

# Webinar | IMI2 - Call 15

## Emerging translational safety technologies and tools for interrogating human immunobiology

10.07.2018

# Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Isabella Tamagnini, IMI
- The Call topic – Jonathan Moggs, Novartis
- Involvement of SMEs, patient groups, regulators – Isabella Tamagnini, IMI
- Questions & answers

# How to use GoToWebinar

Expand / minimise control panel →

Microphone status →

Full screen →

Raise / lower your hand  
e.g. if you want to ask a  
question orally

Send a question in writing →

The screenshot shows the GoToWebinar interface with several key elements highlighted by a red border and green arrows:

- Expand / minimise control panel:** A red circle highlights the right-pointing arrow icon at the top of the control panel.
- Microphone status:** A red circle highlights the microphone icon with a slash through it, indicating it is muted.
- Full screen:** A red circle highlights the full-screen icon (a square with a smaller square inside).
- Raise / lower your hand:** A red circle highlights the hand icon with a green dot, indicating the hand is raised.
- Send a question in writing:** A red circle highlights the text input field containing the placeholder "[Enter a question for staff]" and the "Send" button.

The interface also displays the following information:

- File View Help (menu)
- Audio (title bar)
- Sound Check (status)
- Computer audio (selected) / Phone call (unselected)
- MUTED (status)
- Transmit (Plantronics Savi 7xx-M) (dropdown)
- Receive (Plantronics Savi 7xx-M) (dropdown)
- Talking: Liz Davis (status)
- Questions (title bar)
- Webinar Housekeeping (title bar)
- Webinar ID: 608-865-371 (text)
- GoToWebinar (logo)

# How to use GoToWebinar - audio

To listen via your computer, select **Computer audio**

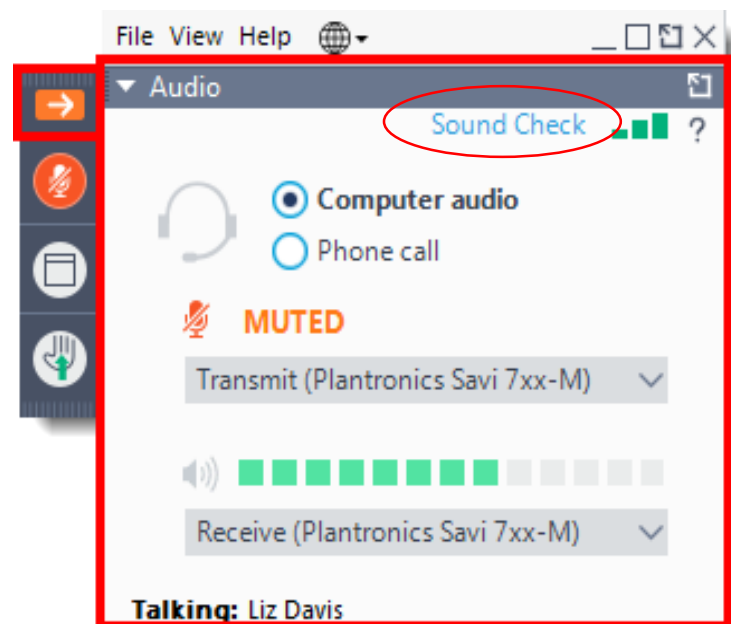
## Can't hear us?

- Check your **speakers are switched on and not muted**
- Do a **Sound Check** to make sure GoToWebinar is picking up the right speakers
- Still not working? Select **Phone call** and dial the numbers given on your phone

To listen in via your phone, select **Phone call**, pick your country, and dial the numbers given

## Can't hear us?

- Check you have selected **Phone call** in the audio panel
- Try **another country's** phone number
- Still not working? Select **Computer audio** and listen over your computer's speakers



# 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 and published on the website
- 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.



**Webinar | IMI2 - Call 15**  
**Emerging translational safety technologies and tools for interrogating human immunobiology**

Isabella Tamagnini

# 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

**Tuesday 10 July at 10:30**

# 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.



# 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**.

# 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

# 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

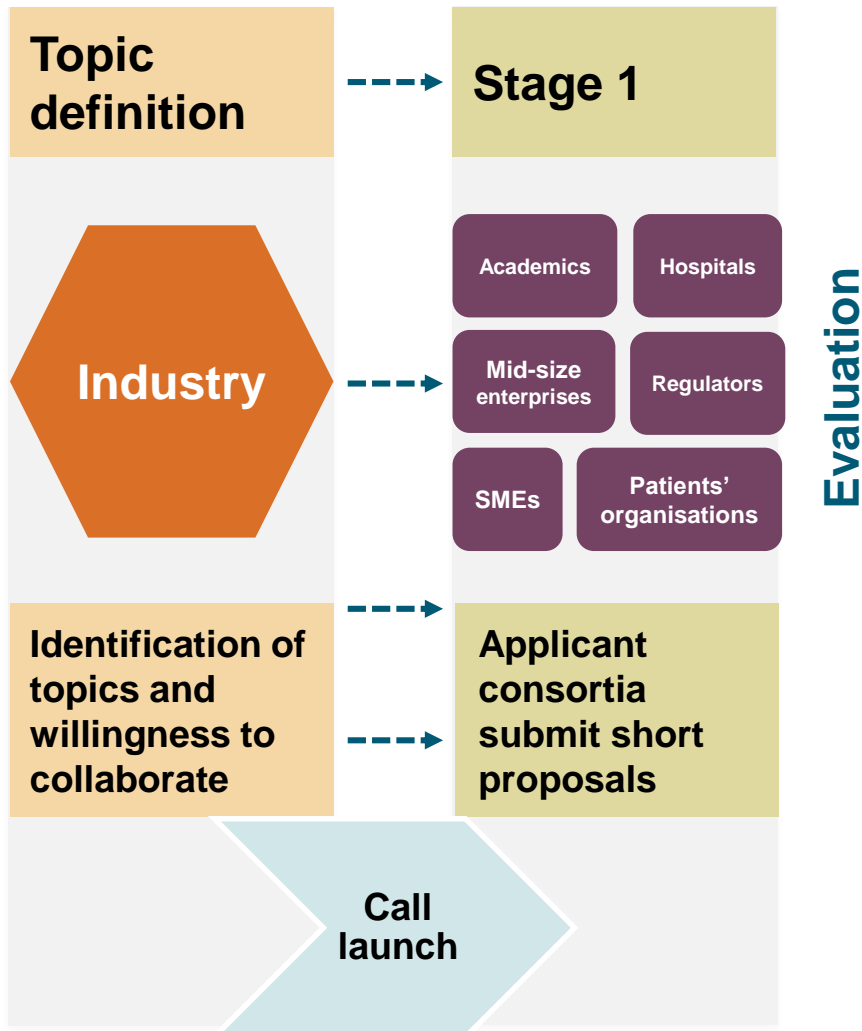
Scale is a key to success and is provided through IMI funding

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

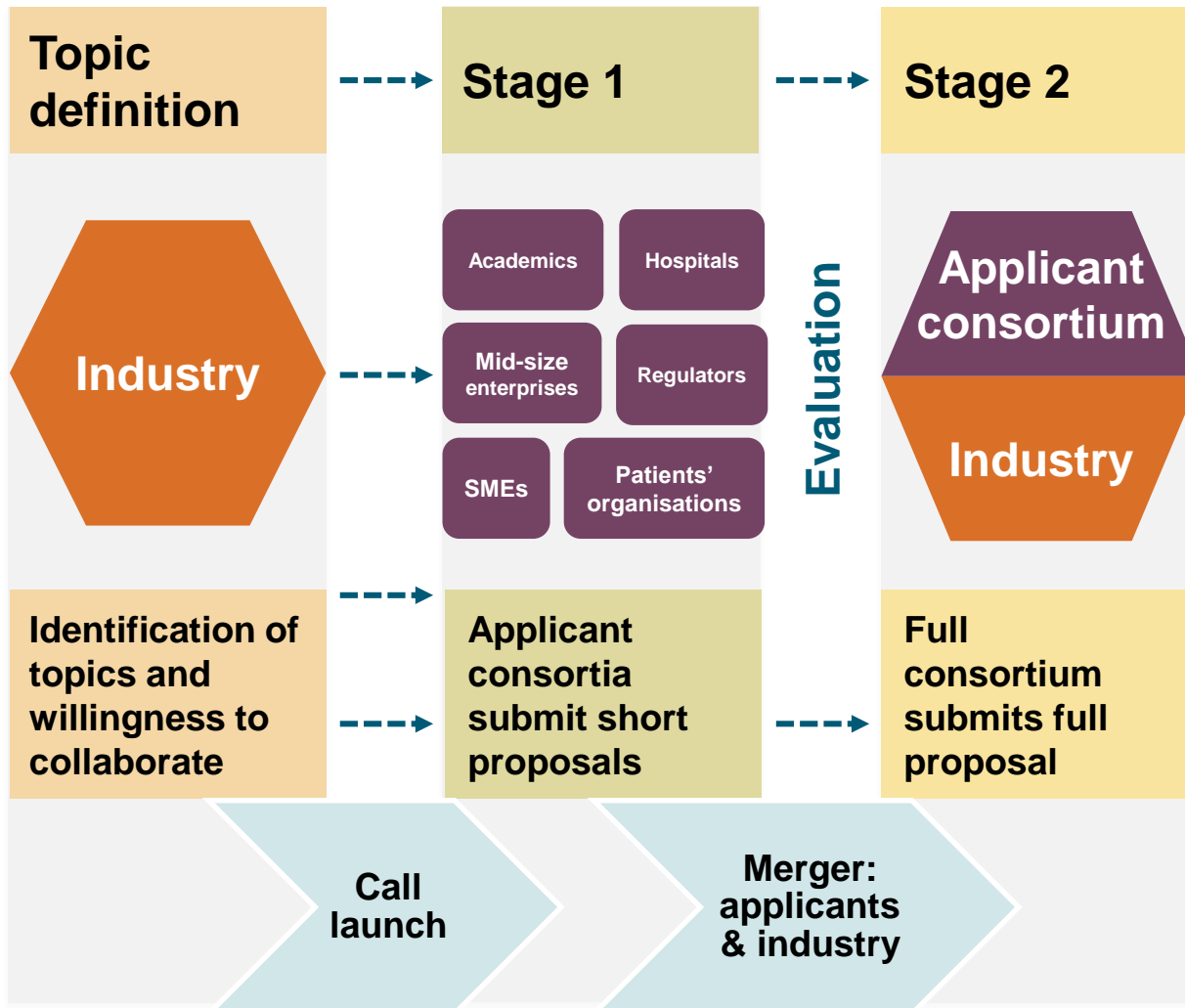
# Typical IMI project life cycle



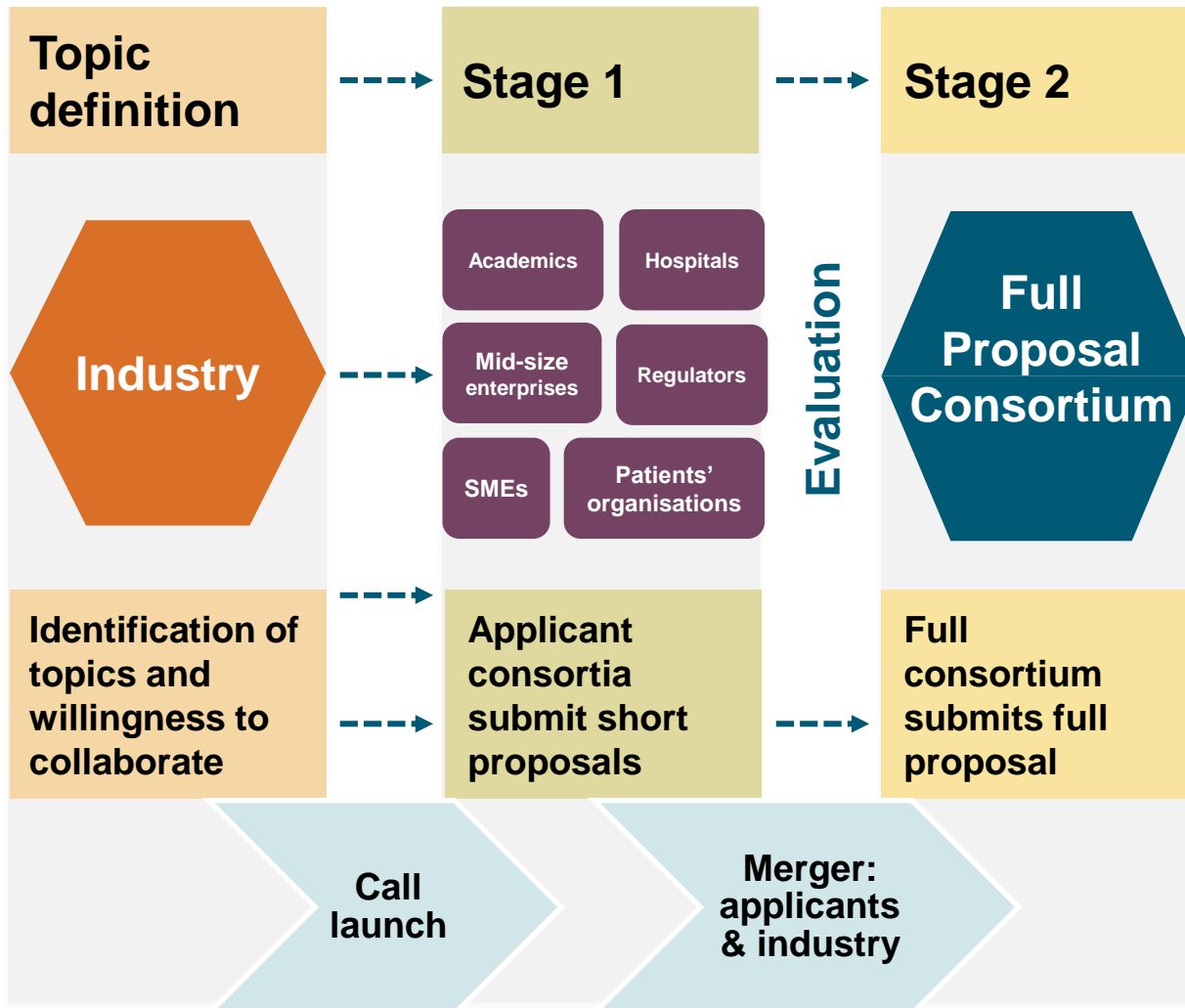
# Typical IMI project life cycle



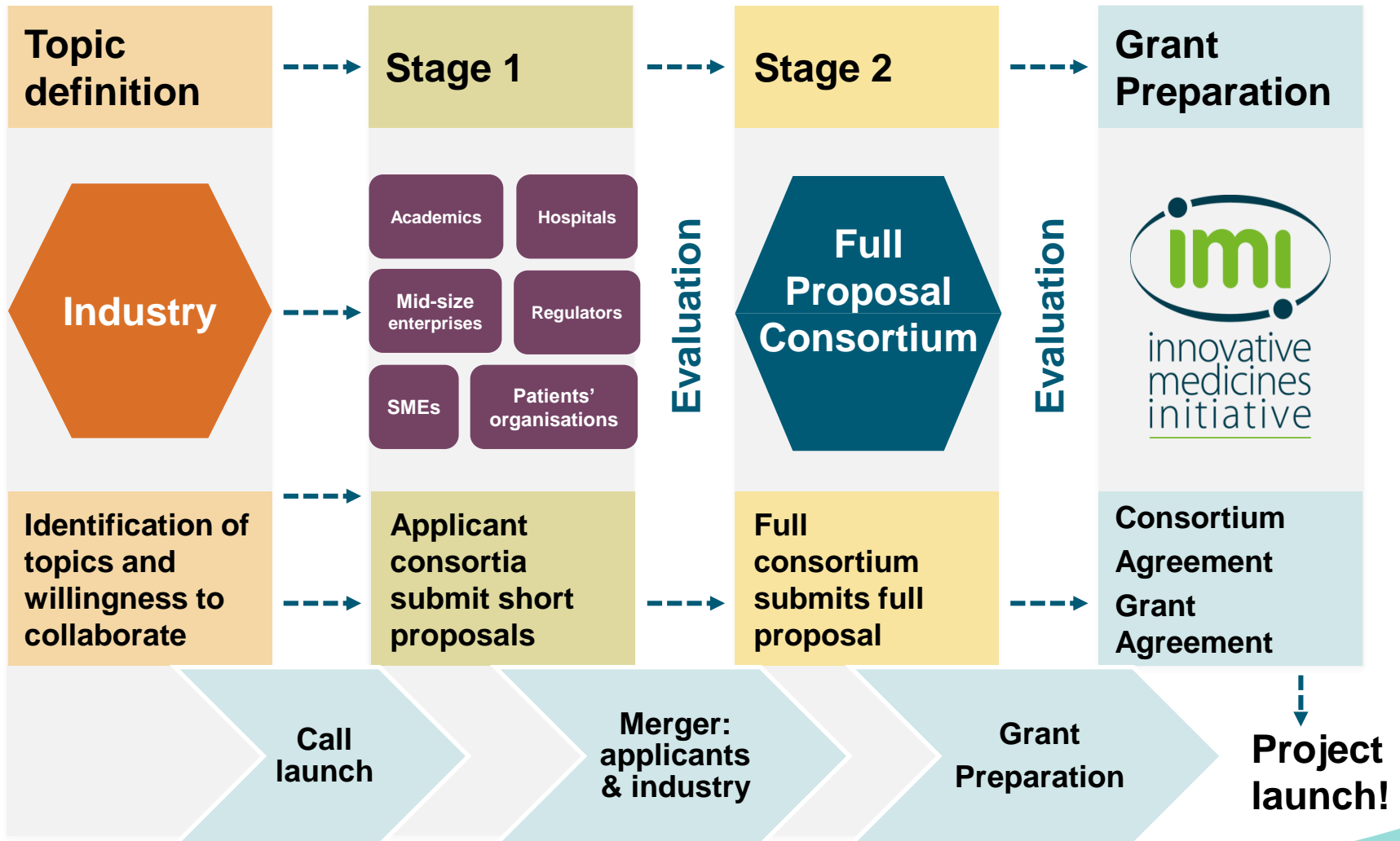
# Typical IMI project life cycle



# Typical IMI project life cycle



# Typical IMI project life cycle





# Submitting a proposal

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

The screenshot displays the 'Participant Portal' for 'RESEARCH & INNOVATION' by the European Commission. The main navigation bar includes 'HOME', 'FUNDING OPPORTUNITIES', 'HOW TO PARTICIPATE', 'EXPERTS', and 'SUPPORT'. A search bar and 'LOGIN'/'REGISTER' buttons are also present. The left sidebar lists 'EU Programmes 2014-2020' with categories like 'Search Topics', 'Updates', and 'Calls', where 'H2020' is selected. The main content area is titled 'Calls for Proposals' and features a 'Horizon 2020' section with a globe icon and a link to 'Advanced search for topics Calls for tenders on TED'. Below this, there are filterable categories: 'Excellent Science' (including ERC, FET, Marie-Sklodowska-Curie Actions, and Research Infrastructures) and 'Industrial Leadership' (including LEIT and ICT). A 'Status' filter is set to 'Calls with forthcoming topics' and 'Calls with open topics'. The 'Sort by' dropdown is set to 'Publication date', and a search filter 'IMI2' is entered in the search box.

# 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

|                                      |   |
|--------------------------------------|---|
| <b>1. EXCELLENCE</b>                 | <b>3. IMPLEMENTATION</b>  |
| 1.1 Objectives                       | 3.1 Outline of project plan — Work packages, and major deliverables |
| 1.2 Relation to the call topic text. | 3.2 Management structure and procedures                             |
| 1.3 Concept and approach             | 3.3 Consortium as a whole   |
| 1.4 Ambition                         | 3.4 Table 3.1a: List of work packages                               |
| <b>2. IMPACT</b>                     | <b>4. PARTICIPANTS</b>  |
| 1 Expected impacts                   | 4.1. Participants (applicants)                                      |

# 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](http://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](mailto:infodesk@imi.europa.eu)

# 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 is not well described.

# 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](https://ec.europa.eu/research/participants/portal/desktop/en/organisations/partner_search.html)
  - German NCP partner search tool: [www.imi-partnering.eu](http://www.imi-partnering.eu)
- Get in touch with your **local IMI contact point**:  
[www.imi.europa.eu/about-imi/governance/states-representatives-group](http://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)

# 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
- Patient organisations
- Regulatory bodies
- Companies / organisations from related fields (e.g. diagnostics, animal health, IT, imaging, etc.)





# Emerging translational safety technologies and tools for interrogating human immuno- biology

Jonathan Moggs and Kara Lassen on behalf of the industry consortium

10.07.2018 • IMI webinar

## ***Primary goal:***

**Enhance safety assessment of innovative immunomodulatory therapeutics by evaluating the utility of integrating non-clinical and clinical safety experience with data derived from human *in vitro* immune cellular models, “engineered” animal models, and innovative immunophenotyping endpoints**

# Specific challenges to be addressed

- Urgent need to better understand inherent risks of innovative immunomodulatory therapeutics during early non-clinical stages of drug development
- Scope includes immuno-oncology and immuno-inflammatory diseases

The collage consists of the following articles:

- Regulatory Toxicology and Pharmacology:** Workshop report: HESI/FDA workshop on immunomodulators and cancer risk assessment: Building blocks for a weight-of-evidence approach. Authors: H. Lebec, F.R. Brennan, H. Haggerty, D. Herzyk, C. Kamperschroer, C.C. Maier, R. Ponce, B.D. Preston, D. Weinstock, R.D. Melion.
- Clinical Microbiology and Infection:** Narrative review: ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Introduction). Authors: M. Fernández-Ruiz, Y. Meije, O. Manuel, H. Akan, J. Carratala, J.M. Aguado, J. Delalaye.
- FDA U.S. FOOD & DRUG ADMINISTRATION:** FDA Public Workshop: Assessment of Cardiovascular Toxicities in Immuno-oncology Trials.
- UNIVERSITY OF LIVERPOOL:** CENTRE FOR DRUG SAFETY SCIENCE. Events: Safety of Immune Checkpoint Inhibitors Workshop. 19 February 2018 | Forensic Centre, University of Liverpool, 1 Brownlow Street, L69 3GE.
- FDA U.S. FOOD & DRUG ADMINISTRATION:** Checkpoint Inhibitor Induced Autoimmunity in a Humanized Mouse Model. Author: Kristina E. Howard, DVM, Ph.D., Division of Applied Regulatory Science, Office of Translational Sciences/CDER, Food & Drug Administration.
- FDA U.S. Food and Drug Administration:** Immunomodulators and Cancer Risk Assessment. The TNF Inhibitor History Illustrates the Scientific & Regulatory Challenges.
- ELSEVIER:** Cytokine. Cytokine release: A workshop proceedings on the state-of-the-science, current challenges and future directions. Authors: Christine Grimaldi, Deborah Finco, Madeleine M. Fort, Daniel Gliddon, Kirsty Harper, Whitney S. Helms, Jane A. Mitchell, Rangan O'Lane, Stanley T. Parash, Marie-Solène Pêche, Daniel M. Reed, Gabriele Reichmann, Patricia C. Ryan, Richard Sebbings, Mindi Walker.
- ELSEVIER:** Chimeric antigen receptor T-cell therapy — assessment and management of toxicities. Authors: Sattva S. Neelapu, Sudhakar Tummala, Partow Kebriaei, William Wierda, Cristina Gutierrez, Frederick L. Lachier, Krishna V. Kammanduri, Yi Lin, Nitin Jain, Naval Daver, Jason Westin, Alison M. Gulbis, Monica E. Logthir, John F. de Groot, Sherry Adkins, Suzanne E. Davis, Katayoun Rezvani, Patrick Hwu, Elizabeth J. Shpall.

**Immunosuppression  
risk: infection,  
malignancy**



**Immune stimulation  
risk: autoimmunity,  
cytokine release**



# Specific challenges to be addressed

- Toxicities induced by immunomodulatory therapeutics in patients are often not detected in traditional animal models:
  - lack of expression of appropriate targets/pathways in young healthy animals
  - differential target genetics/expression/functions in animals versus intended patient populations



- Need innovative translational (human-relevant) safety assessment tools, technologies, models and resources to facilitate the development of novel immunomodulatory drugs

# Need for public-private collaboration

- Focus on immunomodulatory therapeutic modes of action for which there is existing non-clinical and clinical safety experience but suboptimal prediction of human toxicities based on input from pharma industry, academia and regulators
- Assessing the potential utility of integrating safety data derived from innovative non-clinical animal models and/or human in vitro immune cellular systems into IND/CTA-enabling safety assessment packages is unlikely to be within the scope of investment and capabilities for any one company or organisation
- Innovative non-clinical models and endpoints will need to be customised for specific immunomodulatory therapeutic modes of action, disease indications and anticipated toxicities

# Objectives of the full project (1)

- Development of innovative comparative (cross-species) in situ and ex vivo molecular, biochemical tools and cellular profiling of immune cells (including patient-derived clinical samples) and association with functional/phenotypic endpoints to enable:
  - enhanced understanding of therapeutic target and pathway biology,
  - enhanced pharmacological and toxicological mechanistic insight and biomarker identification
  - supporting therapeutic index determination for drug candidates and drug modalities
  - identification of novel endpoints/biomarkers to help support safe starting dose selection for first in human studies e.g. determination of minimum pharmacologically active dose (mPAD) and minimum anticipated biological effect level (MABEL)
  - identification of novel endpoints/biomarkers to help differentiate patient populations that might be more at risk for adverse events

# Objectives of the full project (2)

- Establishment, refinement and validation of non-clinical tools and models to enable the development of novel classes of immunomodulatory medicines supporting in vitro-in vivo and cross-species translation:
  - comparative assessment of performance of established human in vitro immune cell assays based on healthy volunteer versus patient-derived cells representing specific disease states
  - development and validation of human immune-competent organotypic and microphysiological systems for efficacy and safety profiling of immunomodulatory drugs
  - development and validation of animal models (e.g. humanised mice, genetically engineered animal models, disease models) as tools for efficacy and safety assessment of immunomodulatory drugs
  - deployment of computational biology approaches for assessment and integration of large multivariate immuno-biology datasets to reveal novel immune-biology mechanisms and translational biomarkers

# Pre-competitive nature

- The topic requires a strategic consortium that will enable the sharing of experience from regulators, academia, and pharma industry, in fast evolving immune cell phenotyping technologies, complex in vitro model development, and characterisation of engineered and disease state animal models, as well as facilitating access to extensive immune cell and tissue biobanks (including patient-derived material and thus potential engagement of relevant patient organisations)



# Expected impact

- **Help deliver safer medicines to patients via:**
  - provision of new tools and models to enable a better understanding of the inherent safety risks of immunomodulatory therapeutics during early (non-clinical) stages of drug development
  - improvement of drug development processes and regulatory assessments for immunomodulatory therapeutics through the characterisation of innovative immune-biology models and biomarkers that complement and enhance existing non-clinical safety assessment approaches
  - better definition of limitations in the translatability of non-clinical test systems to patients, which will enable the most appropriate and efficient combinations of test systems to be used for future safety assessment of immunomodulatory therapeutics, and will also contribute to the principles of the 3Rs

# Suggested architecture of the project

Regulatory Advisory Group

**Work package 1** – Management, coordination, dissemination and sustainability.

**Kick-off workshop to prioritise immunomodulatory therapeutic modes of action for which there is suboptimal prediction of human toxicities**

**Work package 2** – Innovative models for safety assessment of immuno-oncology therapeutics

**Work package 3** – Innovative models for safety assessment of immuno-inflammatory disease therapeutics

**Work package 4** – Innovative biomarkers for translational safety assessment of immunomodulatory therapeutics

**Work package 5** – Clinical sample management – sourcing and logistics for assay and model development

# Expected contributions of the applicants

- ability to deploy/develop innovative in vivo/ex vivo/in vitro technologies for recapitulating human immuno-biology
- expertise in customised/innovative immune cell assay/model/bioinformatics development
- expertise in innovative technology platforms for molecular, biochemical and cellular phenotyping of immune cells
- regulatory expertise on selection of immunomodulatory therapeutic case studies for assay/model validation
- project management, dissemination and exploitation expertise

# Expected contributions of the applicants

- provision of human blood- and tissue- samples to support deployment of advanced immune cell phenotyping technologies and/or in vitro model development
- given the significant technical and logistical challenges associated with sourcing patient-derived samples to support customised safety assessment studies, experience is also sought for the establishment of a network to facilitate sourcing of human-derived immune cell and tissue samples for specific disease areas (potentially through a combination of Patient Organisations, Medical Technology companies and Academic/Clinical centres of excellence)

# Expected (in kind) contributions of industry consortium

- expertise in in vitro and in vivo safety assessment models and biomarkers
- design and deployment of prospective in vitro and in vivo studies; provision of historical safety-related in vivo phenotypic data for defined therapeutic modes of action (e.g. discontinued development compounds; marketed compounds); in silico prediction of immunomodulatory drug-related adverse events
- provision of advanced technology platforms and bioinformatic support for cross-species molecular, biochemical and cellular phenotyping of immune cells

# Expected (in kind) contributions of industry consortium

- provision of human blood and tissue samples to support deployment of advanced immune cell phenotyping technologies and/or in vitro model development (baseline, antigen-challenged, pharmacologically-stimulated, disease states)
- emerging human-centric ex vivo / in vitro technologies (patient-derived and healthy volunteer-derived) will be evaluated and/or further refined for their potential to recapitulate in vivo human immune biology

# What's in it for you?

- IMI public-private partnership consortium approach enables rapid sharing of scientific and technical experience, tools, models, biobanked samples and databases between regulators, academia, pharma industry, medical technology companies and patient organisations
- Unique opportunity to enhance human immuno-biology knowledge on therapeutically relevant targets, pathways and mechanisms
- Unique opportunity to evaluate utility of new human immuno-biology tools and technologies for practical applications in drug development

# Key deliverables of the full project

- Development/evaluation of human in vitro systems (healthy donor- and/or patient-derived) and ‘engineered’ animal models that are customised for specific therapeutic MoA and patient-relevant cell types/tissue microenvironments in order to recapitulate target engagement, pharmacodynamics and clinically-relevant toxicity phenotypes
- Development/evaluation of innovative molecular and cellular immunophenotyping biomarkers across conventional toxicology models, ‘engineered’ animal models, and human in vitro models:
  - provide enhanced molecular and cellular biomarkers for determination of therapeutic index (TI) and first-in-human (FIH) maximum recommended starting dose (MRSD)
  - benchmark biomarker performance versus patient-derived samples and assess utility for determination of minimum pharmacologically active dose (mPAD) and minimum anticipated biological effect level (MABEL)





**Thank you**

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@IMI\_JU

# Involvement of SMEs, patient groups, regulators

Isabella Tamagnini

# SME participation

IMI encourages the participation of SMEs in applicant consortia as they can offer a complementary perspective to other organisations.

Under this topic, the contribution of SMEs would be considered especially beneficial in the provision of:

- innovative, engineered animal models
- in vitro models that mimic human immuno-biology
- etc.

# Patient participation

Given the significant technical and logistical challenges associated with sourcing patient-derived samples to support customised safety assessment studies, **the input of patient organisations will be fundamental to establish a network to facilitate sourcing of human-derived immune cell and tissue samples via centres of excellence for specific disease areas** (patient organisations / medtech / academic partners).

IMI also encourages applicants to consult patient organisations or patient advocacy groups, e.g. regarding:

- patient consent forms
- relevant communication about the project and its potential value
- dissemination of the project results
- etc.

# Interactions with regulators (1)

- **Have a plan for interaction** with relevant **milestones** and **resources** allocated, as needed
- Consider the **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)
- Consider involving regulators as project participants or in the **advisory board**
- Have 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:

- [Webinar & presentations](#) 'How to engage with regulators EMA / FDA'
- 'Raising awareness of regulatory requirements: [A guidance tool for researchers](#)'

# Interactions with regulators (2)

The consortium is expected to have a strategy on 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 resources allocated should be proposed to ensure this (e.g. qualification advice on the proposed methods for novel methodologies for drug development, qualification opinion).



# Questions & answers

# Questions?

Raise your hand if you want to ask a question orally



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Send a question in writing



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

[applicants@imi.europa.eu](mailto:applicants@imi.europa.eu)





**Thank you!**