

**Webinar | IMI2 – Call 13
Improving the preclinical prediction
of adverse effects of
pharmaceuticals on the nervous
system**

12 December 2017 • 15:00 CET

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Iwona Jablonska, IMI
- The Call topic – Jacques Richard, Sanofi
- Involvement of SMEs, patients and regulators – Iwona Jablonska, IMI
- Questions & answers

How to use GoToWebinar - audio

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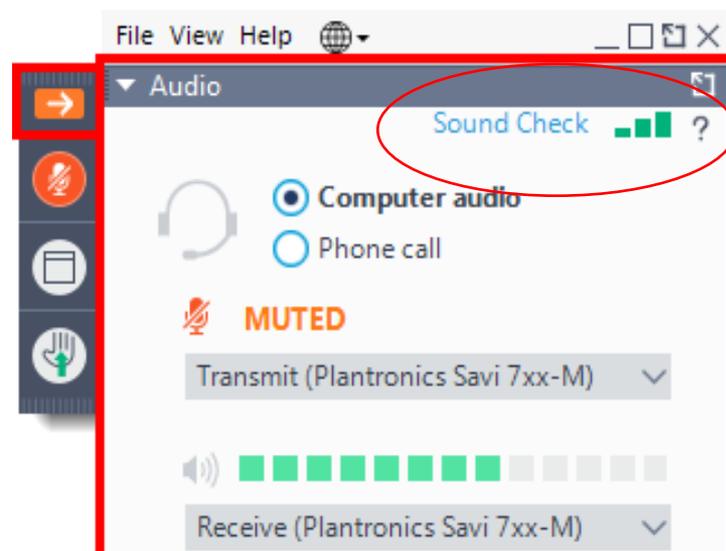
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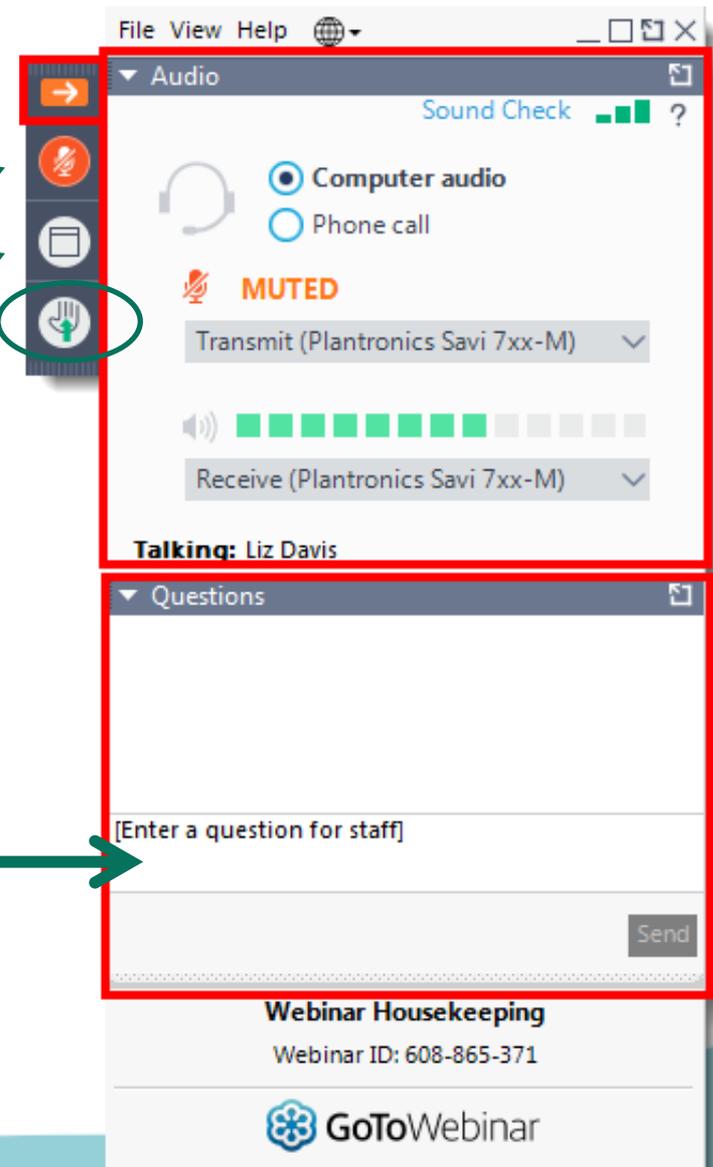
Expand / minimise control panel →

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The screenshot shows the GoToWebinar control panel interface. A red border highlights the main control area. On the left, a vertical toolbar contains several icons: a right-pointing arrow (highlighted with a red box), a microphone with a slash (Microphone status), a square icon (Full screen), and a hand icon (Raise/Lower hand). The hand icon is circled in green. To the right of the toolbar, the 'Audio' section is visible, showing 'Computer audio' selected, a 'MUTED' status, and a volume bar. Below the audio section, the 'Questions' section is shown with a text input field containing '[Enter a question for staff]' and a 'Send' button. At the bottom, the webinar title 'Webinar Housekeeping' and ID '608-865-371' are displayed, along with the GoToWebinar logo.

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

Webinar | IMI2 - Call 13

Topic 10: Improving the preclinical prediction of adverse effects of pharmaceuticals on the nervous system

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

- **Webinars on IMI's rules and procedures and opportunities for SMEs** took place on Thursday 7 December – recordings are available online
- Both will be repeated in January 2018 – sign up via imi.europa.eu

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

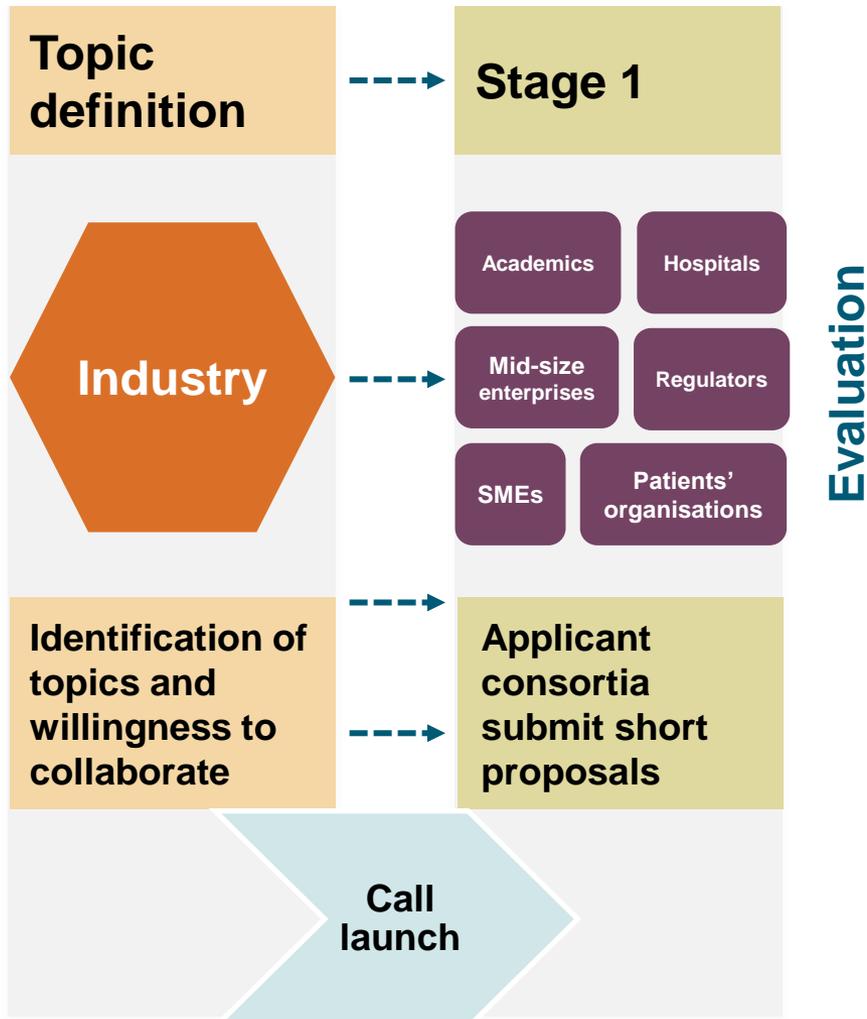
Scale is a key to success and is provided through IMI funding

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

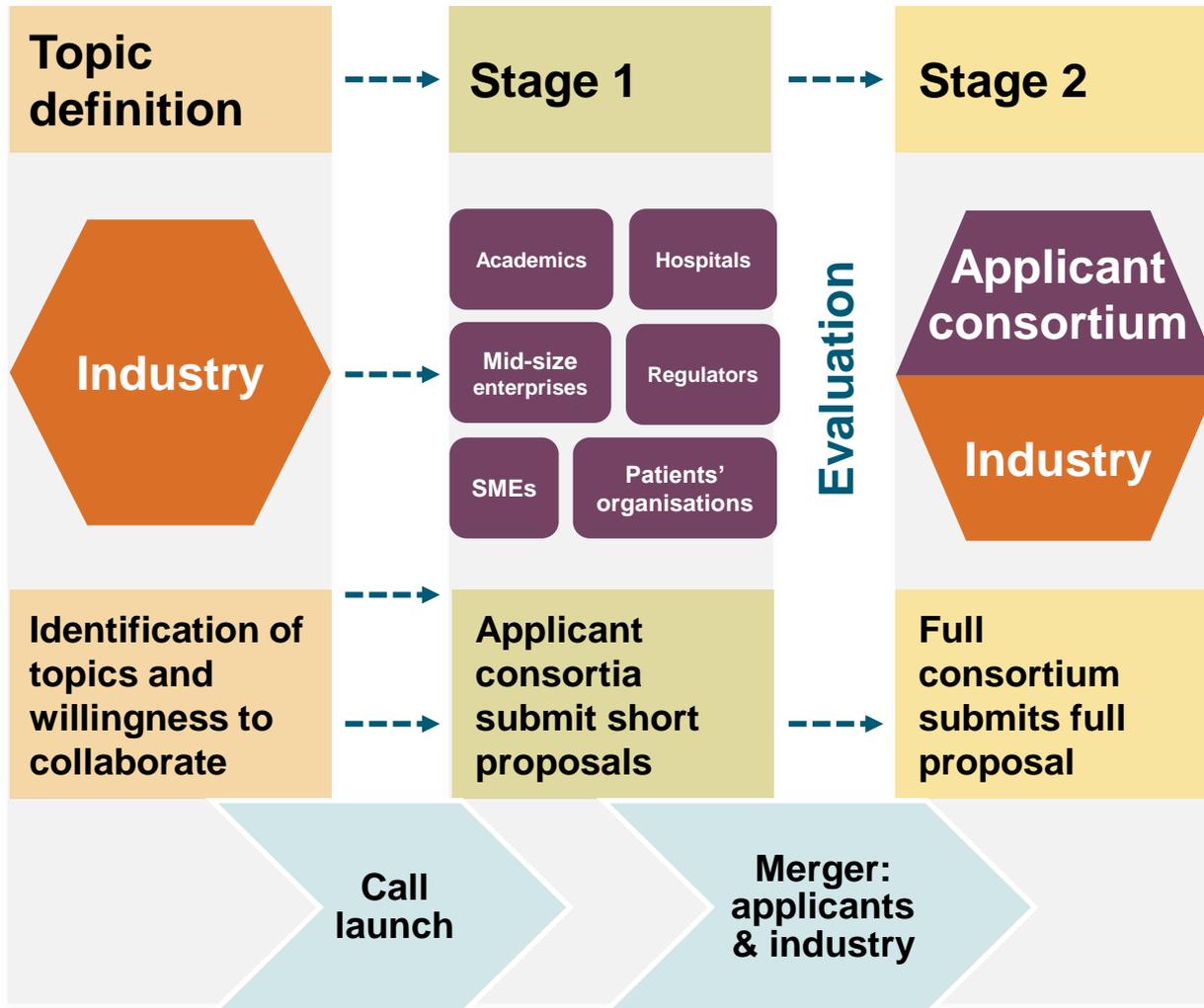
Typical IMI project life cycle



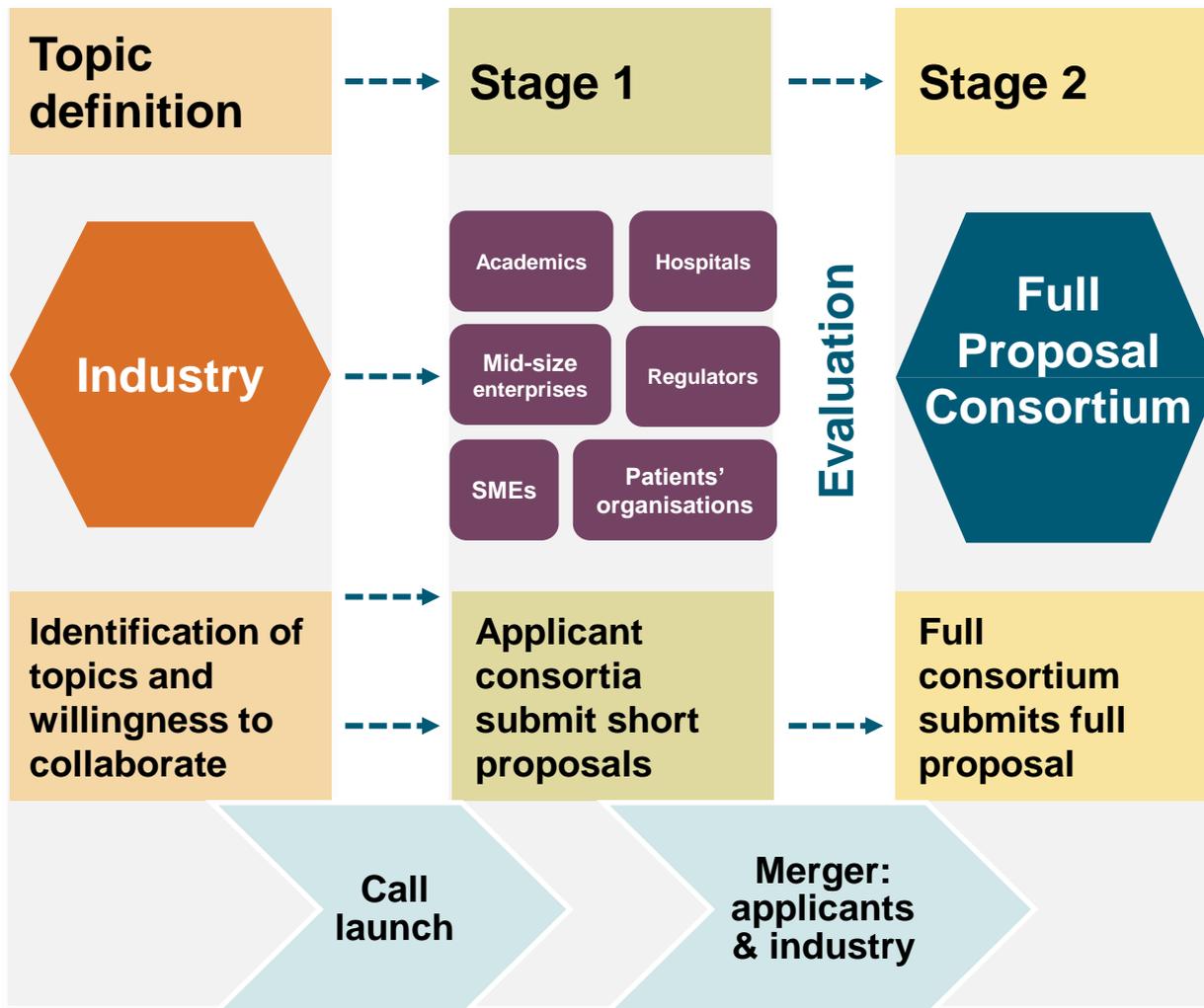
Typical IMI project life cycle



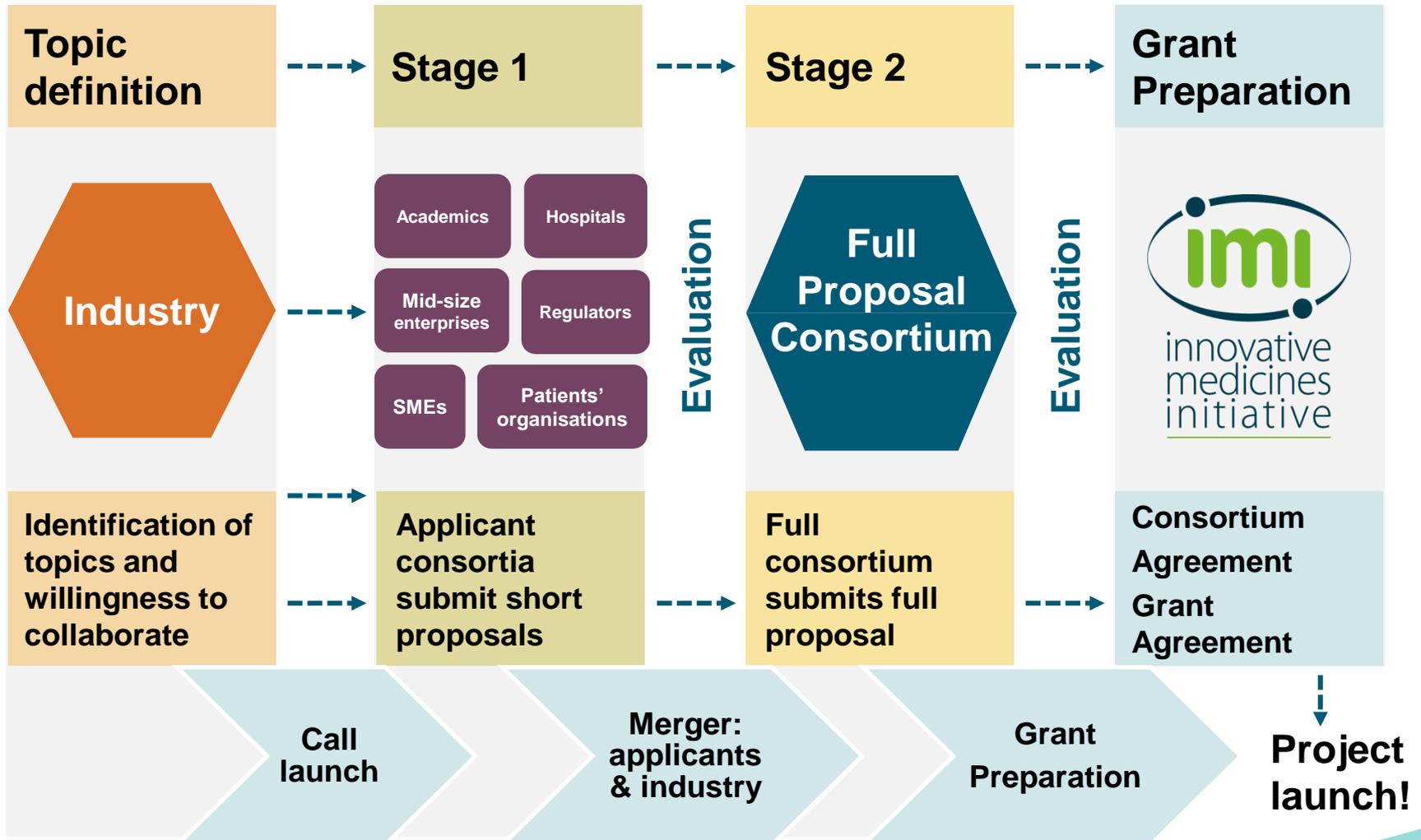
Typical IMI project life cycle



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 'H2020', '3rd Health Programme', 'Asylum, Migration and Integration Fund', 'Consumer Programme', 'COSME', 'Internal Security Fund - Borders', 'Internal Security Fund - Police', and 'Justice Programme'. The main content area is titled 'Calls for Proposals' and features a 'Horizon 2020' section with a globe icon and a link for '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

1. EXCELLENCE	3. IMPLEMENTATION
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
2. IMPACT	4. PARTICIPANTS
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
- 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

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.

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)

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...)

Improving the preclinical prediction of adverse effects of pharmaceuticals on nervous system

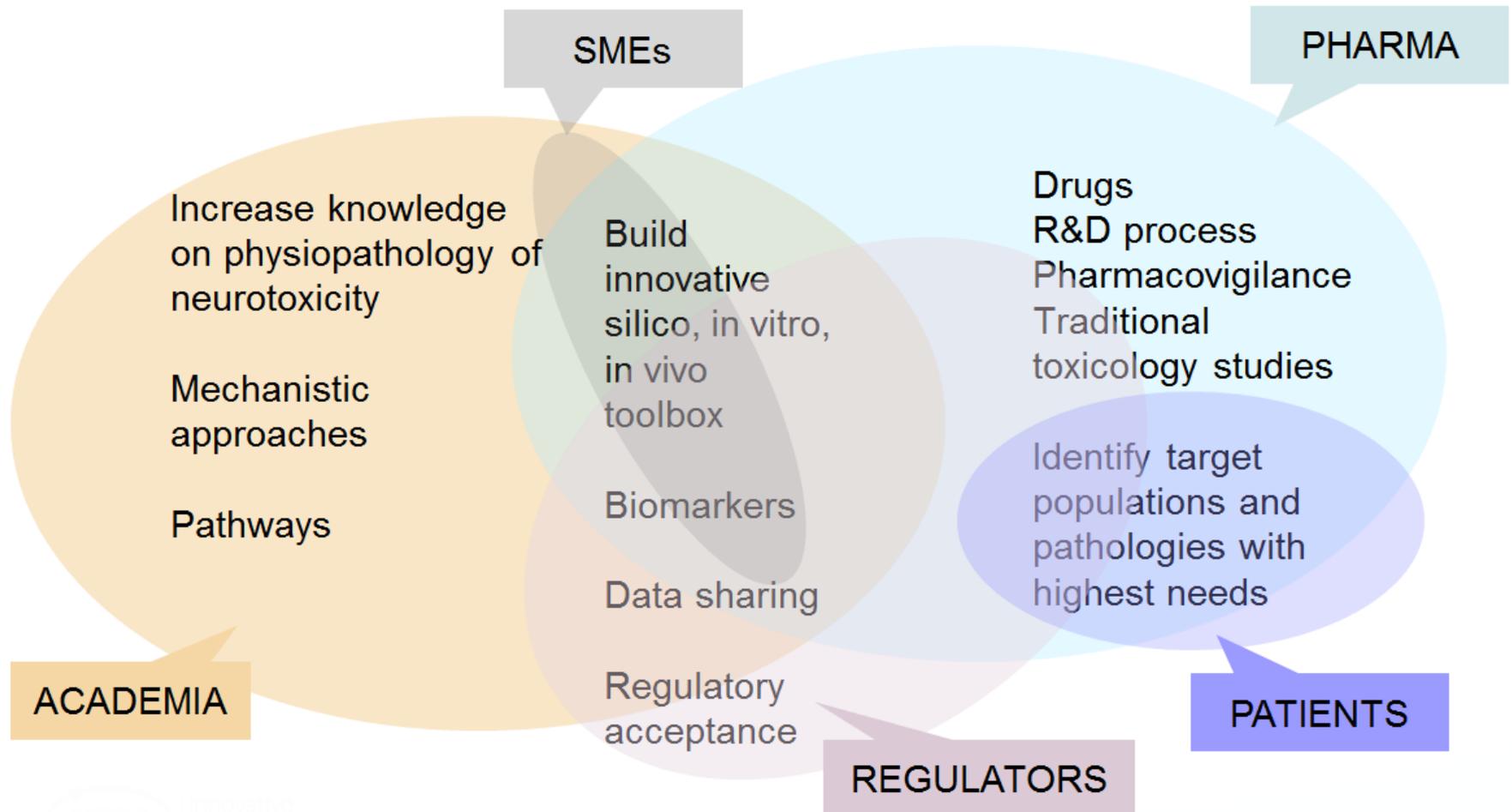
Jacques RICHARD
12.12.2017 • IMI webinar

Why a topic on neurotoxicity?

- **Prediction of adverse effects** on nervous system at preclinical stages is **poor**:
 - Complex physiopathology of neurotoxicity
 - **Insufficient predictability** of the preclinical toolbox
 - Translation «preclinical to clinical» not established
- Consequences:
 - **Risk of adverse effects** during clinical trials or post-marketing
 - **Attrition** during R&D process
- Most critical needs for:
 - Seizures/convulsions
 - Psychological/psychiatric changes
 - Peripheral neuropathies

Need for public-private collaboration

Diverse expertises are needed and cannot be found in a single sector and/or discipline



Objectives of the full project

Build an integrated prediction/evaluation approach to better predict neurotoxicity of drugs:

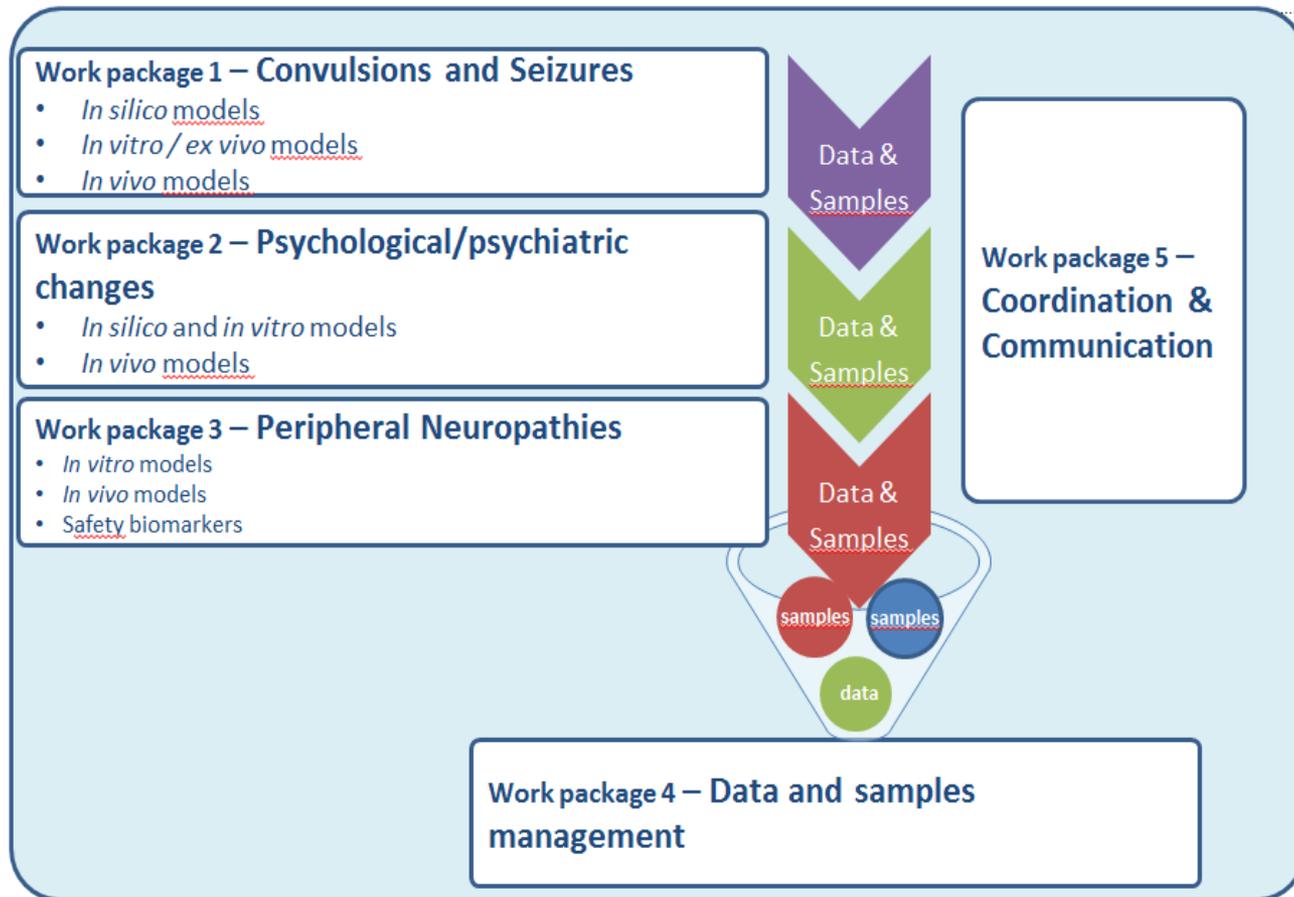
- “Approach”: *in silico* + *in vitro* + *in vivo* tools (assays, studies, biomarkers, etc)
- “Integrated”: holistic mindset allowing risk assessment for decision-making
- “Neurotoxicity”: central + peripheral effects
- “Drugs”:
 - chemical + biological
 - targeting nervous system or not

Expected impact

- On R&D
 - Reduced attrition
 - Increased productivity/reduced costs
 - Reduced drug withdrawals
 - Impact on 3Rs (Reduction, Refinement, Replacement of animal use)
- On volunteers/patients
 - Improved safety
- Overall impact: improved risk/benefit ratio

Suggested architecture of the project

- Exemple of project architecture that could be set up



Scope and objectives of the workpackages (1/3)

- WP1: Convulsions and seizures
 - Detect potential for convulsions/seizures during candidate selection
 - Build refine tools: systems biology, (Q)SAR, ihPSCs, 2D/3D models, neurons, astrocytes, microglia, zebrafish, rodents, non-rodents, EEG, imaging, automated video-monitoring...
- WP2 : Psychological/psychiatric changes
 - Improve prediction of : memory and cognition disorders, mood disorders (including suicide ideation and behaviour) during R&D phases
 - Build/refine tools: systems biology, iPSCs, rodents, dogs, primates...

Scope and objectives of the workpackages (2/3)

- WP3: Peripheral neuropathies
 - Better detect risk of peripheral neuropathy in drug candidates; identify biomarkers for translation to humans*
 - Improve/refine tools: iPSCs-derived neurons, functional and histopathological endpoints
 - Propose biomarkers: rats, dogs, primates

* Biomarkers for central neurotoxicity will be covered by TransBioLine topic

Scope and objectives of the workpackages (3/3)

- WP4: Data and samples management
 - Implement processes for handling and sharing data and samples
- WP5: Consortium coordination and communication
 - Monitor deliverables, budget, timelines, quality, legal aspects, contracts, ethics...
 - Internal and external communication (esp. on 3Rs)

Expected contributions of the applicants (1/2)

- Academics, Research organizations, Universities, etc
 - Scientific input on: physiopathology of neurotoxicity, targets, biological pathways (systems biology/toxicology), physicochemical parameters correlating to Blood-Brain-Barrier, biomarkers of neuropathies, (Q)SAR
- SMEs
 - Innovative assays/techniques: stem cells, organs-on-chip, subcellular systems, MicroElectrode Array, video-monitoring, live brain imaging...
 - Data and samples management, data mining, biostatistics
 - Honest-broker for data sharing and ensure confidentiality
 - Consortium coordination and communication

Expected contributions of the applicants (2/2)

- Patient organizations, clinicians
 - Help focusing on indications, pathologies, therapeutics with highest needs
- Regulatory Bodies
 - Guide on possible implementation in guidelines
 - Advice on eg scientific contents, strategy, validation or qualification (animal models, assays, biomarkers, etc)

Expected (in kind) contributions of industry consortium

- Provide historical control data from already performed in vitro assays and in vivo studies (zebrafish, rats, mice, dogs, primates)
- Provide pharmacovigilance data
- Supply reference and in-house “neurotoxic” compounds
- Perform *in vitro* assays
 - Electrophysiology, calcium oscillation in neurons, brain slices, MEA, nerve conduction, nerve fiber density, expression profiling, neurite dynamics/morphology
 - Any other new assay or endpoint
- Perform *in vivo* studies
 - Already available: EEG, FOB, actimetry, video-monitoring, pathological models
 - Any other new endpoint or technique (eg imaging, automated detection of convulsions...)
- Develop analytical methods to measure safety biomarkers
- PK/PD/TD modeling and simulation

What's in it for you?

- Opportunity to work with Pharma Companies in a mindset based on trust and collaboration
 - Precompetitive nature, guidelines and methodologies for data sharing
- Win-win situation: multistakeholder effort for sharing different approaches, skills and processes
- Translate academic research into deliverables for R&D and ultimately for patients
- Leverage research speed and deliverables through EU funding, allowing to think bigger

Key deliverables of the full project

1. New/improved *in silico* tool(s)
2. Understanding Blood-Brain-Barrier passage and exposure of target structures
3. New/improved *in vitro* assay(s)
4. New mechanistic tools
5. Improved animal model(s)
6. Decision point to select best animal species
7. Identification of safety biomarker(s) for peripheral neuropathies
8. Integration of tools into a single platform
9. Impact on 3Rs

Synergies with other consortia/initiatives, if relevant

- FP7-HEALTH projects PREDICT-IV and NEUROBID
- HESI Committee on Translational Biomarkers of Neurotoxicity (NeuTox)
- NC3Rs Crack-It challenge Neuratect
- IQ Consortium on Preclinical Suicidality and MicroPhysiological Systems
- Ongoing IMI initiatives: TransQST, EBiSC,
- Upcoming IMI initiatives: TransBioLine, Discovery and characterisation of Blood-Brain-Barrier targets

Involvement of SMEs, patient groups, regulators

SME participation

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

The contribution of SMEs could be beneficial for the following activities:

- propose innovative assays/techniques for detection of neurotoxic effects: stem cells, organs-on-chip, subcellular systems (synaptosomes, mitochondria), micro-electrode array (MEA) technology, blood-brain barrier assay (optionally: combined with MEA, in order to correlate brain passage and neurotoxicity), continuous video monitoring in rodents and non-rodents, live-brain imaging of neuronal activity;
- run prospective assays/studies with reference drugs;
- data and samples management:
- data management: data access and data cleaning expertise,
- biostatistics/programming: data analysis and programming expertise;
- coordination and communication:
- ensuring the implementation of the coordinating tasks and running the day-to-day operation, such as project tracking and reporting, meetings, internal communication, budget management, etc.
- ensuring the communication and dissemination with and/or media expertise and in developing tools.

Patient participation

- Patient associations could join as partners, especially in the field of therapeutics indications where adverse effects on nervous system could be viewed as more frequent (psychiatry, oncology, neurology, immunology) as well as providing access to disease-specific donor material for *in-vitro* (primarily induced pluripotent stem cells ((iPSC)-related) work.
- The patient organisations and clinicians could potentially identify indications, pathologies, treatments for which neurotoxicity is a more critical issue.

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

Regulators

- A joint public-private project engaging key stakeholders' expertise could provide clinicians and regulatory bodies with robust data for possible evolutions in the regulatory field. As appropriate, these potential partners will be asked to contribute, e.g. through participation to the advisory board.
- The regulatory bodies could give feedback on tools, strategies, biomarkers that are proposed and their possible implementation in official guidelines (e.g. through qualification advice for biomarkers).



Questions

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**

infodesk@imi.europa.eu