# Webinar | IMI2 – Call 13
# Linking digital assessment of mobility to clinical endpoints to drive regulatory acceptance and clinical practice

**14 December 2017 • 10:30 CET**

# Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Nathalie Seigneuret, IMI
- The Call topic – Ronenn Roubenoff, Novartis
- Involvement of SMEs, patients and regulators – Nathalie Seigneuret, IMI
- Questions & answers

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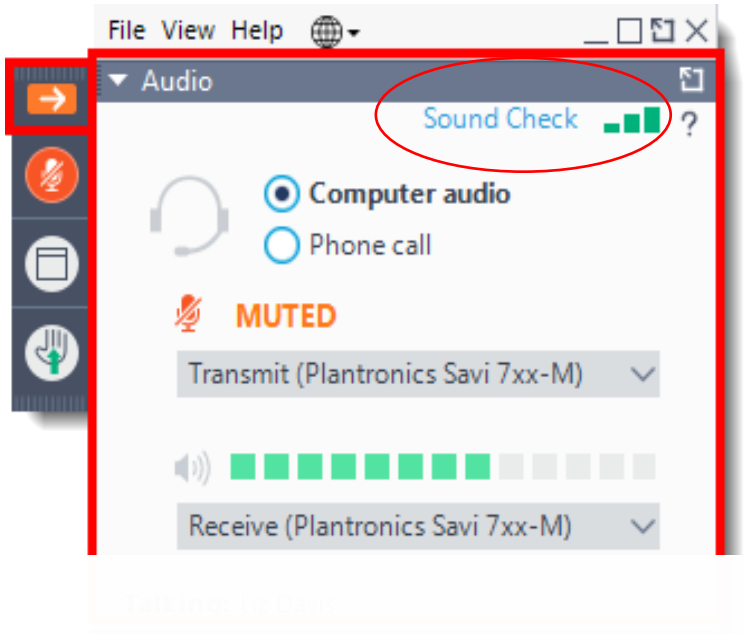


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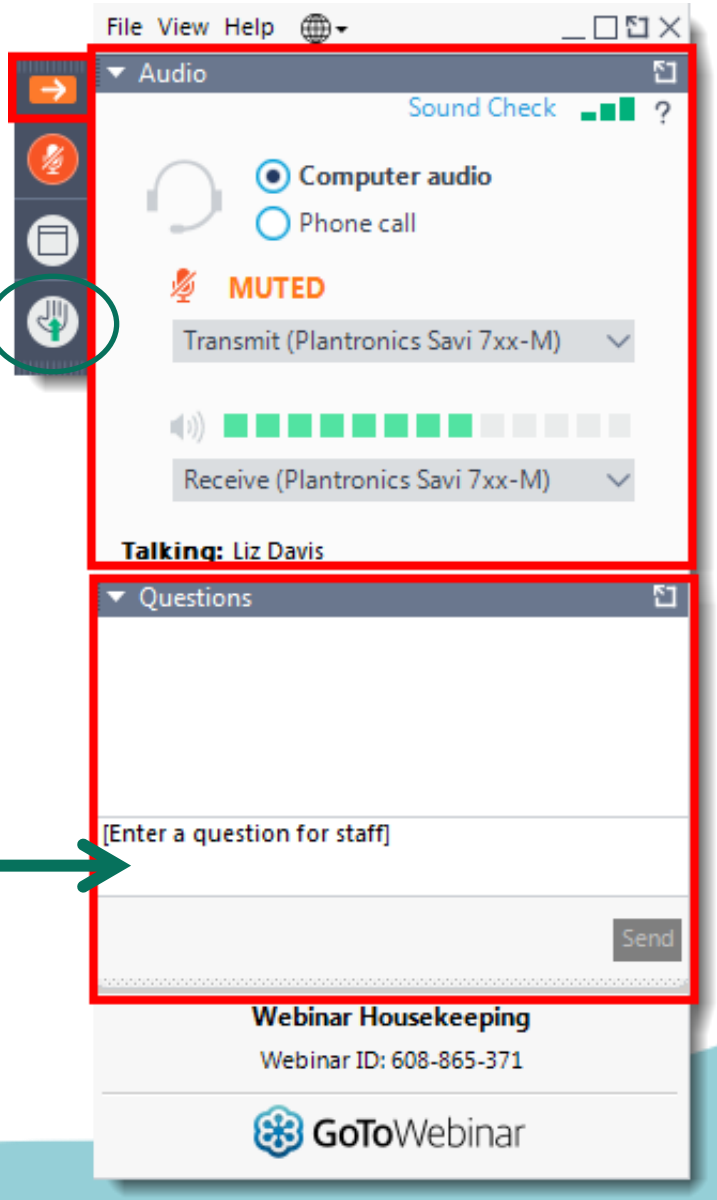


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# Before we start…

- This webinar is being recorded and will be published on the IMI website and / or IMI YouTube channel
- Presentation slides will be published on the webinar web page
- A participant list will be circulated
- IMI2 – Call 13 has been launched and all Call documents & details of how to apply can be found on the IMI website

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# Webinar | IMI2 - Call 13

# Linking digital assessment of mobility to clinical endpoints to support regulatory acceptance and clinical practice

Nathalie Seigneuret

# Today's webinar

**Will cover all aspects of the Call topic**

- Introduction to IMI programme
- Proposed project
  - Objectives, need for public-private collaborative research
  - Key deliverables
  - Structure of the project
  - Expected contribution of the applicants
  - Contribution of industry consortium

**Will not cover rules and procedures**

- A webinar on rules and procedures took place on Thursday 7 December – the recording is online. It will be repeated on Tuesday 16 January 2018 – sign up via the IMI website

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# IMI – Europe's partnership for health

**IMI mission**

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.

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# IMI – Ecosystem for innovative collaborations

- Allow engagement in a cross-sector, multi-disciplinary consortium at the forefront of cutting-edge research
- Provide the necessary scale by combining funding, expertise, knowledge, skills and resources
- Build a collaboration based on trust, creativity and innovative and critical thinking
- Learn from each other - new knowledge, skills, ways of working
- Take part in transformative research that will make a difference in drug development and ultimately patients' lives

IMI is a **neutral platform** where **all involved** in drug development can engage in **open collaboration** on **shared challenges**.

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# IMI 2 budget (2014 – 2024)

**EU funding goes to:**

Universities

SMEs

Mid-sized companies

Patient groups

etc…

**€1.638 bn**

**€1.425 bn**

**Other €213 m**

**IMI 2 total budget €3.276 billion**

**EFPIA companies**

receive no funding

contribute to projects ‘in kind’

Associated Partners e.g. charities, non-EFPIA companies

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# How a topic is generated

Industrial partners align themselves around a real challenge for industry and agree to work together **and commit resources**

New ideas from public sector, universities, SMEs etc. are needed to address the challenge

Scale is a key to success and is provided through IMI funding

Outcomes should be transformative for the industry as well as having a clear “public” value

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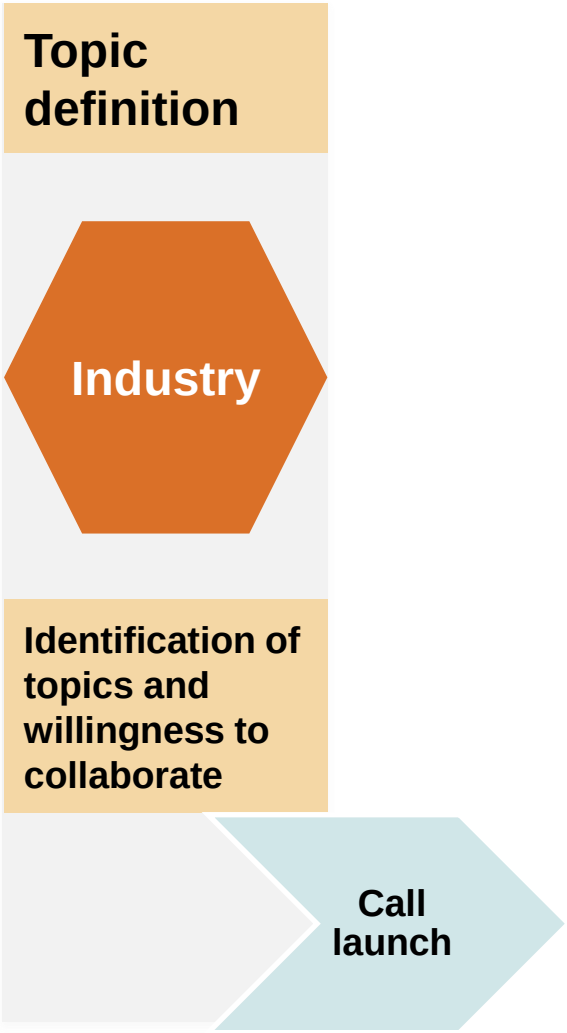
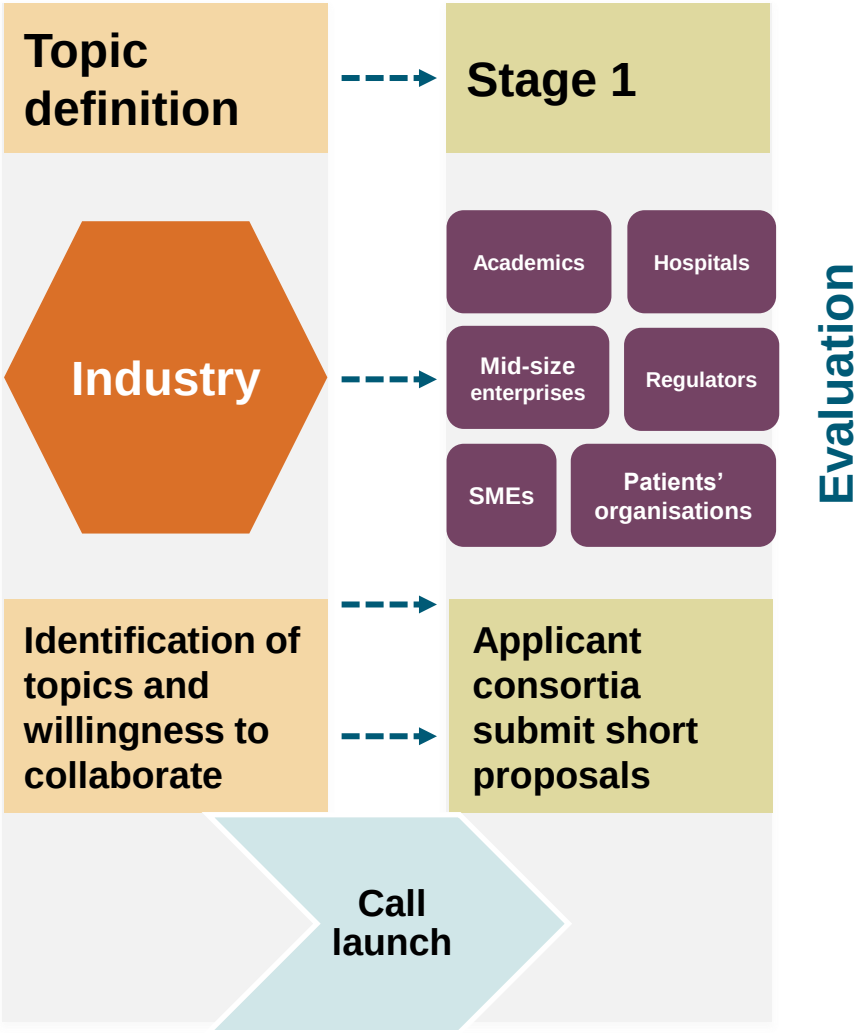
# Typical IMI project life cycle



# Typical IMI project life cycle

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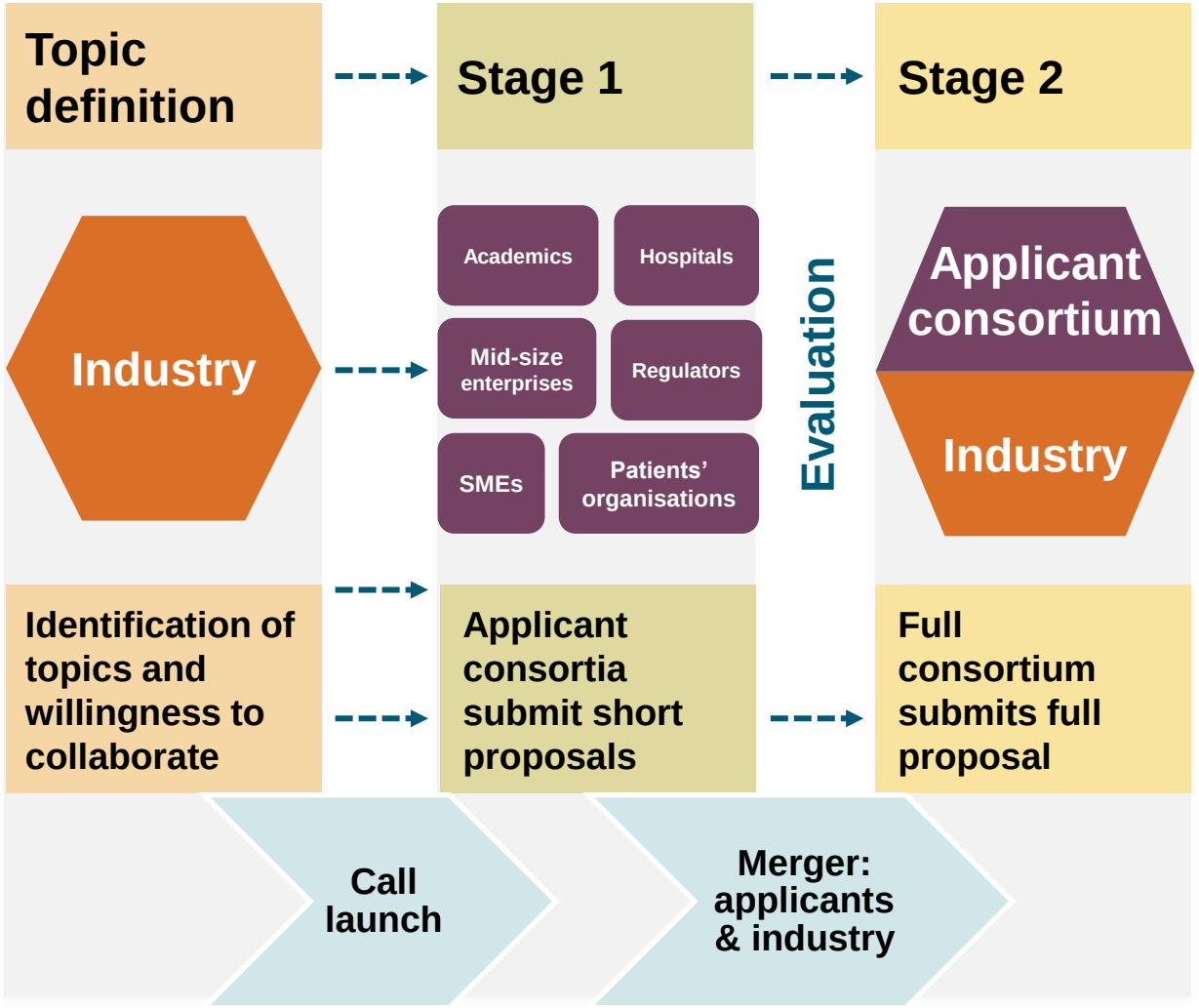
# Typical IMI project life cycle

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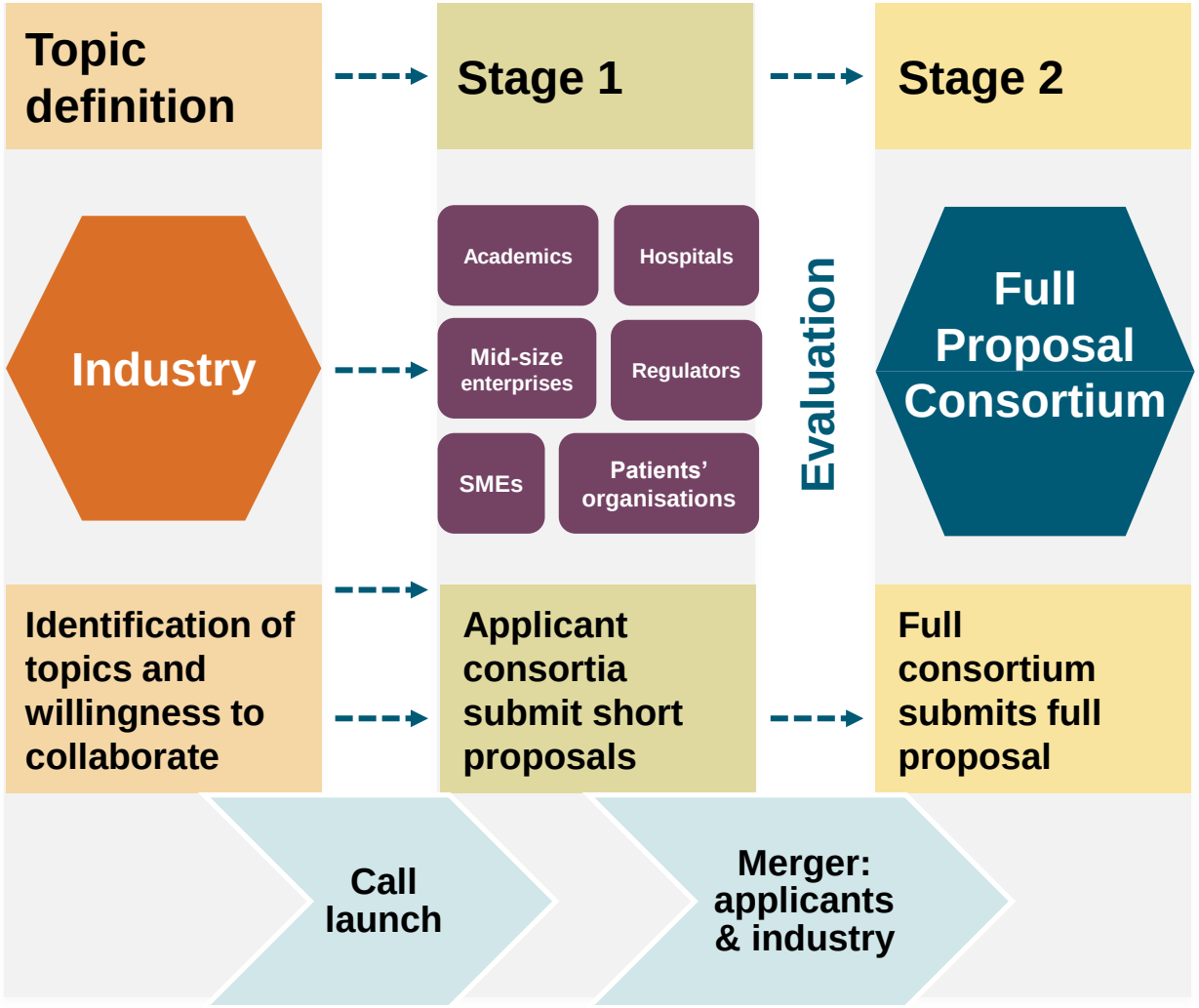
# Typical IMI project life cycle

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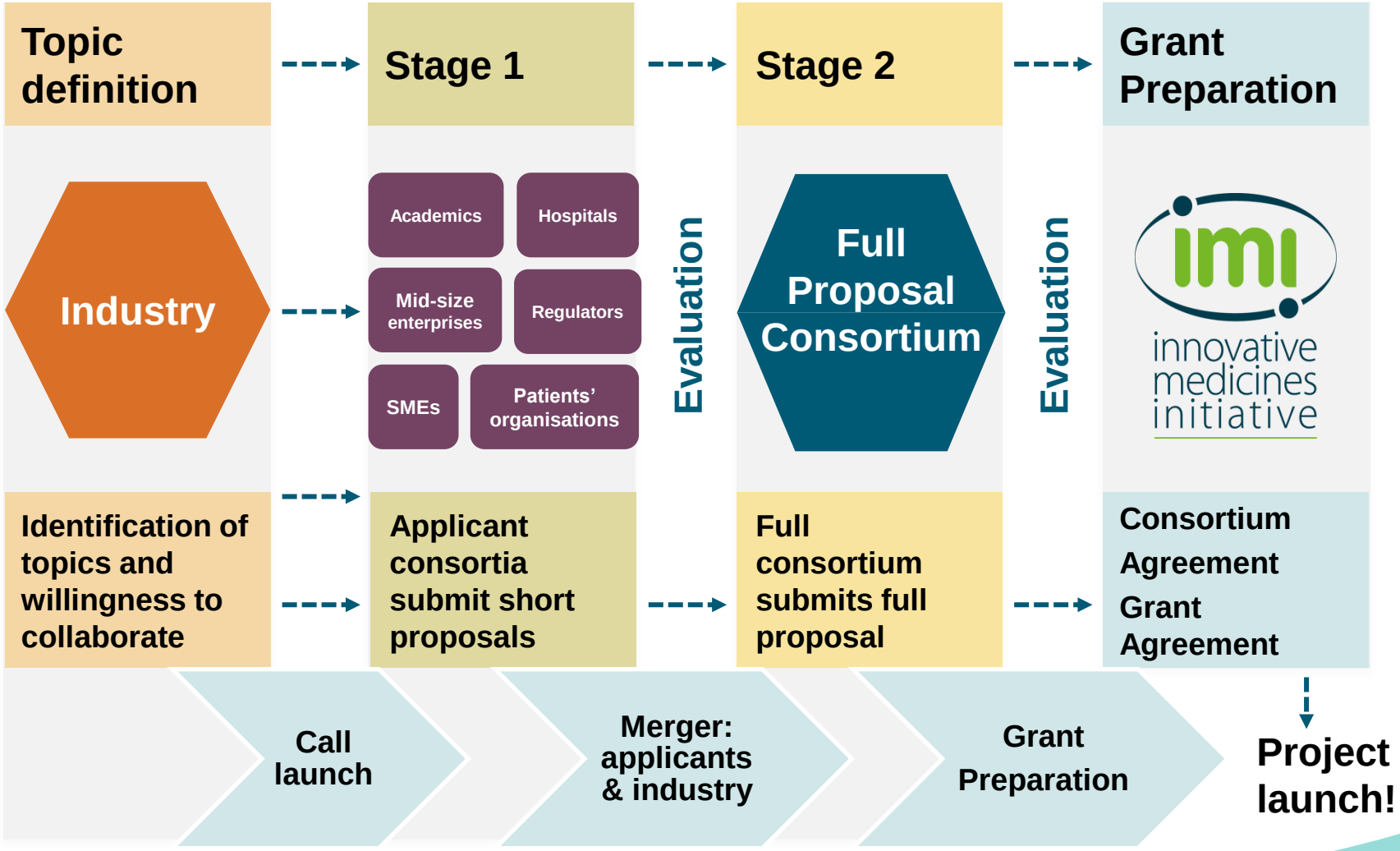
# Typical IMI project life cycle

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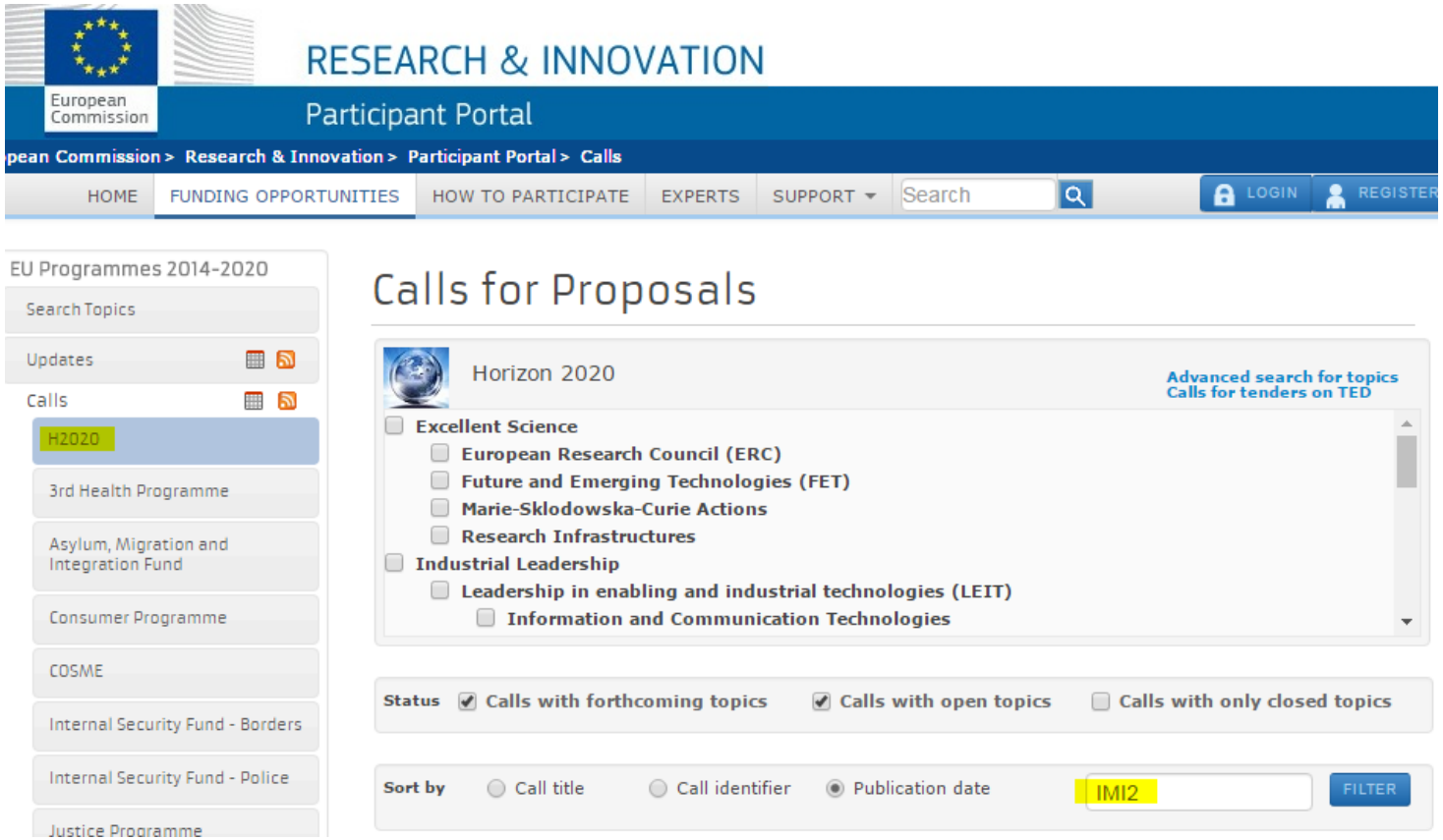
# Submitting a proposal

- https://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/index.html

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# Proposal Template

- Available on IMI website & H2020 submission tool
- For first stage proposals, the page limit is **30 pages**.

**Title of Proposal**

**List of participants**

**Table of Contents**



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# Evaluation Criteria (1/2)

- **Excellence**
  - Clarity and pertinence of the proposal to meet all key objectives of the topic;
  - Credibility of the proposed approach;
  - Soundness of the concept, including trans-disciplinary considerations, where relevant;
  - Extent that proposed work is ambitious, has innovation potential, and is beyond the state of the art;
  - Mobilisation of the necessary expertise to achieve the objectives of the topic, ensure engagement of all relevant key stakeholders.
- **Impact**
  - The expected impacts of the proposed approach as mentioned in the Call for proposals;
  - Added value from the public private partnership approach on R&D, regulatory, clinical and healthcare practice as relevant;
  - Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges;
  - Improving European citizens' health and wellbeing and contribute to the IMI2 objectives.

# Evaluation Criteria (2/2)

- **Quality and efficiency of the implementation**
  - Coherence and effectiveness of the outline of the project work plan, including appropriateness of the roles and allocation of tasks,  resources, timelines and approximate budget;
  - Complementarity of the participants within the consortium (where relevant) and strategy to create a successful partnership with the industry consortium as mentioned in the topic description in the Call for proposal;
  - Appropriateness of the proposed management structures and procedures, including manageability of the consortium.

# Tips for writing a successful proposal

- Read **all the call-relevant material:**
  www.imi.europa.eu
- Begin forming your consortium **early**
  Partner search tools & networking events
- Provide **reviewers** with all the information requested to allow them to evaluate your proposal
- **Finalise and submit your proposal early**
- Contact the **IMI Office** (**NOT** industry topic writers):
  infodesk@imi.europa.eu

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# Common mistakes

- Admissibility/Eligibility criteria not met**:**
  - submission **deadline** missed
  - minimum of **3 legal entities** from **3 member states & H2020 associated countries** not met
- The proposal does **not address all the objectives** of the topic
- A proposal is **scientifically excellent** but will have **limited impact**
- **Complementarity** with Industry consortium not well described.

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# Find project partners

- Network with **your contacts**
- **Network** with fellow webinar participants
- Use **Partner Search Tools:**
  - EU participant portal: https://ec.europa.eu/research/participants/portal/desktop/en/organisations/partner_search.html
  - German NCP partner search tool: www.imi-partnering.eu
- Get in touch with your **local IMI contact point**: www.imi.europa.eu/about-imi/governance/states-representatives-group
- Talk to your **Health National Contact Point** (NCP)
- Network on **social media** (e.g. IMI LinkedIn group)

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# Participation of SMEs, patient groups, regulators

We encourage the participation of a wide range of health research and drug development stakeholders in our projects.

- SMEs and mid-sized companies
  – *check the list of interested SMEs on the Call 13 web page*
- Patient organisations
- Regulatory bodies
- Companies / organisations from related fields (e.g. diagnostics, animal health, IT, imaging etc…)

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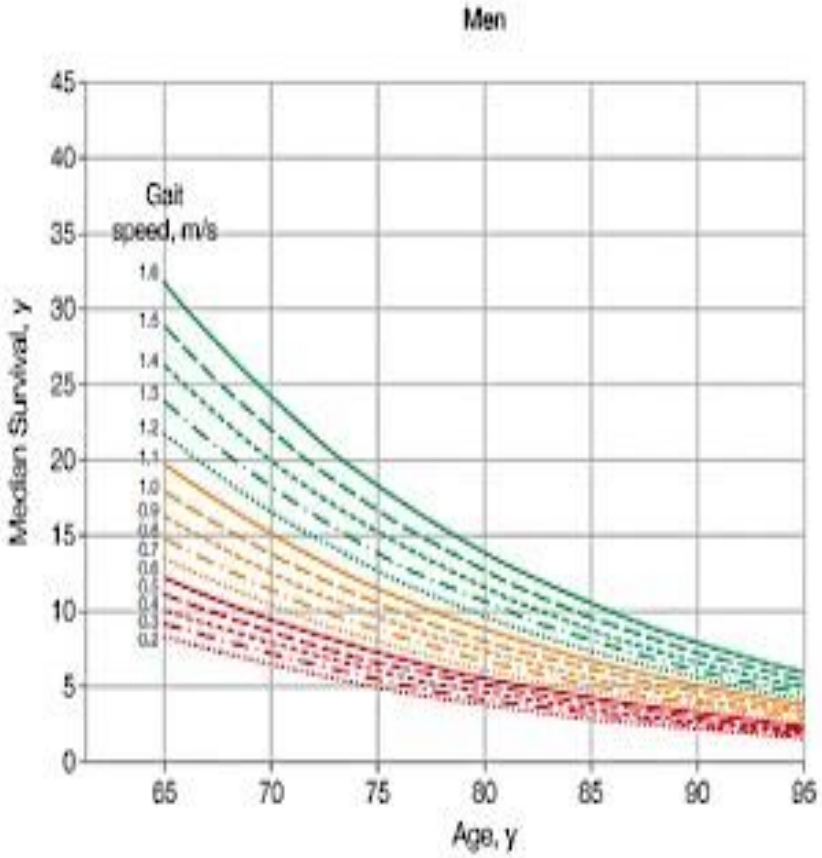
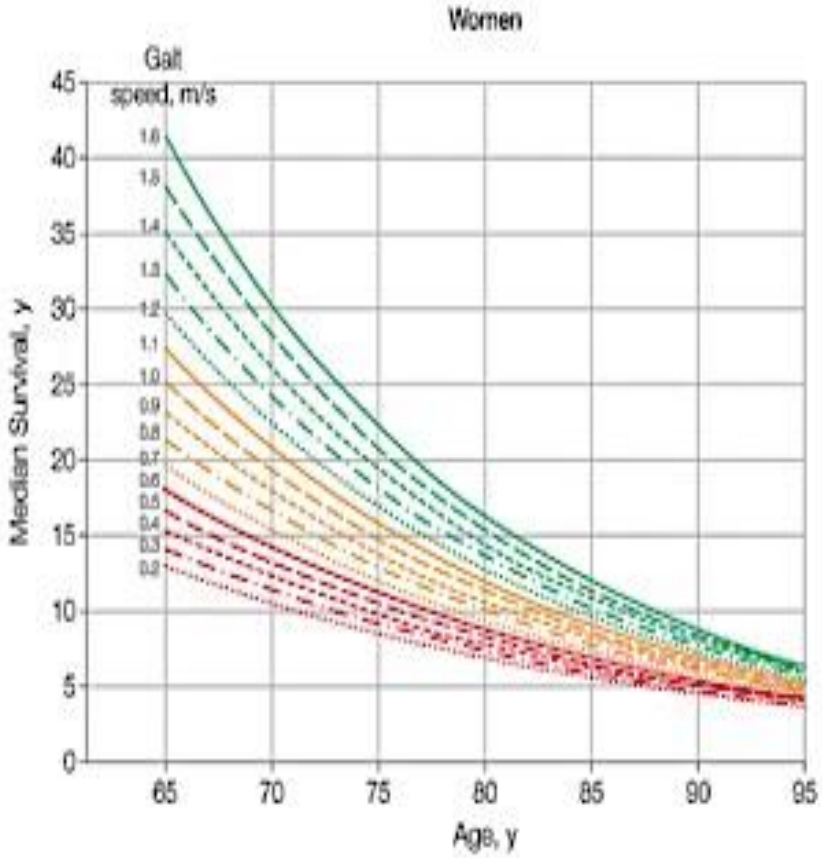
# DIAMOND: Linking digital assessment of mobility to clinical endpoints to support regulatory acceptance and clinical practice

**Ronenn Roubenoff, Novartis**

13 December 2017 • IMI Call 13 webinar

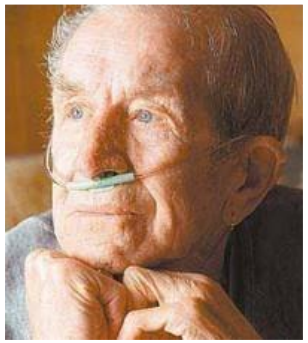
# Predicted Median Life Expectancy by Age and Gait Speed*



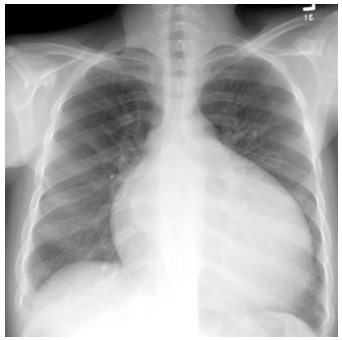




* Studenski *et al*., JAMA 2012

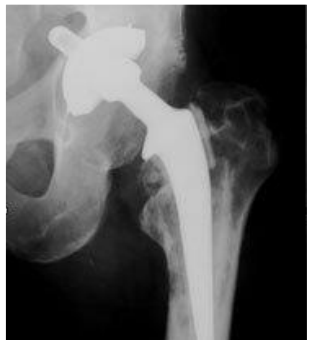
# Slow gait speed predicts bad outcomes in many diseases



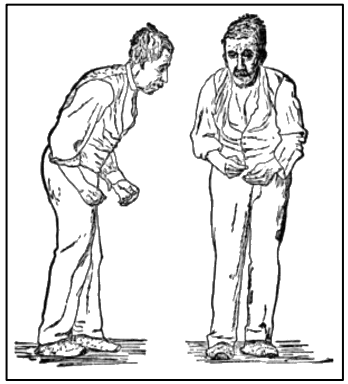
COPD



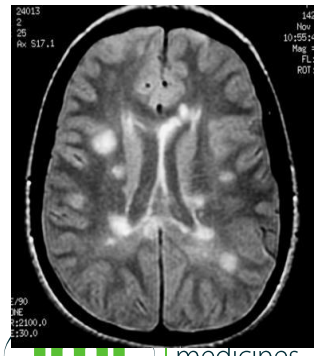
Heart Failure



Hip Fracture Recovery



Parkinson's Disease



Multiple sclerosis

# Translating physical performance into function

*Walking speed, METS and function*

| Walking speed | | METS | Functional capacity |
|---|---|---|---|
| m/sec | mph | | |
| 0.67 | 1.5 | < 2 | Self care |
| 0.89 | 2.0 | 2.5 | Household activities |
| 1.11 | 2.5 | 3.0 | Crossing street during "walk" light |
| 1.33 | 3.0 | 3.5 | Climb several flights of stairs |

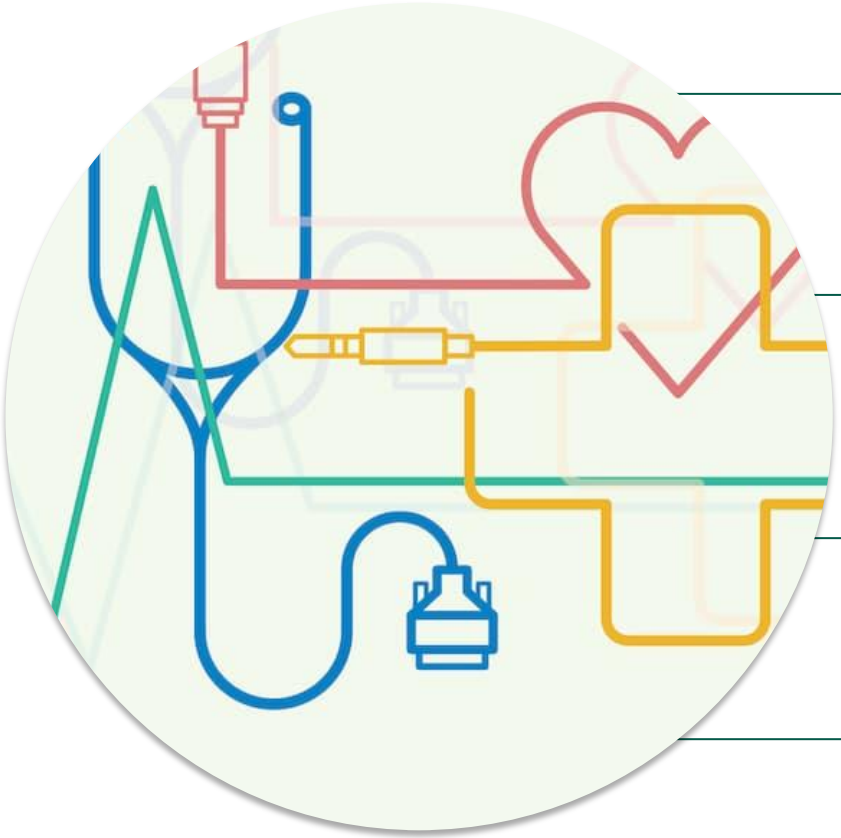
# Need for public-private collaboration

- Disease perspective: The first step in treating loss of mobility and preventing disability is detecting it effectively, with methods that do not require highly complex, hospital-based solutions.
- Digital perspective: The digital assessment of mobility and walking speed is the farthest advanced digital technology, but linking it to hard clinical outcomes is required for regulatory, payer, clinician, and patient acceptance.
- Regulatory perspective: Gaining regulatory and payer acceptance of digital mobility assessment is on the critical path to implementing digital endpoints. If this is successful, dissemination to clinical practice will follow.
- Such an approach can only be done by multiple companies, including EFPIA members, technology companies, and Small and Medium-sized Enterprises (SMEs) working with governmental, academic, and patient advocacy groups, to create a harmonised approach.

# Objectives of the full project

- By validating mobility assessment, the DIAMOND consortium will enable development of novel solutions (pharmacological, digital, nutritional, exercise-based) to a major public health problem – the increasing prevalence of mobility disability due to the aging of the population and chronic diseases.
- The purpose of of the action is to measure in three chronically ill or frail populations:
  - As a primary outcome, real world walking speed (RWS);
  - As secondary outcomes, additional digital mobility assessment (step counts, time walking, gait characteristics, time sitting/standing/walking, cadence, estimated energy expenditure of physical activity, etc.) to be collected and compared (or combined) with RWS to identify outcomes of maximum predictive power.
- The action will demonstrate that RWS or one of the other gait parameters predicts relevant medical outcomes (falls, injurious falls, hospitalisations, loss of ADLs, death), and achieve regulatory recognition of RWS as a surrogate endpoint independently of underlying disease diagnosis. To do this, regulatory submission for qualification opinion is anticipated.

# Digital Endpoint Acceptance Strategy



Replace Poor Endpoints

Reduce Patient Burden and Cost

Increase measurement accuracy

Validate to regulatory standards

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# Pre-competitive nature

- The specific aims are to develop and apply algorithms that will subsequently become publicly available
- The validated endpoint consists of the measurement algorithm, the analytic method, and the range of normal or abnormal results that predicts relevant clinical outcomes.
- This construct should support a variety of wearable hardware and inertial sensor types, and provide design-control characteristics that allow any manufacturer to receive medical device approval by demonstrating comparable performance characteristics to the tested device (i.e., a CE mark and reimbursement approval in the EU or 510(k) process in the USA).
- For the purposes of the action, however, the successful consortium will only be asked to demonstrate the validity of a single device-algorithm pairing; expansion to subsequent devices will be outside the scope of this action.

# Expected impact

- The mission of IMI is to improve health by speeding development of, and patient access to, innovative medicines, particularly in areas of high unmet medical or social need.
- As the fastest-growing population in Europe is people >80 years of age, and many previously fatal illnesses have been converted into chronic diseases, mobility disability is going to continue to grow in the 21st century.
- The first step in treating loss of mobility and preventing disability is detecting it effectively, with methods that do not require highly complex, hospital-based solutions.
- By making mobility assessment feasible, and indeed an integral part of medical care, the consortium could enable development of novel solutions (pharmacological, digital, nutritional, exercise-based) to a major public health problem – the increasing prevalence of mobility disability due to the aging of the population and chronic diseases.
- DIAMOND has the potential to revolutionise the care of frail populations and of the development of drugs to treat them.

# Suggested architecture of the project

**WP1: Project Management and Oversight**

**WP2: Algorithm development and technical validation**

**WP3: Database development and data management**

**WP4: Validation of RWS vs. Clinical Outcomes and definition and validation of RWS/mobility clinical endpoints**

**WP5: Regulatory, HTA, and Payer Consensus over Operational Definitions**

**WP6: Statistical analysis, evaluation of results, and data availability**

**WP7: Stakeholder information and results dissemination**

Applicants may propose different project architecture but must justify their selections.

# DIAMOND Sponsors – Pharma and Technology Companies

EFPIA (Pharma) Sponsors:

Novartis (Lead)
Amgen
AZ
Bayer
Grünenthal
Merck KGaA
Pfizer
Roche
Sanofi
Teva

DIAMOND

Tech Co Sponsors*:

ERT
Icon
Microsoft

Regulators:

EMA

Academic/Tech Consortia:

To Be Selected

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# Expected contributions of the applicants

- Identify centres with ongoing longitudinal cohort studies in relevant populations.
- Collaborate to select a digital activity detection device, develop or obtain an algorithm for step detection, purposeful walking detection, and walking speed measurement, and pursue technical validation against a reference method.
- Provide project management capabilities, ideally by an entity with experience in large PPP projects
- Develop and host the clinical and technical database to support the Project and provide access to all consortium members.
- Server hosting, database development and maintenance; creation of processes for data security, privacy, and transfer; provision of data anonymization procedures when necessary, definition of data standards that can be used for capture of raw and processed data from a range of inertial sensor types and sensor positioning.
- Analyse the data and collaborate with EFPIA sponsors on data interpretation and publication.
- Participate, actively contribute to constructive discussion with regulators and payers to promote and achieve consensus over operational definitions. (Co)-author reviews and white paper(s).

# Expected (in kind) contributions of industry consortium

- Support for project management, including planning, budgeting, follow up and tracking, and consolidation of work package reports to IMI.
- Advice and oversight based on member companies' expertise with database development and function, including privacy assurance and data anonymization experience
- Making fully available the member companies' expertise in clinical study initiation and conduct, providing oversight over the study management,
- Planning, hosting and organising workshop(s) with regulators and payers, contributing to discussion of available evidence (including unpublished data), literature analysis, publication support, co-authoring of reviews and white paper(s).
- providing Regulatory Affairs expertise to the Consortium;

# DIAMOND: Key Deliverables

- Longitudinal cohorts in relevant populations
- Algorithm and one (or more) digital devices
- Consensus on data collection, data quality, and analysis algorithms that will be publicly available and can function across multiple devices.
- Digital mobility and clinical outcome assessment over 2-3 years in each of 2-3 populations
- Outcome prediction analysis and thresholds for increased risk of clinical outcomes (falls, hospitalizations, loss of ADLs, death) in these populations.
- Meta-analysis across populations: Will one algorithm apply to all populations are are disease-specific algorithms necessary?
- Collaboration with and submission of algorithm validation for mobility assessment to health authorities and HTA bodies.
- Validation of RWS or other endpoints with cut-offs for predicting increased risk of the clinical endpoints for
    1. surrogate primary or secondary endpoints for clinical trials
    2. recognition by payers and health technology assessment (HTA) bodies
    3. clinical decision making in real-world settings

# DIAMOND Key deliverables

Part A (1-2 yrs)

- Development of the appropriate actimetry measurement algorithm and one (or more) digital mobility assessment devices
- Consensus on data collection, data quality, and analysis algorithms
- Submission of validation for mobility assessment to health authorities and HTA bodies

Part B (3-5 yrs)

- Digital mobility and clinical outcome assessment over 2 years in each of 3 populations (COPD, heart failure, multiple sclerosis, neurodegenerative diseases, sarcopenia/frailty, hip fracture recovery, etc.)
- Analysis of the predictive capacity and thresholds for increased risk of clinical outcomes (falls, hospitalizations, loss of ADLs, death) in multiple populations
- Meta-analysis of mobility across populations as a predictor of adverse clinical outcomes
- Submission of data to health authorities and HTA bodies for consideration as a surrogate endpoint for clinical trials, and for payer recognition of the endpoint for clinical use, respectively

# DIAMOND: Confounding variables

- Important confounding variables should be considered, including but not limited to:
  - Postural stability
  - Balance
  - Dizziness
  - Symmetry of gait
  - Medications
  - Comorbid conditions
  - Weather/external conditions/location.
- In general, the goal of the project is to validate low gait speed and/or inadequate walking as a whole-body function, rather than gait asymmetry due to arthritis, neurological deficits (stroke, etc.) that affect primarily one limb or joint.

# What's in it for you?

- Academic researchers
  - Enhance longitudinal studies with digital assessments
  - Differentiate from other centres/PI's
  - Multiple publications expected
- SMEs
  - Ensure device recognition in algorithm development
  - Ensure algorithm works with your device!
- Patient organisations
  - Deliver value to patients with enhanced digital assessments that are clearly linked to medical outcomes
- Regulators
  - Participate in project that is designed to deliver results geared to regulatory needs

# Involvement of SMEs, patient groups, regulators

Nathalie Seigneuret

# SME participation

- IMI encourages the participation of SMEs in applicant consortia as they can offer a complementary perspective to other organisations.
- For example, solutions that are co-created with SMEs can provide an economic stimulus that can be enduring. Their involvement in the action might offer a complementary perspective to industry and the academia, and help deliver the long-term impact of the project.
- In particular, in this topic, SMEs can participate providing the relevant technology, expertise in complex data management and analysis, project management and professional communication among others.

# Patient participation

There are many ways you can improve project performance by working with your patient partners e.g:

- patient input to the development and validation process.
- community outreach and dissemination on digital mobility assessments

***"The patient, doctor and researcher – each is a different kind of expert."***

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# Interactions with regulators

- Consider having a **plan for interaction** with relevant **milestones**, **resources** allocated
- You may need to go through a **formal regulatory process** to ensure **regulatory acceptance of project results** (e.g. qualification procedure for biomarkers)
- Get familiar with **services offered for dialogue** (e.g. at EMA through qualification advice, Innovation Task Force, briefing meetings)
- If regulators are not project participants, consider including them in an **advisory board**
- Consider also a plan for dialogue with **HTA bodies / payers** if relevant

**To maximise impact of science generated by projects**

**Engage in dialogue with regulatory authorities**

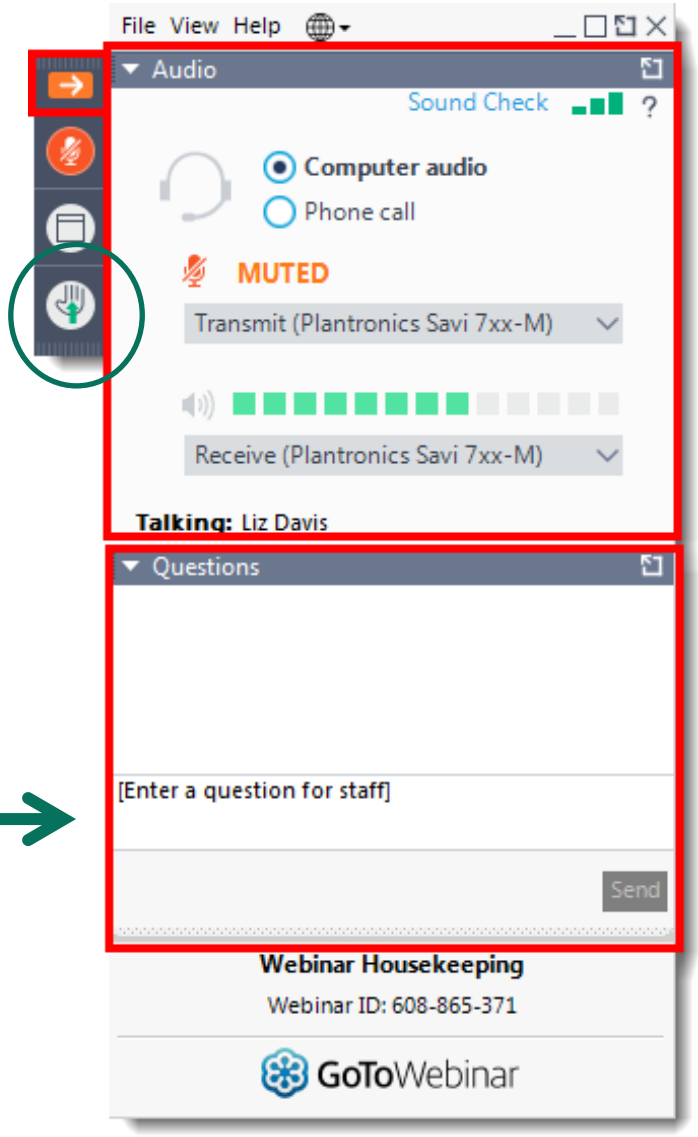
More info: 'Raising awareness of regulatory requirements: A guidance tool for researchers'

www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/RegulatoryRequirementsGuide.pdf

# Questions

# Questions?

Raise your hand if you want to ask a question orally




Send a question in writing

After the webinar, send any questions to the **IMI Programme Office**

**infodesk@imi.europa.eu**

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