

CN-BIO

Organ-on-a-chip contract research services

Rapid access to organ-on-a-chip,
powered by **PhysioMimix®** and
the expertise of our team!



visit cn-bio.com



About us

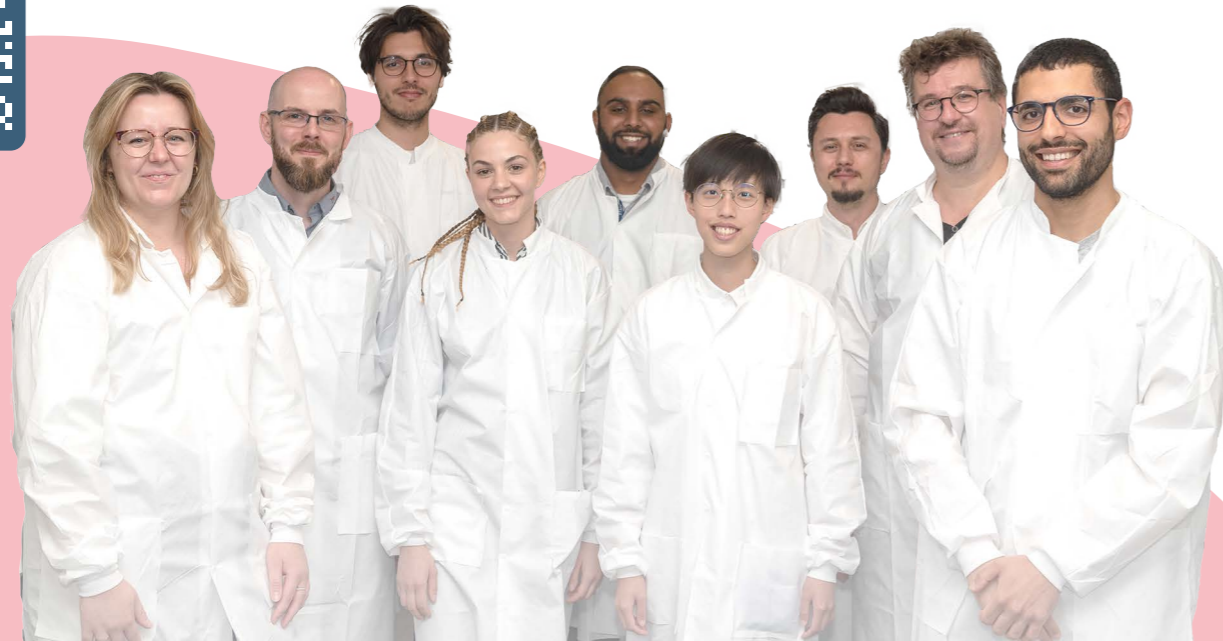
We are a passionate and creative thinking team, working together towards our shared goal – a future where drugs are discovered faster, brought to patients more cost-effectively, and through the use of less animal experimentation.

CN Bio's PhysioMimix® Organ-on-a-chip (OOC) range recreates human tissues and organs in the lab, enabling researchers to perform rapid, tissue-based studies that more accurately predict human responses to drugs.

Our technology bridges the gap between traditional *in vitro* methods, like cell culture, and *in vivo* studies to help you develop safe and efficacious therapeutics, faster and more cost effectively than ever before.

Access the technology and CN Bio's expertise through our Organ-on-a-chip Contract Research Services.

Learn more at cn-bio.com/in-vitro-services



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Enrich decision making with advanced *in vitro* organ-on-a-chip models that offer the highest physiological relevance and rapid access to human-relevant data.

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Services overview

We offer advanced *in vitro* studies to screen your therapeutic candidates, investigate mechanisms of action, and fast-track clinical trial design

Our services are ideal for for customers who:

- 1 wish to benefit from the insights of Organ-on-a-chip (OOC) without investing in equipment or developing in-house expertise.
- 2 require a rapid turnaround, when there is a time pressure (such as with a clinical asset).
- 3 want to predict human outcomes for human-specific targeting drugs that lack suitable *in vivo* models.

We have over a decade's experience in the field to ensure you get answers quickly and cost-effectively.

Our objective is to rapidly answer your most urgent and unanswered questions so that you can make data-driven decisions that improve your chance of clinical success.

Our team will work collaboratively to design a bespoke study that matches your research goals. A dedicated project lead will remain in close communication and provide regular updates throughout the duration of your study, and **deliver actionable data within weeks.**

Studies are performed using the PhysioMimix® OOC range of microphysiological systems, which provide large scale tissue and media volumes to obtain high content multi-omics and microscopy data.

- Endpoint assays from our in-house menu
- Sample delivery back to you for further profiling
- Transfer of samples to specialist analytical service providers

The technology

Studies are performed using PhysioMimix® OOC

We co-culture physiologically-relevant combinations of primary human cells under perfused conditions to form healthy or diseased single- and multi-organ microtissues that recapitulate the key pathophysiology, phenotypes and functions of human organs *in vitro*.

Our complex organ models accurately predict human drug responses and remain functional for up to one month, enabling both acute and chronic dosing studies that improve the translatability of data between the laboratory and the clinic.

The technology underpins our *in vitro* NAFLD¹/NASH (also known as MAFLD²/MASH³), DILI and ADME⁴ Services.

- 1 Non-alcoholic fatty liver disease
- 2 Metabolic dysfunction-associated fatty liver disease
- 3 Metabolic dysfunction-associated steatohepatitis
- 4 absorption, distribution, metabolism and excretion



Get started with a proof of concept study



Ensure our approach matches your needs before fully investing with rapid turn around proof of concept studies.



Non-alcoholic steatohepatitis (NASH)

A sophisticated *in vitro* model to accurately study a complex human disease

Access a human-relevant model that replicates key disease phenotypes and reports clinical biomarkers to allow translatability to clinical trials.

Utilizing our extensive expertise, we adapt our industry-validated PhysioMimix® NAFLD/NASH assay, as necessary to explore the effects of your therapeutic(s).

- ✓ The model uses validated cells with known NASH-related genotypes
- ✓ Captures clinical markers with proven translatability
- ✓ Assesses inflammation, fibrosis, steatosis, and cell health biomarkers

We found CN Bio has developed a system that has steatotic, inflammatory, and fibrotic features that have been very useful in evaluating our lead compounds. The scientists at CN Bio are very knowledgeable and have worked with us on the study details to obtain the best quality of results in a timely manner.

Heather Hsu, Chief Scientific Officer, Inipharm



CN Bio supported Inipharm to evaluate drug candidate INI-822 for metabolic liver disease, which is now successfully in clinical trials.

The approach was adopted to circumvent cross-species issues within preclinical development.

Learn more at
cn-bio.com/ini-822

Key endpoints

Functionality biomarkers

Albumin production
Urea production

Clinical liver health biomarkers

Lactose dehydrogenase (LDH) release
Aspartate transferase (AST)
Alanine amino transferase (ALT)

Disease biomarkers

Luminex®/ELISA assays

Fibrosis (e.g. TIMP-1, Pro-collagen, Fibronectin)
Inflammation (e.g. IL-6, IL-8 TNF-α)

Confocal microscopy

Smooth muscle actin (alpha-sma)
Collagen
Fat accumulation (Nile Red staining)

Service flexibility

To ensure you get the most out from your study, we can:

- **adjust the time course** (10 days standard) and dosing frequency
- apply **alternative endpoint assays**, including RNA isolation for transcriptomic analysis.
- implement **periodic media sampling** to enable secreted biomarker assessment.

Our NASH service

Through the co-culture of primary human hepatocytes and non-parenchymal cells, and the evaluation of multiple endpoints, our assay offers a complete assessment of NASH drug efficacy.

We complete your study within two to three months of receiving an order. You benefit from a dedicated contact, who will work facilitate seamless collaboration from project kick-off to completion.

1

Design and finalize the experimental plan

2

Customer supplies the required amount of drug(s)

3

Three to four weeks to complete cell culture

4

Three to four weeks to run endpoint assays, analyze data, and complete the report

Drug-induced liver injury (DILI)

A sensitive and specific means to predict human hepatotoxicity

Employing our Liver-on-a-chip hepatic co-culture model (evaluated by collaborators at the U.S. FDA), our PhysioMimix® DILI assay can screen molecules of any type, and gene editing reagents, to establish human DILI risk.

We assess at least six hepatic health parameters, simultaneously, to achieve the sensitivity and specificity required to identify hepatotoxins that may be missed in animals, and other *in vitro* assays.

- ✓ Explore a range of conditions: healthy, inflammation, fatty
- ✓ Compare acute vs chronic toxicity responses
- ✓ Investigate drug-drug interaction events
- ✓ Check for CYP induction or inhibition

I worked with CN Bio on a DILI services project to predict which formulation of the same test agent would be safe for humans. Previous **in vivo studies demonstrated inter-species differences** between the formulations in animals but thanks to the expertise of CN Bio, I was able to **rapidly gain human-relevant data** that helped to move my project forward.

**Professor Gerry Boss
M.D. UCSD**

**Professor Gerry Boss M.D.
UCSD Distinguished Professor
of Medicine, Department of
Medicine.**

Key endpoints

Functionality biomarkers

Cytochrome P450 enzyme activity
Albumin production
Urea production

Clinical liver health biomarkers

Lactose dehydrogenase (LDH) release
Adenosine triphosphate (ATP)
Aspartate transferase (AST)
Alanine amino transferase (ALT)

Optional profiling analysis

Quantitative PCR
Transcriptomics

Service flexibility

To maximise the scope of your OOC study, we

- **Assess compound availability and drug metabolism** through media sampling for LC-MS.
- **Adjust experimental methods** - the time course (4 days standard), dosing frequency, and biomarker assessment.
- Apply **alternative endpoint assays**, including transcriptomics to explore idiosyncratic DILI.
- **Design bespoke studies** (e.g. multi-organ, or with circulating immune cells) on request.

Our DILI service

Through the co-culture of primary human hepatocytes and Kupffer cells, and the evaluation of multiple endpoints, our assay offers a complete assessment of DILI risk.

We complete your study in approximately two months of receiving an order. You benefit from a dedicated contact, who will work facilitate seamless collaboration from project kick-off to completion.

1

**Design and finalize
experimental plan**

2

**Customer supplies required
amount of drug(s)**

3

**Two weeks to complete
cell culture**

4

**Two to three weeks to run endpoint
assays, analyze data and complete
the report**

ADME

Predict human tissue drug exposure outcomes with greater efficiency

Studies investigating drug metabolism, metabolite concentrations over time, permeability, and bioavailability are conducted using our highly functional, human-specific PhysioMimix® single- and multi-organ models.

We offer metabolically active, long-term cultures to derive unique *in vitro* data to better inform the selection of lead candidates with desirable ADME properties.

- ✓ Hepatic clearance including low clearance, compounds, plus Phase I and II metabolite identification
- ✓ Gut metabolism and permeability
- ✓ Lung permeability in upper and lower airway models
- ✓ Multi-organ (Gut/Liver, Lung/Liver) models that simulate route of administration to predict bioavailability
- ✓ Method developed with protein-free cell culture medium, and low non-specific binding multi-chip assay plates

Working with CN Bio has been a pleasure, the team **listened to our non-trivial requirements** and made useful suggestions to help meet objectives.

During the course of the project, the **team were responsive and helpful.**

The results were delivered as agreed and helped us to move towards our goals.

Dr Giuseppe Ferrandino
Senior Translational Scientist,
Owlstone Medical

Key endpoints

Liver

Functionality biomarkers

Cytochrome P450 enzyme activity
Albumin production
Urea production
Lactose dehydrogenase (LDH) release

Profiling analysis

Media samples ready for LC-MS analysis
Quantitative PCR assessment of
Cytochrome P450 enzyme functionality

Gut, or Lung

Functionality biomarkers

Trans epithelial electrical resistance (TEER)
Lactose dehydrogenase (LDH) release

Profiling analysis

Media samples ready for LC-MS analysis

Service flexibility

To ensure you get the most out of your OOC study, we offer

- **Alternative endpoints**, such as transcriptomics or confocal imaging to assess areas such as mucus production.
- **Adjustments to experimental methods** - dosing regimens and time courses.

Our ADME service

Using single- or multi-organ models, our assays generate insights into the human body's effects on drugs previously only possible using animals.

We complete your study in approximately **two months** of receiving an order. You benefit from a dedicated contact, who will work facilitate seamless collaboration from project kick-off to completion.

- 1. Design and finalize experimental plan**
- 2. Customer supplies required amount of drug(s)**
- 3. Assay dependent preparation of organ models - between four and 21 days**
- 4. Compound dosing and sample collection over one to four days**
- 5. One to two weeks to run endpoint assays, analyze data, and complete the report**
- 6. Approximately two months to complete the study**
- 7. Media samples sent to the customer, or a third party for LC-MS analysis**

Bespoke service offering

At CN Bio, we believe in meaningful partnerships

We will help you find the right solution for your drug discovery and development needs.

Our standard assays can be adapted to suit your research objectives as required. We welcome mutually-beneficial collaborative project opportunities.

If you would like to find out more, please get in touch to arrange an exploratory meeting.

sales@cn-bio.com

Data compliance

CN Bio places great importance on the privacy and protection of your data. When you deal with CN Bio, you can be assured that your data is in good hands. We have processes and procedures in place that maintain strict levels of confidentiality between our scientists and your project team at all times.

To learn more about our data protection policy please contact us.



Meet the team



Dr. Gareth Guenigault - Lead Scientist

Gareth leads the CRS team, managing projects using our PhysiMimix® OOC technology to better understand the bioavailability, efficacy, and toxicity of therapeutic compounds against diseases such as MASH*. With a background in virology and innate immunology, he has always had an interest in using the relevant *in vitro* models to best reflect human disease. He has a PhD in immunology from Cardiff University and a BSc in molecular medicine from the University of Sussex.



James Christophi - Research Assistant

James has MSc in genetic approaches to drug discovery from the University of Sheffield. He was instrumental in the development of our NASH-in-a-Box responsible for validating cell lots for the kit, alongside the completion of research projects using the PhysiMimix Organ-on-a chip system.



Christina Skarlatopoulou - Scientist

Christiana graduated from King's College London with an MRes in biomedical and molecular sciences, with a focus on tissue engineering and hepatic fibrosis using organoids. As part of the CN Bio CRS team, she is involved in the successful and timely delivery of contract research projects utilizing the PhysiMimix OOC microphysiological systems and working on our MASH and DILI** models.



Dr. Rachel Wong - Senior Scientist

Rachel completed her PhD from UCL, where her project involved growing 3D optic tissue using iPSCs from patients with congenital deafblindness, and also creating decellularized scaffolds. As a senior scientist in the CN Bio CRS team, her role involves managing contract research projects using the PhysiMimix OOC systems.

*metabolic associated steatohepatitis, ** drug-induced liver injury

The lab

We established our dedicated contract research laboratory in July 2022 at our existing Cambridge Science Park site, doubling the workspace to meet increasing market demand for OOC services.

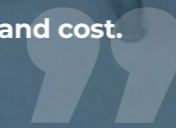
New Alternate Methodologies (NAMs), such as OOC, can better predict human-relevant clinical outcomes and have the potential to reduce and replace animal models – especially for the testing of new drug modalities with human-specific modes of action.

The rising demand reflects the acceptance of OOC data by pharma and biotech companies in their therapeutic programs. This is further fuelled by repeat business and growing interest from regulatory agencies.



Animal models don't always get it right, nor are ethically desirable, we are poised to offer solutions that fit researchers' individual needs by utilizing the power of OOC technology to provide early stage, clinically-translatable data across a range of applications. We hope to give customers greater confidence in the success of their projects, in a fraction of the time and cost.

- Dr. Gareth Guenigault, Lead Scientist



Resources hub

Dive deeper into our technology, its applications, and how its helping enhance the development of tomorrow's medicines around the world.



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CN-BIO

332 Cambridge Science Park
Milton Road, Cambridge, CB4 0WN

+44 (0) 1223 737941

sales@cn-bio.com

visit **cn-bio.com**