CN-BIO

2021 WEBINAR SERIES

Towards a Body-on-a-Chip

The Value of Multi-Organ MPS for Human-Relevant Drug Assessment

Q&A

A full run down of questions & answers from our March 24th webinar

Abbreviations

3D: Three dimensional

ADME: Absorption, distribution, metabolism, and excretion

BBB: Blood Brain Barrier

COC: Cyclic olefin copolymer

DMPK: Drug metabolism and pharmacokinetics

ECM: Extracellular matrix

FDA: U.S. Food and Drug Administration

iPSC: Induced-pluripotent stem cell

MIT: Massachusetts Institute of Technology

MPS: Microphysiological system

OOC: Organ-on-a-chip

PBPK: Physiologically-based pharmacokinetics

PDMS: Polydimethylsiloxane

NASH: Non-alcoholic steatohepatitis

TEER: Trans-epithelial electrical resistance

Q&A participants

Tomasz Kostrzweski

Director of Biology

CN Bio

Audrey Dubourg

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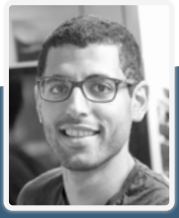

Yassen Abbas

Bioengineer

CN Bio

Another question?

Drop an email to one of our experts - **sales@cn-bio.com**

Missed the webinar?

Watch an on demand - **recording of the webinar here**

Questions

Q1

Q: What other models do you offer? Do you have a gut only model? Do you have more 2-organ models?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Our **PhysioMimix™ Microphysiological Systems** (MPS) are versatile, providing users with the flexibility to generate advanced *in vitro* models that meet their experimental requirements. We provide users with access to various CN Bio validated single- and dual-organ model SOPs (such as **liver**, **gut, lung and gut-liver**) and currently have many more models in development.

The system's open architecture, however, means that customers may also integrate their own bespoke tissue or organ mimics, use commercial inserts, or design new models from scratch. For example, dual-organ models, such as lung-liver, or skin-liver, can be developed using our bespoke **MPS-TL6 consumable plate** and commercial inserts such as ReadyCell® or MucilAir®, or by generating the tissue in-house using Transwell® inserts.

Q2

Q: How long exactly can one culture 3D liver tissues in your system?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Our **Liver-on-a-Chip**, or liver MPS, model allows for the long-term culture of primary liver cells in either mono- or co-culture. We have successfully cultured 3D Liver tissues for over 30 days internally without loss of cell function or dedifferentiation which offers real benefits to PhysioMimix users - examples being the analysis of low clearance compounds and the induction of chronic liver disease pathophysiology i.e., fibrosis, to better model fatty liver diseases.

Q3

Q: How many endpoint markers (soluble and from the tissues) can you measure for one sample?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Thanks to the large sampling volumes of the system (up to 1 mL of media and relatively large 3D tissues grown on scaffolds or Transwell® inserts), a wide and diverse set of end point parameters can be measured from each sample either by repeat sampling

over time and/or at the termination point of the experiment. These include: cell health (LDH, Albumin, Urea), metabolic activity (CYP assays), clinical biomarkers (ALT/AST), metabolite determination, mechanistic signatures of cytotoxicity, RNAseq to –omics and microscopy analysis.

To learn more, watch **our animated video**

Q4

Q: How many parameters must be included in the Physiologically-based pharmacokinetic (PBPK) modelling to extrapolate the data generated with the PhysioMimix system? Do you have to increment each different flow?

A: From Dr Yassen Abbas, Bioengineer, CN Bio:

For predictive modelling, two main parameters are required: hepatic clearance rate and compound permeability through the intestinal barrier. We are working on a mathematical model that will take data generated from the **MPS-TL6 consumable plate** and generate fittings for the parameters. Flow can easily be adjusted in the model and this allows us to understand the effects of different mixing rates.

To learn more, read our **Multi-Organ Application Note**: Drug metabolism in a gut-liver microphysiological system.

Q5

Q: Is the flow connecting the 2 organs physiologically relevant? How do you scale it to the human body?

A: From Dr Yassen Abbas, Bioengineer and Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

In the human body, not one organ operates in isolation. Therefore, the reason for connecting lab-grown organs or organ-like tissues by flow is to mimic this *in vitro*, uncovering the sorts of insights that would normally require animal models but, without any cross-species concerns.

By connecting two organs by flow, many applications can be investigated using the system. For example, compounds may be transferred from one organ to the other enabling compound distribution and bioavailability to be assessed alongside its metabolism and toxicity. The most important aspect to consider here is for the medium to be well mixed as this ensures a uniform drug concentration and distribution in the system. The rate and direction of the medium flow are accurately controlled by the PhysioMimix Multi-Organ Controller and this can simply be altered

by the user for different experimental set-ups. These experiments are also combined with PBPK modelling to match physiological relevance.

By connecting a barrier model, such as the gut, to a 3D liver tissue, users can recreate human drug ADME as compounds are first absorbed through the gut tissue before being delivered to the liver to be metabolised. To learn more, read our **Multi-Organ Application Note**: Drug metabolism in a gut-liver microphysiological system.

Interconnected multi-organ models can be used to uncover the following physiologically-relevant insights:

- obtain a deeper mechanistic knowledge of disease states and drug behaviour
- analyse human inter-organ crosstalk effects
- study reactive metabolite-driven toxicity and multi-organ toxicity
- evaluate drug absorption and metabolism to understand bioavailability.
- investigate drug-induced liver injury (DILI) susceptibility due to underlying disease

We are currently working on PBPK mathematical models that will enable scaling of data-derived using the PhysioMimix Multi-Organ MPS-TL6 consumable plate for *in vitro* to *in vivo* extrapolation.

Q6

Q: How complex is it to generate a common media that is beneficial for 2 connected organ types?

A: From Dr Yassen Abbas, Bioengineer and Dr Audrey Dubourg, Product Manager, CN Bio:

The complexity greatly depends on the cell types used, the 2-organ model set-up and the application. For a barrier-liver model set-up, such as our gut-liver for ADME assays, a slightly optimised version of the media can be used. Initially, each organ is cultured individually until both tissues are fully formed.

Gut cells are seeded and grown on the apical side of a Transwell® insert and liver cells are seeded directly into the liver chamber of the **MPS-TL6 consumable plate**. Once the organs are cultured, flow between the compartments is activated and drugs are added, however, the gut's media, remains separated by the Transwell insert, its membrane and the physical barrier of the gut microtissue. Only drugs that are absorbed by the gut transfer through to the

basolateral side of the chamber, which is perfused with media to support liver function.

However, if two organs are both seeded in the MPS-TL6 consumable plate, one common media would be required to maintain the health, phenotype, and function of both individual organs which would require some optimisation. When optimising media, the end application also has to be considered. For example, serum is usually used to culture Caco-2/goblet cells, however, for PBPK studies we use a serum-free gut media to reduce the risk of the drug binding to serum proteins. Gut cells tolerate this remarkably well with no drop in epithelial barrier integrity (TEER).

If you'd like to learn more about multi-organ models, read our Nature Comm paper on 7- and 10-organ models: **Edington et al., 2018**.

Q7

Q: How long can the gut-liver model be used for?

A: From Dr Yassen Abbas, Bioengineer and Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

The length of an experiment will depend on the application, for example, drug metabolism studies (as reported in our multi-organ application note: **Drug metabolism in a gut-liver microphysiological system**) are typically shorter than studies focussing on organ crosstalk. Here, the **PhysioMimix Multi-Organ MPS** enabled an interconnected gut and liver model, cultured in a **MPS-TL6 consumable plate**, to remain viable for the required two weeks with media changes every 2-3 days. However, as long as the functionality and health of the cells is maintained there is no reason that this could not be extended for longer periods.

Q8

Q: You mentioned being able to do pharmacology and toxicology studies at the same time with your liver-on-a-chip model. Can this also be done in the PhysioMimix Multi-Organ System?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Absolutely yes! The **PhysioMimix Multi-Organ System** provides a large volume of media (up to 1 mL) and tissue from which to sample, enabling pharmacological and toxicological studies to be combined. For example, using the gut-liver model to mimic *in vivo* drug transit conditions, on-board pharmacokinetic profiles for the drug can be generated. The exposure of the target tissue to a dynamic concentration of the drug's metabolites can then be assessed, from

which any toxic effects can also be determined.

Q9

Q: Can the gut-liver multi-organ model be linked to disease states such as IBS or fatty liver?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

To date our aim has been to develop the gut-liver model as a human alternative to animal or *in silico* first pass metabolism studies in order to improve *in vivo* PK/PD predictions. Here we use healthy gut and liver tissue to characterise the effects of increasing therapeutic drug concentrations versus a range of pharmacological and toxicological endpoints, however, in prior studies (using the **PhysioMimix Single-Organ System**) we have successfully developed and validated many **disease models** which could easily be incorporated into a multi-organ format. Currently, we have several internal and collaborative research projects, including fatty liver diseases and COVID 19 infection, where our PhysioMimix Multi-Organ Systems are being used.

Q10

Q: Does the gut tissue in your gut-on-a-chip generate villi and/or crypt-like structures?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

Our gut microtissues display similar tight junction formation, mucus secretion and metabolic function to *in vivo* gut tissue. Whilst the microtissues that form under perfusion in our **gut-on-a-chip** model mimic the 3D shape of *in vivo* gut villi, they are not recreated to the same depth.

Q11

Q: Regarding the 7-organ and 10-organ models presented here, what are the timelines regarding incorporating this capability into a user-friendly set-up such as your system?

A: From Dr Audrey Dubourg, Product Manager and Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

The DARPA **body-on-a-chip** program that we completed in collaboration with The Massachusetts Institute of Technology (MIT), set the ball in motion towards the development of complex and interconnected systems (**Edington et al, 2018**). It was a very exciting endeavour and an enormous undertaking which uncovered many challenges in terms of scaling and interconnection that are still being worked through and optimised for commercial use almost

a decade later. For example, discovering a common medium for all interconnected organs is a necessary step but developing a universal solution that maintains the health, phenotype and function of so many organs is far from a simple task in practice. Additionally, the more organs that are interconnected, the more complex the system microfluidics become. Ideally, system microfluidics should recreate a physiologically-relevant flow rate and cardiac output within each organ as well as between each organ in the system. On top of that, the solution needs to be easy to operate with the ability to plug and play different organ combinations, a prerequisite for an easy integration into laboratory workflows.

To provide user-friendly workable solutions for use in commercial settings, we have stepped back from the full body-on-a-chip of DARPA days, taken the time to develop gold-standard single-organ models, and are now addressing the challenges of linking those organs together to form less extensive but more usable multi-organ systems that provide the next dimension of safety and toxicity data. For example, by connecting liver tissue with another "route of entry" organ (liver-gut or liver-lung models), PhysioMimix users can now study reactive metabolite-driven toxicity whilst simultaneously evaluating drug absorption and metabolism.

The more we develop and understand complex models, the easier it will be to develop body-on-a-chip models for personalised medicine in the long run, but this is not something we see happening in the near future. Although CN Bio's vision is to become the first commercialised body-on-a-chip provider, we currently see a greater value in developing a broader portfolio of applications for single- and dual-organ models which will enable end-users, particularly in the pharmaceutical industry but also wider industries such as cosmetic or food, to benefit from improved data translation over standard techniques.

Q12

Q: In the liver-Gut MPS, how do you calculate the volume of liver and gut. Also, how do you calculate the fluidic flow for each organ?

A: From Dr Yassen Abbas, Bioengineer and Dr Audrey Dubourg, Product Manager, CN Bio:

If by volume of liver and gut you mean scaling of gut tissue versus liver tissue, this is something that is still challenging to do *in vitro* as the gut is one of the largest organs in the body. Our gut-liver MPS model currently does not scale the gut and liver tissues to match their *in vivo* counterparts as we use standard 24-well Transwell® inserts and our proprietary scaffold to generate both tissues

respectively. To scale and extrapolate *in vitro* data generated from our system into an *in vivo* prediction, we use physiologically-based pharmacokinetics (PBPK) modelling. By comparing the behaviour and toxicity of a compound in our gut-liver MPS to PBPK, we provide users with a physiologically relevant picture of a drug's behaviour and the crosstalk between gut and liver tissues.

To know more, read our multi-organ application note: **Drug metabolism in a gut-liver microphysiological system**.

An extensive amount of research effort has been invested into ensuring that the PhysioMimix's organ-specific flow rates physiologically match that of the *in vivo* counterpart organ. Here is an example of how we calculated the flow rate for the liver: **Domansky et al, 2009** during the development of the PhysioMimix in collaboration with MIT. Note fluidic flow rates were calculated for single (gut and liver) organ models. When considering multi-organ models, the calculations to determine fluidic flow rate and cardiac output for each organ and between organs can be really challenging. The more organs, the more parameters have to be considered. A good example of this can be found in our 7- and 10-organ model publication: **Edington et al, 2018**.

Q13

Q: What about the behaviour of the tissues in the absence of hormones, nerve endings, individual genetic compositions, etc.?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

That is a very interesting question. MPS were originally developed to fill certain gaps i.e. to improve the translatability of *in vitro* data and address the cross-species differences observed between *in vivo* animal models and human. Although complex 3D MPS models do not fully recapitulate the human physiology in terms of vasculature, hormones or individual genetic compositions, we can recreate the physiological shear stress experienced by organs, by putting the tissues under perfusion, and we can isolate the signals occurring within that organ to mimic its environment and functions. Simple vasculature can be recapitulated by including endothelial cells, specific hormones can be added to the media to match the organ's physiology, we can replicate specific genetic compositions by using specific donors (or genetically altering cells) and, with the new **PhysioMimix Multi-Organ System**, two organs or more can be interconnected to enable organ-organ crosstalk.

So, although MPS systems are not able to completely represent the human body, they do create complex organ mimics. These

advanced *in vitro* models allow researchers to answer specific questions about specific human physiology or drug reactivity and deliver results with improved translatability over standard techniques.

To know more about how the flow enables the creation of physiologically-relevant organ models, watch our webinar: **The Rhythm of Life – Using Microfluidics to Mimic Blood Flow in Single- and Multi-Organ-on-a-Chip Models.**

Q14

Q: How does CN Bio model vasculature in MPS?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

To recreate vasculature, endothelial cells can be added into our current tissue models e.g., **gut or lung**, alongside epithelial cells. In principle, endothelial cells can either be added as networks between the tissue models or to line the fluidic channels, however, this has not been fully validated internally. Some of our collaborators have successfully incorporated endothelial cells into their liver models. The further development of vascularised models is on our roadmap.

Q15

Q: Are MPS setups being used to observe and determine human enhancement capabilities?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Whilst the number of MPS models and applications has steadily increased over the last decade, their development has predominantly focussed on recreating healthy, or diseased, human organ physiology to improve the clinical relevance of *in vitro* drug discovery and academic research models.

These advanced models comprise human cells and tissues whose phenotypes and functions mimic those *in vivo*. When drugs are added, they generate translationally relevant pre-clinical data. As such, if you were able to adequately recreate e.g., the heart's microenvironment, cardiac output and vasculature in the lab and subjected it to extensive validation to ensure *in vivo*-like phenotype and function then, in theory, there is no reason that MPS models could not be developed for the purpose of human enhancement.

However, before starting human enhancement projects, any ethical issues surrounding their development should be carefully considered, for example, recent work being done to develop brain-on-a-chip and cerebral organoids models has sparked a debate about consciousness in those models and the ways to potentially

assess it by introducing biologically-engineered tissues into an animal (**Sawai et al, 2019** and **Sawai et al, 2021**).

Q16

Q: Could this technology be used on non-human species - say canine, feline, bovine, or even aquatic vertebrate?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Our work at CN Bio has mainly focused on developing physiologically relevant human models for drug discovery, however, the PhysioMimix OOC is an open and versatile system that can be used to develop non-human species models. The key to success is selecting the right extracellular matrix (ECM) to support the tissue/cell of interest as well as cell culture condition optimisation.

We have worked with **primary rat liver cells** alongside our collaborators at MIT and a number of collaborators are working with alternative species, such as the Pirbright Institute, who currently use the PhysioMimix to **develop avian models to study avian flu** and other viruses.

Q17

Q: Have you tried to use the system to mimic a cancer microenvironment?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

Our PhysioMimix™ System has, and still is, being used by some of our collaborators to recreate the effects of breast cancer metastasis on the liver and study the effects of specific chemotherapies on those metastasis (**Beckwitt et al, 2018**). If you'd like to know more about their work, you can watch the on-demand webinar: **A Microphysiological Model of Metastatic Progression.**

Our system can also be used to house precision-cut slices of tumours which can be challenging to keep alive for extended periods of time. With perfusion, tissues are kept alive for longer than the standard few days (unpublished work). If you'd like to know more, please contact us at **enquiries@cn-bio.com**.

The PhysioMimix can also be used to culture patient-derived tumour organoids within a multi-organ environment. This project is currently being developed and validated internally but, please, contact us if you'd like to know more: **enquiries@cn-bio.com**.

Q18

Q: Can you comment on how you work with the microbiome in the gut model and how long culturing can take place for?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

Including the gut microbiome into a gut MPS model is very challenging due to the anaerobic environment required for many bacterial species. With our collaborators at MIT, we have been developing an adapted MPS set up that will allow the culture of anaerobic bacteria along with a 3D-like gut model under flow which shows that it is possible to develop such *in vitro* models (**Zhang et al, 2021**). If you would like to know more about this technology, you can watch the on-demand webinar: **Engineering mucosal barriers**.

Q19

Q: How about models with cardiomyocytes or neurons? What would the readout be?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

We worked with cardiomyocytes and neurons when developing our 4-, 7- and 10-organ models with MIT for the DARPA Body-on-a-Chip program (**Edington et al, 2018**), however, we have not fully validated cardiac or neuronal models. As both models are grown on removable scaffold/insert in our platform, a wide range of readouts can be performed from each recovered microtissue and media (up to 1 mL) sample. Moreover, for the cardiac model, beat frequencies can be assessed using appropriate tools, such as an RCTA Cardio Analyzer, during an experiment.

Q20

Q: Can you talk about the brain-on-a-chip?

A: From Dr Audrey Dubourg, Product Manager and Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

Although researchers have made tremendous progress in recreating brain organoids and other complex 3D models of the brain, recreating an *in vitro* model of the entire brain still represent an enormous challenge since the all the different cell populations and the surface dimension of the brain need to be considered. Incorporating the blood brain barrier (BBB) into those models is also currently extremely challenging and therefore limits the range of applications for such models.

Our work internally has not significantly focussed on brain-on-a-chip models, however in a recent publication, our collaborators at MIT describe the use of brain culture in a protype multi-organ set-up

to study Parkinson's disease and other neurodegenerative diseases (**Trapecar et al, 2021**). In this study, they cultured a mixture of iPSC-derived neurons, astrocytes and microglia to assess inflammation-related changes in cerebral pathology. This research demonstrates the potential of MPS platforms for culturing complex *in vitro* 3D brain models under perfusion, however, more work is required before these models are validated for disease modelling purposes.

Q21

Q: Which application among them is very close to potentially replace/reduce animal use?

A: From Dr Audrey Dubourg, Product Manager and Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

Before answering, it is important to highlight that MPS models were not originally designed to replace animal models but to provide researchers with a tool to use alongside current *in silico*, *in vitro* and *in vivo* models to address translatability limitations. However, as these advanced *in vitro* models continue to develop and prove to predict human biology better than animal models, we envisage that our reliance on animal studies will become reduced, and in some cases potentially replaced by MPS along the way.

For example, our collaborators at Charles River Laboratories have developed a Liver MPS model using the **PhysioMimix** that provides a reliable assessment of a compound's genotoxicity in the human liver compared to gold standard animal models. If you'd like to know more about their work, you can watch their on-demand webinar: **Go With the Flow**.

The study of fatty liver disease represents another area where improved models are desperately needed as animal models do not adequately represent the pathophysiology of complex human metabolic diseases such as non-alcoholic steatohepatitis (NASH). A recent human MPS model of fatty liver disease, however, demonstrates an improved pathophysiology that more accurately recapitulates long-term fibrotic and inflammatory NASH phenotypes (**Kostrzewski et al, 2019**) and, in response to therapeutic treatment, this model delivers more clinically-relevant responses. If you'd like to know more, watch our upcoming webinar in collaboration with AstraZeneca: **Pathologically Scarred by Fibrosis**.

The U.S Food and Drug Administration (FDA), has also recognised the potential for MPS to improve the predictability of drug discovery. Through a collaboration with CN Bio, the FDA is evaluating the performance of MPS models versus gold standard techniques

for applications, that include drug metabolism, drug safety, and disease modelling. In a recent publication (**Rubiano et al., 2021**), the superior performance of the PhysioMimix's Liver-on-a-Chip model for drug safety and metabolism applications was demonstrated over standard *in vitro* culture. The data within this study provides decision-makers with the collateral to justify adoption of MPS into their workflows and by adopting these powerful systems, we offer an option to help replace, reduce and refine the number of animal tests.

Q22

Q: How do you ensure a constant regular flow in the multi-organ chip?

A: From Dr Tomasz Kostrzewski, Director of Biology, CN Bio:

CN Bio has adopted a programmable approach which enables flow rates and profiles (pulsatile or continuous) to be tuned, more accurately mimicking each individual organs exposure to the fluid shear forces and dynamic mechanical stresses that occur *in vivo*. This is achieved through use of robust materials, tightly controlled pneumatics and micropumps embedded into the MPS consumable plates which accurately and reliably move media around tissue structures or between organ mimics for weeks to maintain the performance of that culture over extended periods of culture (up to 30 days).

For a detailed explanation, please watch the on-demand webinar: **The Rhythm of Life**.

Q23

Q: How do you differentiate CN Bio from other organ-on-chip (OOC) players such as Emulate, Synvivo etc?

A: From Dr Audrey Dubourg, Product Manager, CN Bio:

There are many OOC models and platforms available, most of which are chip-based, such as Emulate or Synvivo. Each delivers an individual set of benefits and limitations that should be investigated and matched to user requirements before any investment is made. Many factors, however, differentiate CN Bio's PhysioMimix from other providers, for example, our microfluidics capabilities (touched upon in Q22) which offer improved physiological relevance, culture longevity and the unique ability to uncover insights that only the interconnection of organs and tissues can bring. Another is the ease of use of our systems. We enable incredible biology through:

- the co-culturing of human cells to faithfully recreate human tissues,

- scaffolds that promote 3D organ model formation,
- recirculating fluidic flow that delivers biomechanical stimulus, oxygen and nutrients,
- adjustable inter- and intra- “organ-specific” flow rates to enhance physiological relevance
- viability, function and phenotype that is maintained over many weeks

However, we take away the fiddliness and complexity often associated with OOC technologies. Our platform has been built with the end-user in mind, making it very easy to set-up and use. No engineer is needed to install the platform, it can be set-up in less than an hour and ready to use as soon as it is installed. The user interface on the controller makes our system also very user-friendly, simply select the right program and press play, no need to fine-tune anything but the flow rate.

When developing our platform with MIT, we purposefully chose a completely different approach to chip-based providers, adopting an open-well cell culture set-up that researchers are well accustomed with to decrease adoption barriers. This open-well plate format provides many additional benefits. With up to 1 mL of media available and microtissue that can easily be recovered, users can analyse a huge number of end points from each sample to gain deep mechanistic insights into disease states or drug action.

Our **consumable plates** approach also permits 6 to 12 experiments, or conditions to be run per plate (depending on the plate you use), which brings down the cost of a PhysioMimix experiment significantly and increases throughput capability compared to most OOC solutions where you can only run one experiment, or condition per chip. If you’d like to learn more watch the on-demand webinar presented by our collaborators at Charles River laboratories: **Go With the Flow**.

Another differentiator is the use of a low-binding material, Cyclic olefin copolymer (COC), in our consumable plates. We specifically chose COC, instead of polydimethylsiloxane (PDMS), to ensure that researchers can confidently assess a drug’s DMPK for example without worrying about binding of their compounds to the plate.

One final point worth mentioning is our long-standing collaboration with the U.S. Food and Drug Administration (FDA) which has led to a recent co-publication comparing our liver MPS model to the gold standard of *in vitro* liver cell culture (**Rubiano et al, 2021**). This first ever co-publication between a regulator and an OOC developer showcases the great potential of OOC technologies for improving the predictivity of preclinical drug development.

Our 2021 webinar series continues

27th Apr

Pathologically Scarred by Fibrosis:

How To Model and Quantify Human NASH in a Microphysiological System

Dr Gareth Guenigault, Senior Scientist, CN Bio

Dr Samantha Peel, Principal Scientist, Functional Genomics, Discovery Sciences AstraZeneca

Register here

8th June

Webinar details to be announced soon

Registration coming soon

22nd June

Webinar details to be announced soon

Registration coming soon

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