

# Webinar | IMI2 - Call 7 'Validation of translational imaging methods in drug safety assessment (TRISTAN)'

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# Need for public-private collaboration

- Leverage the potential of available imaging techniques in order to improve drug safety analysis and translatability of findings from animals to humans by validating imaging procedures as biomarkers.
- Initiate a novel collaborative framework for standardization and validation of non-invasive diagnostic imaging methods and procedures by combining expertise from imaging vendors, pharma industry and academic groups in the fields of DMPK, drug safety, toxicology, imaging, software solutions and medical excellence
- Opportunity to promote the translatability of pre-clinical toxicological results to humans and improve patient monitoring in early clinical trials

# Objectives of the full project

- 1. Liver Transporter Assessment** by means of dynamic Gadoxetate enhanced MRI to assess Mrp2 / OATP function in animals and in humans. Additional imaging approaches are welcome. Create a validated tool for translational liver toxicity and toxicity mechanism assessment.
- 2. Pulmonary Toxicity Assessment** by establishing and validating imaging biomarker procedures to assess, characterize and quantify the extent of interstitial lung disease in order to introduce a tool for translational lung toxicity evaluation
- 3. Bio-distribution of Biologicals** by developing and utilizing invasive and non-invasive imaging methods to assess distribution of biologicals, locally and systemically, with the aim to improve efficacy and translatability of preclinical safety assessment.

# Objectives of the full project

- 4. Standardization** and validation of image acquisition procedures, image evaluation procedures and result reporting, in order to establish the imaging approaches as powerful medical assays/tools
- 5. Translation** and verification of the additional value of non-invasive imaging methods in longitudinal studies with individuals serving as their own controls as well as verification of translatability of pre-clinical results in clinical studies with few volunteers or vice versa

# Pre-competitive nature

- Improve the quality of pre-clinical data and the possibility for improved patient monitoring in early clinical trials.
- Advance safety evaluation through a better understanding of longitudinal profiles associated with mechanisms of toxicity
- Support technical advances, better standardization across imaging community to ensure protocols, biomarkers, analysis and data interpretation are well recognized and equivalent.
- Provide a basis for improved acceptance of imaging technologies and imaging biomarkers by healthcare authorities and regulators.

# Expected impact on the R&D process

- Appropriate imaging procedures used as imaging biomarkers have a strong potential to improve translatability of pre-clinical results to healthy volunteers and patients
- They help to avoid late stage attrition of development programs
- Opportunity of confirming drug toxicity mechanisms in humans, including the potential for determining drug-drug interactions
- Tracking drug molecules longitudinally by means of imaging includes the potential to reduce animal numbers in pre-clinical studies. Hence the work in this program strongly supports the 3R principle (refinement, reduction, replacement) in substantially reducing the number of animals needed in pre-clinical research

# Suggested architecture of the project

WP 1: Project Coordination

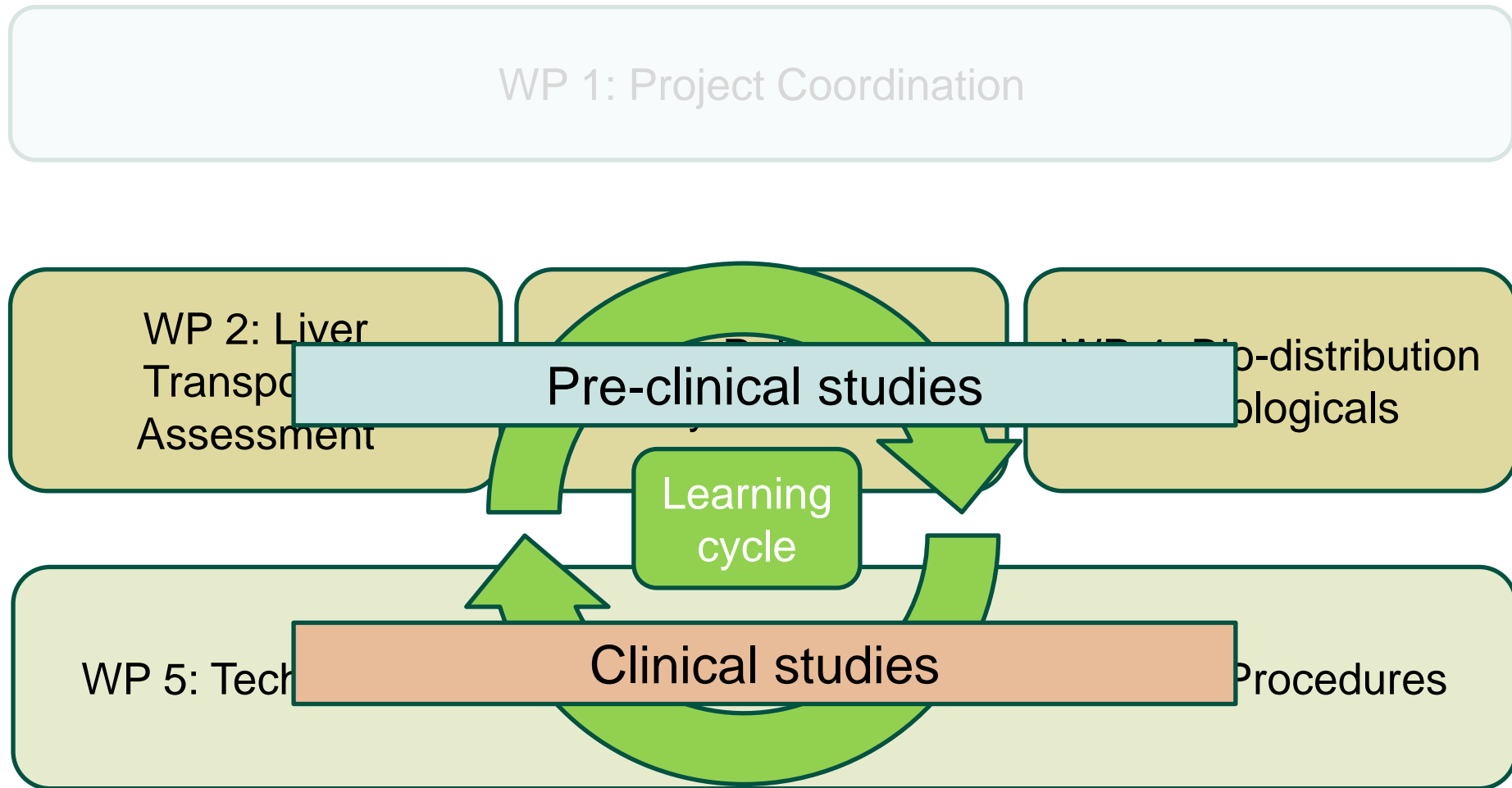
WP 2: Liver  
Transporter  
Assessment

WP 3: Pulmonary  
Toxicity Assessment

WP 4: Bio-distribution  
of Biologicals

WP 5: Technical Standardization and Validation of Imaging Procedures

# Suggested architecture of the project





# Expected contributions of the applicants

- Contribution with relevant animal models and imaging expertise at multiple sites
- Competency in biochemical and biological validation of imaging results
- Expertise in pharmacokinetic modelling of imaging data
- Experience in setting up data evaluation tools for concerted evaluation of different types and formats of data incl. storage and exchange
- Expertise in translating pre-clinical and clinical imaging research demands into standardized, work-flow oriented tools
- Expertise in tracer or contrast agent design and medicinal chemistry
- Radiochemistry expertise and infrastructure for synthesis and use of required PET tracers for pre-clinical and clinical use
- Experience in conducting clinical imaging studies

# Expected (in kind) contributions of EFPIA members

- Key expertise and pre-clinical data to shaping precise needs for standardization and workflow organization
- Contribution of non-clinical data and expertise:
  - Pre-clinical imaging (MRI & CT) and contrast agents
  - Relevant biologics as tool compounds, biochemical and biological analytics
  - Imaging technology validation
  - Image acquisition and analysis including multi-modality approaches, image co-registration, workflow optimization, PK modelling, consulting for hyperpolarization techniques
  - Support in radiochemistry and PET-tracer development
- Consulting for clinical trial set-up and conduct

# What's in it for you?

- Academic researchers:
  - Access to industry resources and safety assessment expertise
  - Access to imaging compounds and tool drug compounds
  - Cooperative advancing of diagnostic imaging application in drug safety assessment
- Regulatory scientists:
  - New proof-of-concept data for improved safety evaluation and patient monitoring
- SMEs:
  - A forum to contribute to standardization of imaging procedures incl. image evaluation, work-flow organization and reporting
- Patients' organisations - improved efficacy in advancing safe therapies

# Key deliverables of the full project

- Validated *translational* imaging methods or procedures (e.i. biomarkers) that have the capability to refine safety assessment and/or toxicological mechanistic hypothesis.

## 1. Liver:

- Provide a database of existing human data of various compounds on transporter function and match to generated imaging data
- Imaging method(s) that allows to assess liver transporter function in longitudinal studies in animals and humans and is validated against biochemical function assessment

# Key deliverables of the full project

## 2. Lung:

- Provide a comprehensive library of imaging biomarkers that represent the breadth of lung disease from early stage through to the chronic condition.
- Imaging technologies exploited to further our understanding of disease and toxicity identification and mechanism in the lung
- Determine biomarkers of disease and toxicity that would lend themselves to the development novel “smart” contrast agents; target cell surface markers to determine the inflammatory/fibrotic/cell involvement/etc condition of disease or of toxicity.

# Key deliverables of the full project

## 3. Bio-distribution:

- Support dose finding and drug response monitoring by assessment of bio-distribution
- For s. c. application, improve understanding on pain on injection, bio-distribution, correlation of local to plasma levels, (sub-/extra-) cellular distribution, degradation, ADA formation

## 4. Standardization and Translation:

- Standardized image acquisition, image evaluation, reporting and respective tools
- Verify the additional value of non-invasive imaging methods in longitudinal studies; verify translatability of pre-clinical results in clinical studies with few volunteers

## Questions?

Contact the IMI Programme Office  
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