Webinar | IMI2 – Call 13
Translational safety biomarker pipeline (TRANSBIOLINE): enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease

4 December 2017 • 15:00 CET

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Isabella Tamagnini, IMI
- The Call topic – Jiri Aubrecht, Pfizer
- Involvement of SMEs, patients and regulators - Isabella Tamagnini, IMI
- Questions & answers

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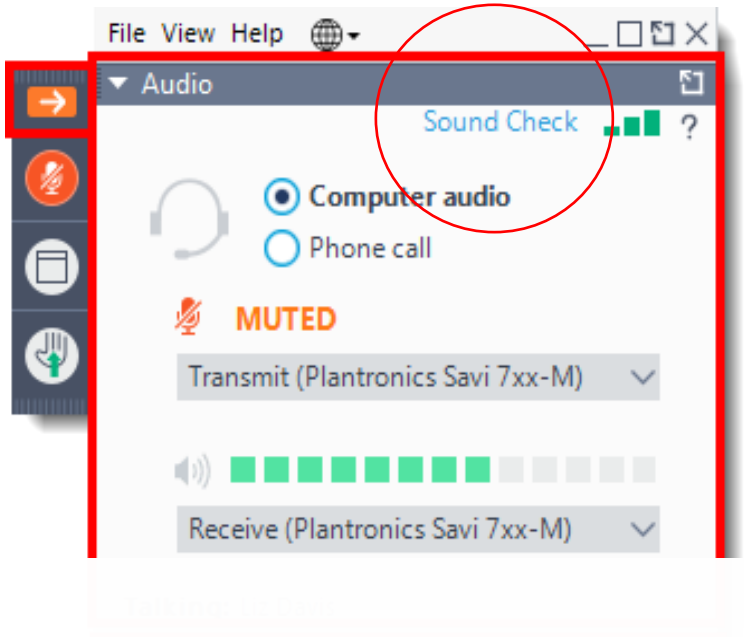

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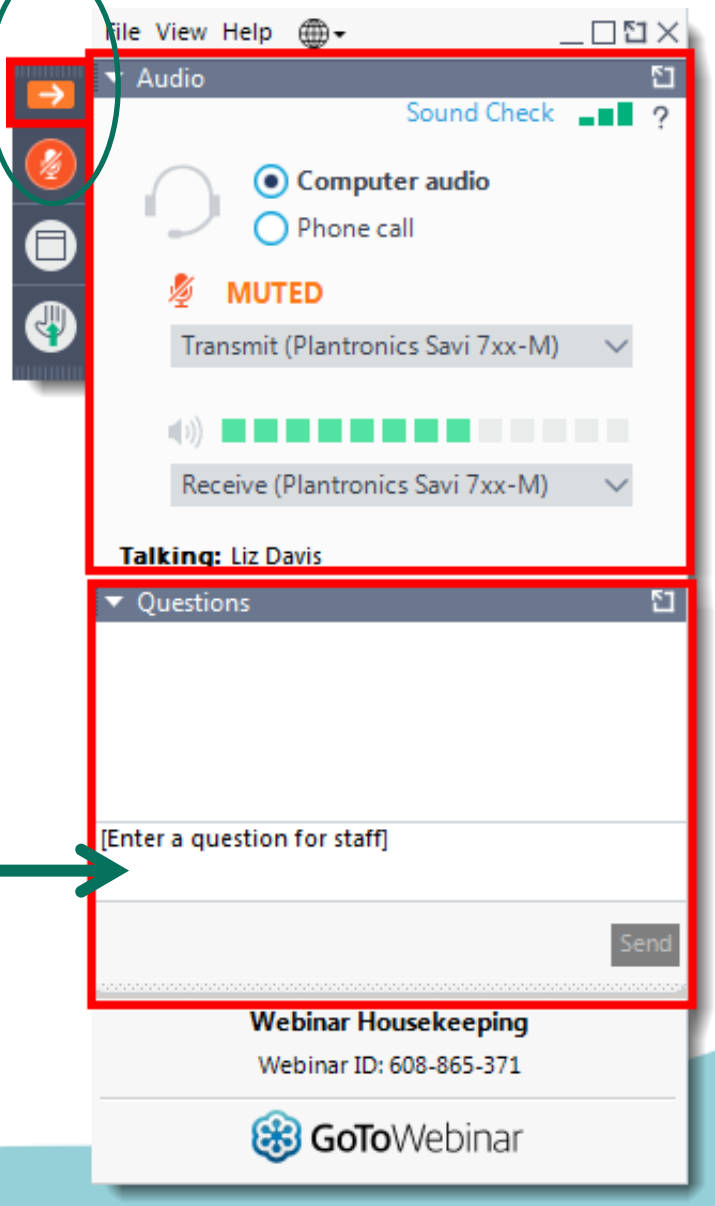

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Before we start…

- 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

Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease

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 will take place on Thursday 7 December, 15:00-16:30

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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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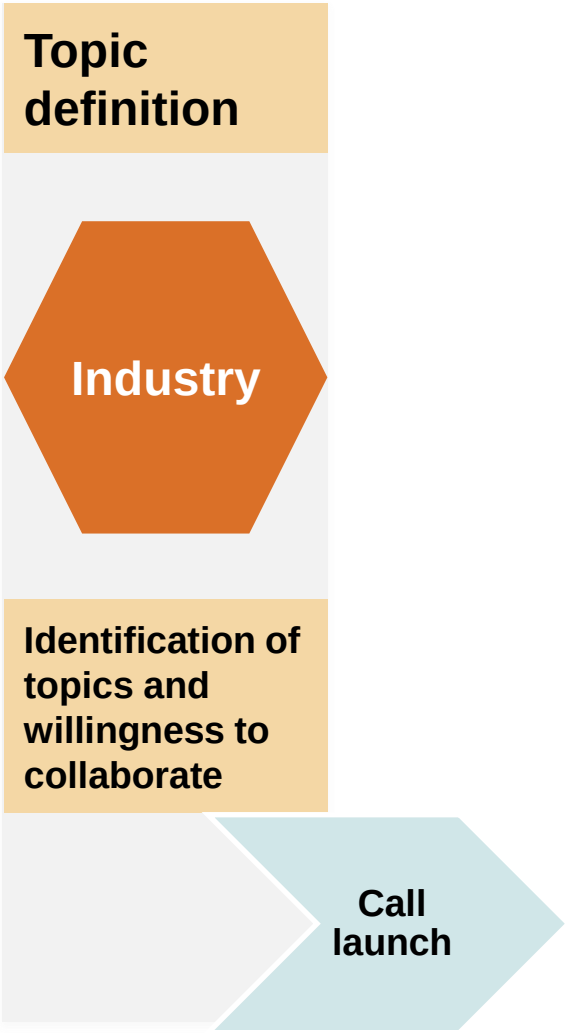
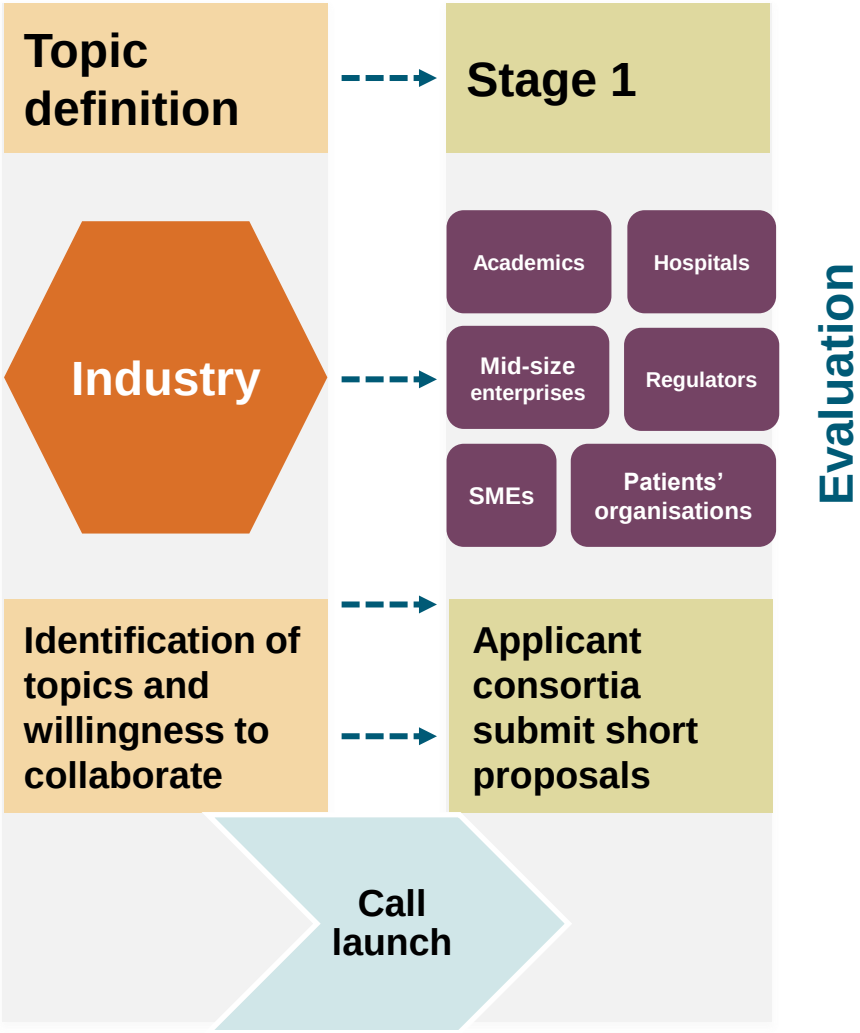
Typical IMI project life cycle



Typical IMI project life cycle



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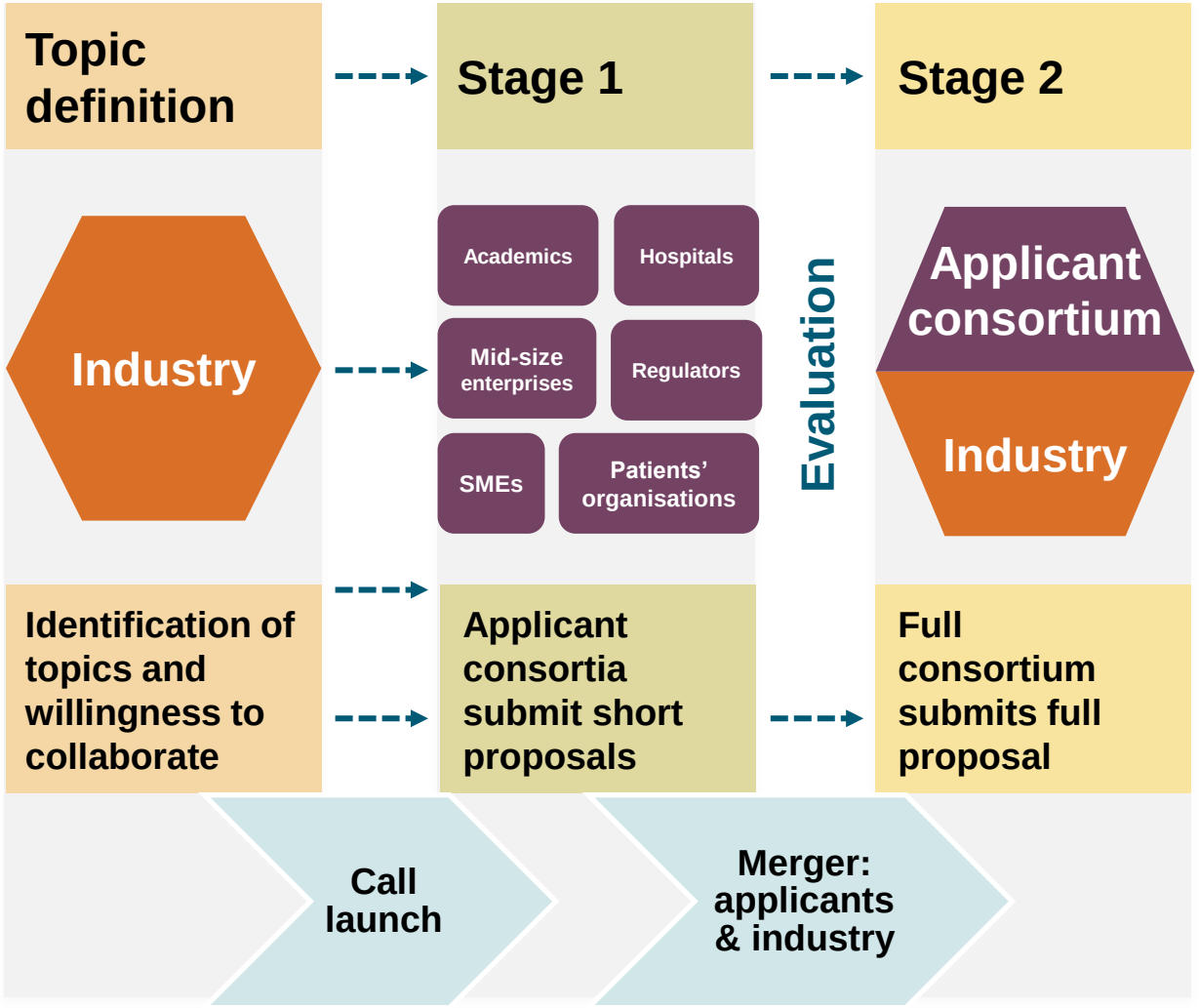
Typical IMI project life cycle



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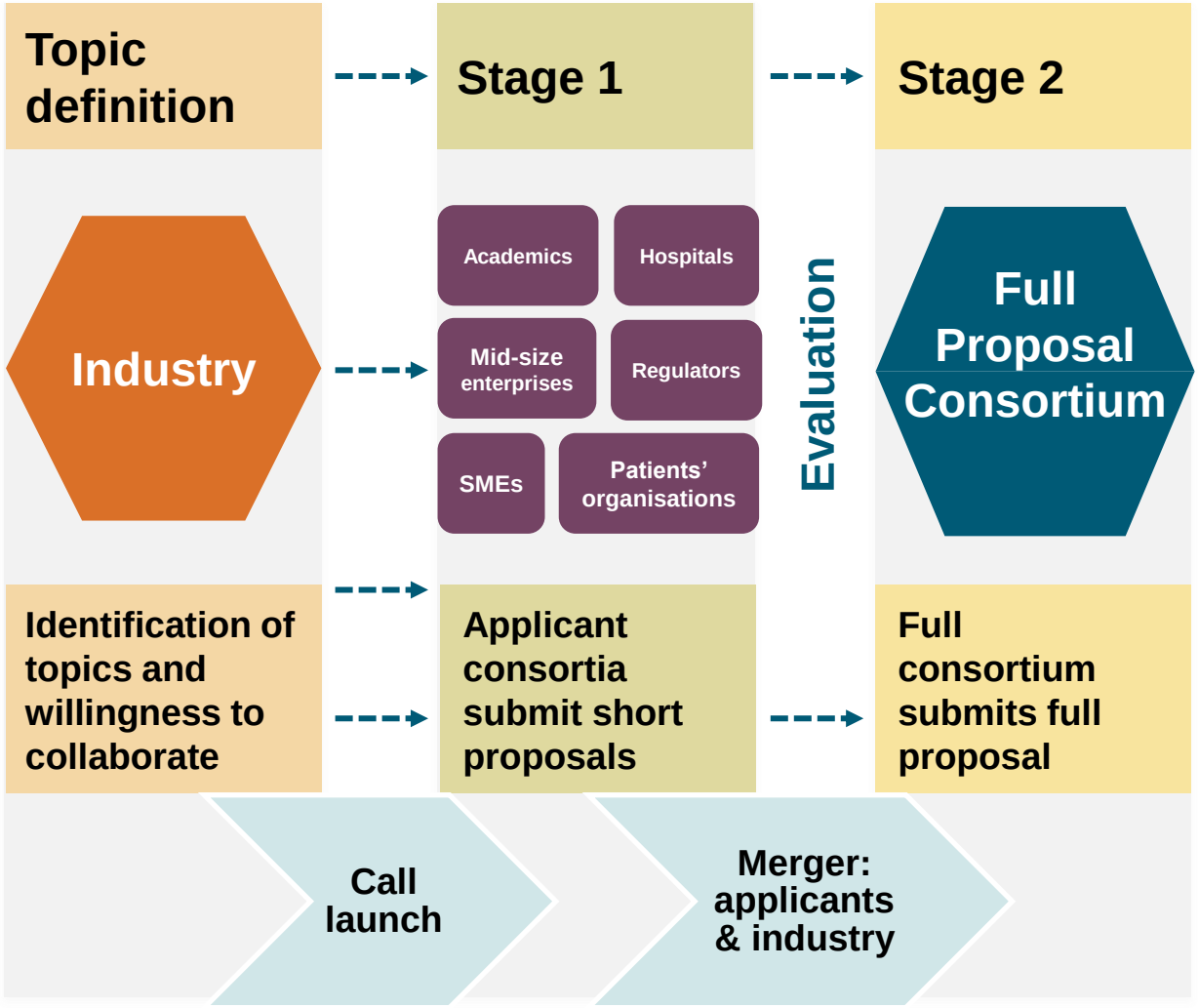
Typical IMI project life cycle



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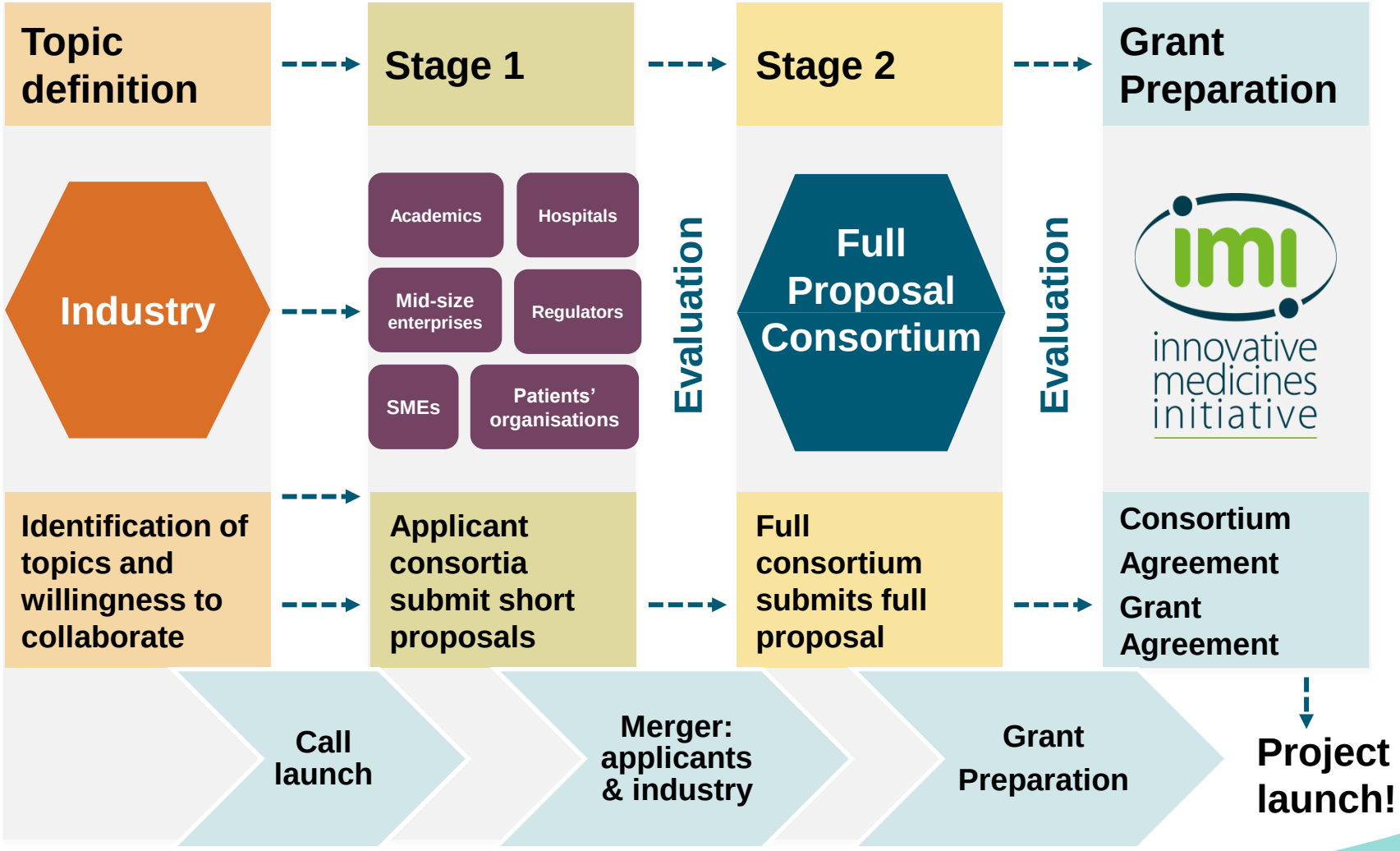
Typical IMI project life cycle



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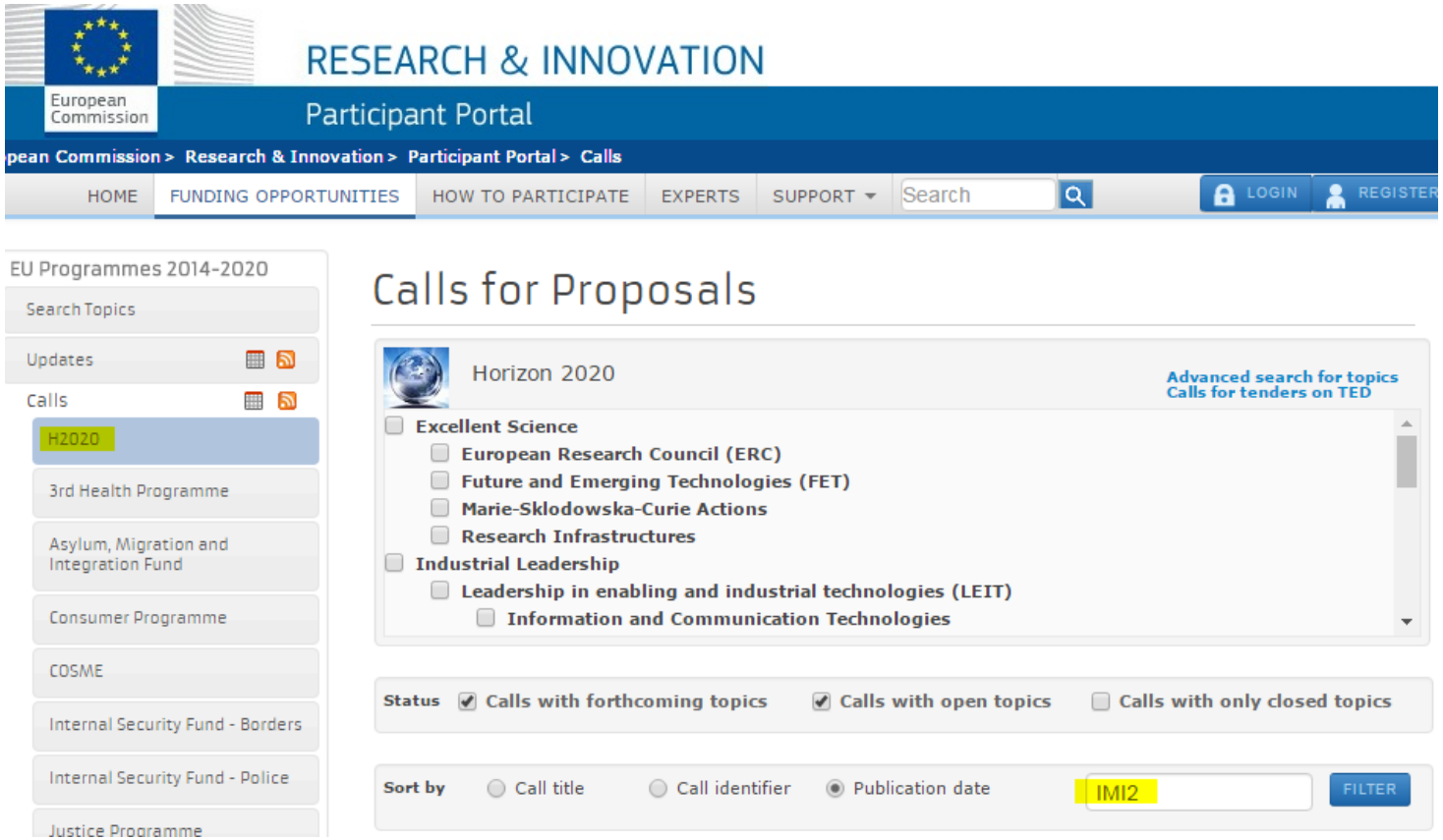
Submitting a proposal

- 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

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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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TransBioLine

Enabling implementation of novel safety biomarkers in clinical trials and diagnosis of disease

Jiri Aubrecht, PharmD, PhD

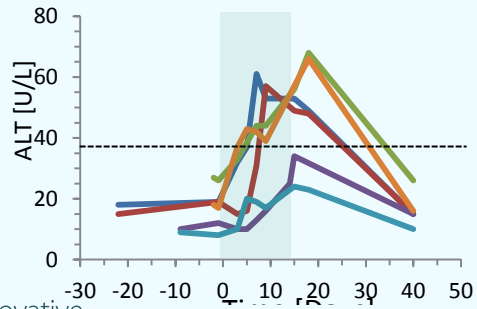
03.12.2017 • IMI webinar

Need for public-private collaboration

- Limited capability to assess **the relevance of isolated safety biomarker changes** in clinic
- Lack of biomarkers for assessing **human relevance of preclinical findings**
- Standard safety biomarkers detect injury but lack **mechanistic** Lack of **sensitive and specific translational biomarkers**
- **Lack of acceptance by regulatory agencies**
- **Improve diagnosis of disease**

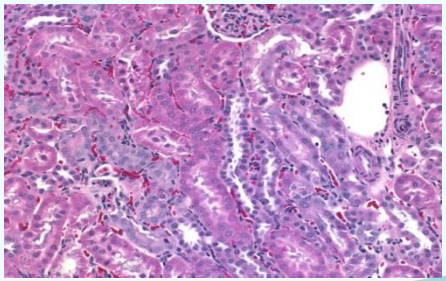
Liver

What is the significance of small increases of ALT? Will subject recover or progress?



Kidney

Drug in clinic and kidney lesion seen in only sub-chronic non-rodent study with no increase of sCr



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Objectives of the full project

- Enable implementation of emerging safety biomarkers in clinical trials and/or diagnosis of disease
  - Liver, kidney, pancreas, vascular, CNS
- Develop non-invasive mechanistic biomarkers of tissue damage (“liquid biopsy”)with potential to revolutionize drug development and diagnosis of disease
- Develop and standardize assays and technologies for detection of biomarker responses
- Achieve regulatory acceptance of novel biomarkers

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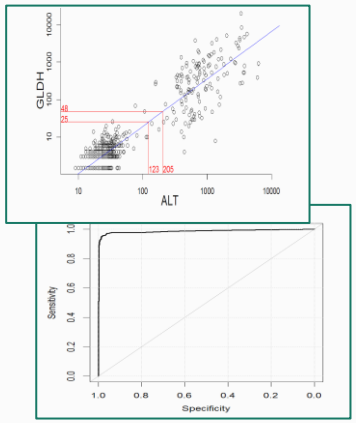
Summary of objectives

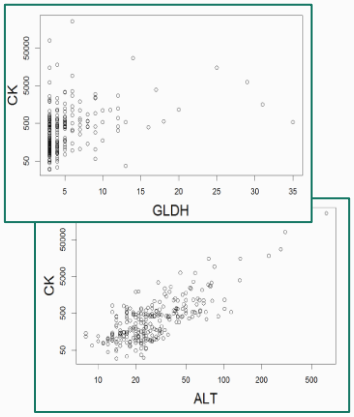
Goal	Emphasis	Approach	Impact
1) Enable implementation of safety biomarkers	• Value added CoUs • Emerging biomarkers for kidney, liver, pancreas, vascular and muscle • Develop large datasets for qualification	• Prospective studies with retained samples from clinical practice and clinical trials • Available data sets • Focused prospective trials • Focused non-clinical studies	• Fast adoption of emerging biomarkers in clinical trials and diagnosis of disease • Accepted by regulators under IND
2) Develop non-invasive mechanistic biomarkers	• Liquid biopsy approach • Integrate systems biology • Mechanisms of toxicity and disease		• New innovative non-invasive approach and capabilities for drug development and diagnosis of disease
3) Develop Assays/Diagnostic	• Evidentiary standards • Establish SMEs for service	• LDT • IVD • Evidentiary standards	• Better diagnostics • Key enablement for biomarker implementation
4) Achieve regulatory acceptance	• Qualification submissions • Develop and nurture scientific interactions with regulatory agencies	• EMA/FDA/PMDA • Evidentiary standards	• Enables using biomarker for decision making • Formal qualification

Prospective studies with retained samples from clinical practice and clinical trials

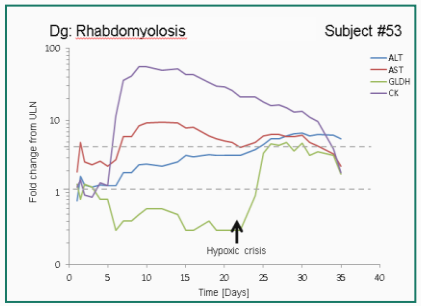
1. **GLDH performance for liver injury**
   750 subjects - healthy and liver diseases



2. **GLDH liver specificity**
   220 subjects healthy and muscle diseases



3. **GLDH detects onset of liver injury in subject with muscle injury**



4. GLDH differentiate muscle injury in subjects treated with statins (study with 3400 subjects)

TOXICOLOGICAL SCIENCES 132(2), 276–283 2013
doi:10.1093/toxsci/kft009
Advance Access publication January 20, 2013

Assessment of Emerging Biomarkers of Liver Injury in Human Subjects

Shelli Schomaker,* Roscoe Warner,† Jeff Bock,* Kent Johnson,† David Potter,* Joyce Van Winkle,‡ and Jiri Aubrecht*,1

Drug Safety R&D, Pfizer Inc., Groton, Connecticut; †Department of Pathology, University of Michigan Medical School, Ann Arbor, Michigan; and ‡Clinical Research Unit, Pfizer Inc., New Haven, Connecticut

- GLDH applied for monitoring of liver safety in development of treatments of MDs
- Partnering with medical community and patient advocates to bring GLDH to medical practice

Pre-competitive nature

Partnership of industry, academia and regulatory agencies

SCIENCE TRANSLATIONAL MEDICINE | PERSPECTIVE 22 November 2017

REGULATORY SCIENCE

What evidence do we need for biomarker qualification?

Chris Leptak,[1]* Joseph P. Menetski,[2]* John A. Wagner,[3]* Jiri Aubrecht,[4] Linda Brady,[5] Martha Brumfield,[6] William W. Chin,[7] Steve Hoffmann,[2] Gary Kelloff,[8] Gabriela Lavezzari,[9] Rajesh Ranganathan,[10] John-Michael Sauer,[6] Frank D. Sistare,[11] Tanja Zabka,[12] David Wholley[2†]

Biomarkers can facilitate all aspects of the drug development process. However, biomarker qualification—the use of a biomarker that is accepted by the U.S. Food and Drug Administration—needs a clear, predictable process. We describe a multistakeholder effort including government, industry, and academia that proposes a framework for defining the amount of evidence needed for biomarker qualification. This framework is intended for broad applications across multiple biomarker categories and uses.

Expected impact

- Enable application of novel biomarkers in clinical trials
  - Facilitate drug development by bringing therapies to patients faster and more effectively
  - Precision medicine
- Develop new tools to diagnose diseases
  - Patient advocates
- Develop approaches for regulatory acceptance of biomarkers
  - Partnership among academia, industry and regulatory agencies
- Opportunities for SMEs to commercialize assays and open new markets

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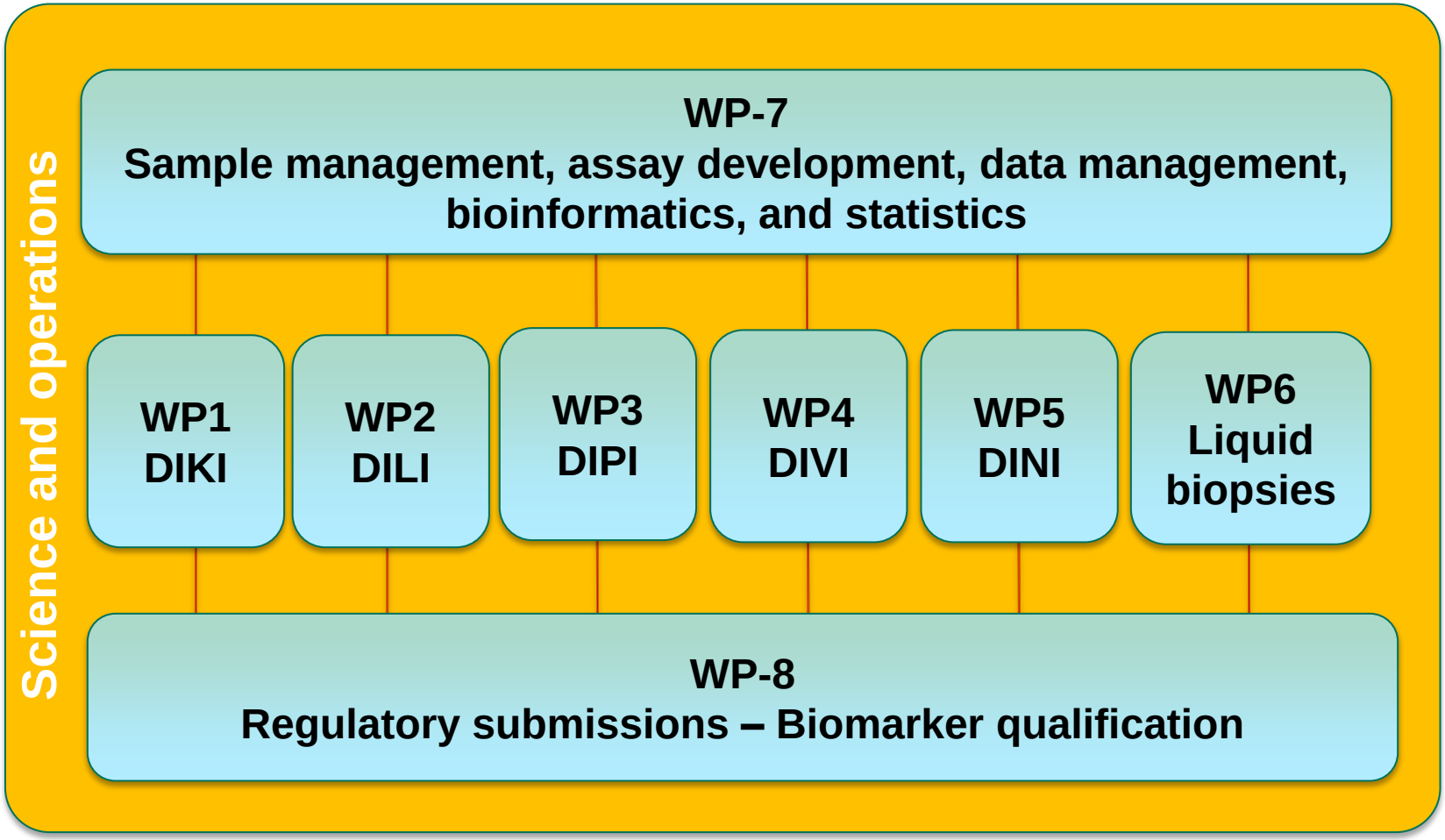
Suggested architecture of the project



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Expected contributions of the applicants

- Sample collections
  - Capability to identify, retain and manage remaining serum, CSF and urine samples from healthy subjects and subjects with relevant disease phenotypes, including a broad range of etiologies and/or treated with a variety of therapeutic modalities as specified by individual WPs.

  - Capability to obtain appropriate patient consent forms, access detailed medical records data for all subjects/samples, and adjudicate the data.

Expected contributions of the applicants

- Analytical technologies 1-6
  - Expertise in pertinent biomarker assay technologies needed to conduct TransBioLine research
  - Analytical capabilities such as immunoassays, LC-MS, biochemical, clin chem etc.

- Molecular technologies and informatics (liquid biopsies)
  - Expertise in analysis and normalization of circulating miRs in human subjects using next generation sequencing and state-of-the-art bioinformatics with expertise in generating signatures of circulating miRs for specific disease phenotypes and/or toxicities in human subjects.
  - NextGen sequencing, state-of the art bioinformatics

Expected contributions of the applicants

- Regulatory science
  - Expertise in regulatory science, biomarker qualifications including preparation of regulatory submissions to regulatory agencies (EMA and/or FDA), and interactions with regulatory agencies world-wide.
- Laboratory information systems and management
  - Expertise and capabilities in sample management systems, patient compliance statements, data management including database systems that comply with managing clinical data, state-of-the-art statistical and bioinformatics tools including tolls for next generation sequencing data.
  - Proven expertise in efficiently managing and maintaining time lines for large, multi-institutional scientific projects and proven expertise in project management.

Expected (in kind) contributions of industry consortium

- Sample collections
  - Samples from healthy volunteers, disease populations in clinical trials
  - Samples from subjects with drug induced organ injuries
  - Samples from different populations
- Assay technologies
  - Expertise in assay validation as LDT and IVD
  - Assay conduct
- Study conduct
  - Nonclinical study conduct under GLP
  - Conduct of clinical studies if required (food effect etc)

Expected (in kind) contributions of industry consortium

- Clinical science
  - Adjudication of cases of organ injury
- Regulatory science
  - Expertise in biomarker qualification, evidentiary standards
  - Interaction with regulatory agencies EMA, FDA, PMDA
  - Expertise in filing regulatory documenters
- LIMS and management
  - Expertise in management of samples and compliance

Key deliverables of the full project

- Short term (1 year)
  - Validated standardized biomarker assay platforms
  - Annual biomarker qualification workshops with regulatory agencies
- Medium term (2-4 years)
  - Evaluation of biomarker performance WP1-WP5
  - Enabling application of emerging biomarkers for specific drug development programs in case by case basis via IND
- Longer term (4-5 years)
  - Biomarker qualification submissions and qualification decisions
  - Liquid biopsy approach implementation

What's in it for you?

- Excellent opportunity to make impact on drug development and patient care
- Unique opportunity for partnership among scientists from industry academia and regulatory agencies
- Developing state-of-the art science and technologies
- Publications in prestigious peer review journals
- SME will have opportunity to commercialize assay technologies, open new markets
- Patient advocates will have opportunity to facilitate adoption of new biomarkers in medical practice, identify new contexts of use, improving medical care
- Industry will have access to new biomarkers that facilitate drug development bringing therapies to patients faster and more effectively

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Thank you

www.imi.europa.eu
@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 areas that include:

- diagnostic assay development
- bioinformatic analysis
- data mining
- data and sample management
- etc.

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Patient participation

IMI 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.

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

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

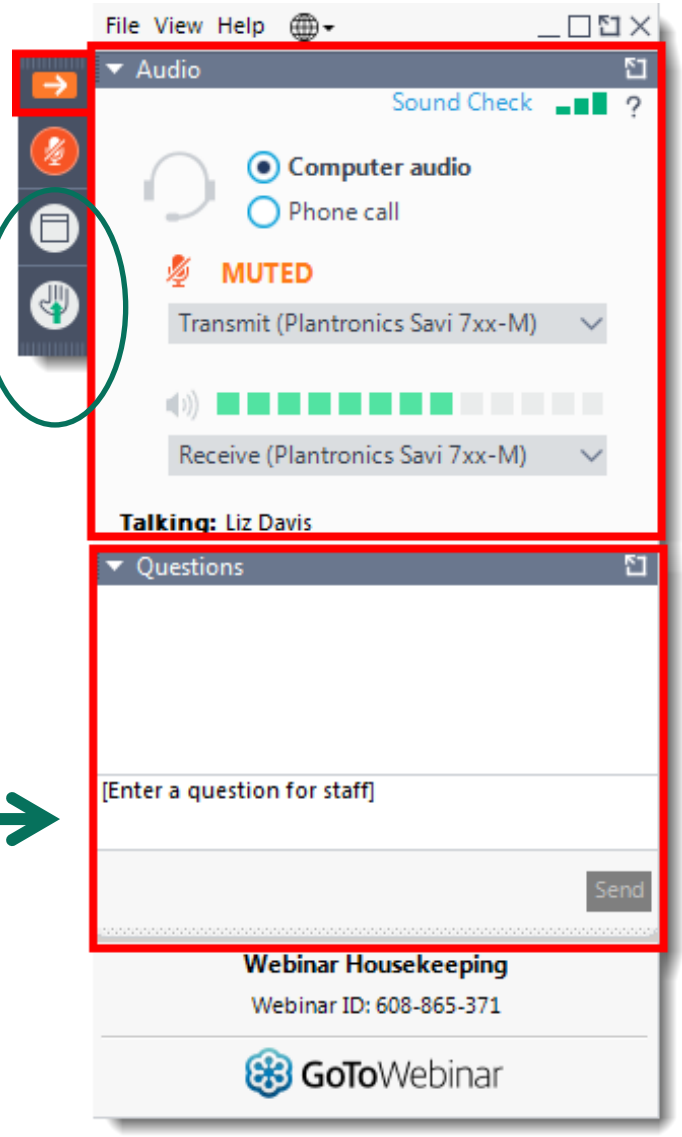
More info: 'Raising awareness of regulatory requirements: A guidance tool for researchers'

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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