Interreg North-West Europe
Co-funded by the European Union
STEP4NAMs

APPLY

Challenge-based SME support

#10 Immune competent perfusable human Liver on Chip to quantify therapeutic antibody–small molecule DDIs driven by cytokine modulation (IL 6 axis + extensions)

EXPECTED DELIVERABLE

Indicative duration: 6 – 9 months

Develop and qualify a 3D perfusable human liver co culture chip (perfused 3D hepatocytes + Kupffer cells + one peripheral immune component (e.g., PBMCs)) that maintains hepatic function long enough to assess pre/post cytokine modulation and quantify antibody–small molecule DDIs (drug–biologic interactions) via cytokine mediated CYP regulation, including readout of inflammatory signaling (cytokine release/acute phase response).

Augment the liver chip with immune system functionality sufficient to evaluate cytokine release scenarios relevant to biologics (e.g., immune activation/CRS-like cytokine bursts) and determine the downstream impact on hepatic drug metabolism and transport.

- Platform description
- Cell sourcing & characterization
- Baseline liver functionality dataset (≥14 days): Albumin, urea (optional), LDH/ALT/AST (optional), morphology/viability imaging, CYP3A4 activity longitudinal readout (and optional other CYPs)
- Inflammation response" dataset (e.g. IL 6) : IL 6 doses response with CYP3A4 suppression, CRP and other IL 6 response markers
- Antibody reversal" DDI dataset (tocilizumab benchmark): Two phase design: IL 6 suppression then tocilizumab de suppression, Small-molecule substrate kinetics (e.g., simvastatin hydroxy acid) with exposure/clearance metrics, Evidence the directionality matches published clinical logic (qualitatively at minimum)
- Cytokine release / immune activation dataset: Cytokine panel time course (IL 6, TNF α, IL 1β, IFN γ minimum suggested), Link to CYP activity changes and recovery, Controls showing specificity (negative controls, vehicle, non-activating antibody)
- Device binding/adsorption report: Recovery of small representative molecules and antibodies through the chip, Stability in tubing/reservoirs, nonspecific loss estimates, Mitigation strategy (surface treatment, alternate plastics, pre-conditioning)
- Reproducibility & robustness (fit for purpose qualification)

LONG-TERM COLLABORATION POTENTIAL

Subject to scientific and strategic alignment

Yes. If the benchmark and reproducibility gates are met, potential long-term collaboration may include:

- Expansion to additional cytokine axes (IL 23/IL 1/IFN γ) and transporter endpoints
- Use in internal DDI risk assessment workflows for therapeutic proteins (supporting regulatory aligned packages)

CANDIDATE SELECTION

Initial eligibility check by MPR. Final selection by the challenge provider based on fir, relevance, readiness and innovation potential

Minimum required Technology Readiness Level (TRL)

- Working prototypes demonstrated in the laboratory and validated in a relevant environment.
- Demonstrated experience with perfused microphysiological systems / organ on chip and long-term culture
- Ability to run primary human hepatocytes and at least one immune component (Kupffer cells minimum)
- Quantitative bioanalysis: LC MS/MS (in house or via partner) for substrate kinetics and immunoassays (ELISA/Luminex) for cytokines/CRP
- Quality mindset: SOPs, QC checkpoints, documented variability targets (fit for purpose reproducibility).
- Clear experimental plan that reproduces cytokine release scenarios relevant to biologics and determine the downstream impact on hepatic drug metabolism and includes controls.
- Strategy to address donor variability (≥2 donors, or justification and risk mitigation), HLA matching liver cells and peripheral immune cells.

Additional selection criteria

- > 50 employees preferred, sufficient staffing to deliver (typical expectation: dedicated project lead + cell culture + bioanalysis + data/modelling)

Completion of EDUCATE	Core Module
Company status	SME under EU criteria
Maximum number of supported companies	1 – 2
Confidentiality: NDA/ CDA required	Likely required
Geographic area	SME from across EU are welcome. SMEs from Interreg NEW are prioritized, particularly partner regions

APPLICATION

Directly via the STEP4NAMs Moodle platform

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SUPPORT

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