capture of data of potential sensitivity related to personal activities;
- expertise in device and sensor development (including SMEs): latest remote assessment technologies (wearable, off-body) that could be further developed or modified for use in the consortium;
- IT/analytics partners (including SMEs): data management architecture, hardware/software platform, state-of-the-art algorithms to process and analyse time-series data from sensors/devices, expertise in data privacy and security;
- expertise in the development and regulatory qualification of novel digital technologies, in particular if applied to health care problems
- some expertise in HECOR and patient outcome research

Applicants should bring an existing data management platform as part of their proposal. An assessment of performance, versatility, data access, sustainability, and security explaining the reasons for the selection should be included.

Applicants should include a mix between already validated digital tools and some novel methods (Technology Readiness Level 5-9) to probe the ADLs or other endpoints not fully addressed in the literature.

In addition, in their proposal, applicants should:

- identify and engage existing longitudinal cohort studies in the four relevant populations;
- design a statistically powered clinical trial to validate the digital solution to measure ADL and show capacity to detect treatment effects with higher precision;

- demonstrate access to sufficient clinical trial subjects and a proven track of clinical trial recruitment and management expertise for NMD and IMID;
- allocate funding for EMA scientific advice and to access HTA expertise;
- allocate funding for a final public conference (additional dissemination activity);
- allocate funding to interact in joint meetings with future topics.

Suggested architecture of the full proposal

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

The final architecture of the full proposal organised in work packages will be defined by the participants in compliance with the IMI2 rules and with a view to the achievement of the project objectives.

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

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

Regulatory strategy

As indicated above, the consortium is expected to have a strategy for the translation of the relevant project outputs into regulatory, clinical and healthcare practice. A plan for interactions with regulatory agencies/health technology assessment bodies with relevant milestones and sufficient resources should be proposed to ensure that advice on the proposed methods for using novel digital methodologies in clinical trials and, possibly, qualification opinion can be obtained[10].

Sustainability

A draft plan for aspects related to sustainability, facilitating continuation beyond the duration of the project should be provided in the short proposal and further detailed in the full proposal.

Dissemination

A draft 'plan for the dissemination and exploitation of the project's results' should be provided in the short proposal and further detailed in the full proposal.

Data management plan

A draft data management plan (DMP) outlining how research data will be handled and made available during the project, and after it is completed, should be provided in the short proposal and further detailed as part of the full proposal.[11]

[10] See http://europa.eu/!ww84Xw

[11] See http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/oa_pilot/h2020-hi-oa-data-mgt_en.pdf

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