Novel Picodroplet-based Single Cell Analysis Platforms

Find, analyze and isolate your most valuable cells, with ease and speed.

sphere FLUIDICS

work small, think big.

spherefluidics.com

Contents

sphere FLUIDICS work small, think big.

Platforms

Cyto-Mine®

Cyto-Mine® can simplify and accelerate your day-to-day operations in antibody discovery, cell line development, and beyond. It's powered by our picodroplet technology to screen and analyze millions of individual cells and isolate those rare 'hits' with monoclonality assured. And all in a single, integrated platform with minimal 'hands-on' time.

Pico-Mine®

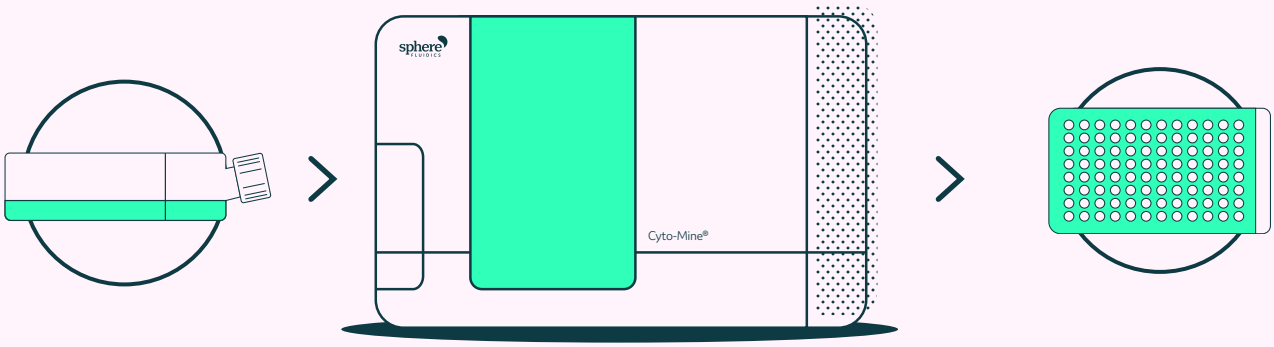
Pico-Mine® is our semi-automated, flexible and easy-to-use platform, designed to find your highly valuable and rare biological variants among vast cell populations.
By radically increasing throughput and reducing cost, our picodroplet technology can help you save on resources whilst boosting your chances of success!

sphere FLUIDICS
work small, think big.

Cyto-Mine® Single Cell Analysis Platform

Cyto-Mine® provides a powerful, proven way to screen hundreds of thousands, or even tens of millions, of cells with a range of assays in a single day.

Leveraging our proprietary picodroplet technology, Cyto-Mine® streamlines cell isolation, titer determination, sorting, imaging and clonality assurance into one automated instrument. This fully-integrated workflow accelerates timelines and reduces costs for biologics discovery and development.



Complex cell population

0.5h

Cell count

Resuspend in fresh cell culture medium

Add assay reagents

Load to Cyto-Cartridge® and into Cyto-Mine®

Cyto-Mine®

4-6h

Picodroplet generation and cell encapsulation

Picodroplet incubation and antibody secretion assay

Picodroplet sorting

Picodroplet imaging and cell dispensing

High-value cells collected to 96 or 384-well microplates

1-2w

Reverse transcription

PCR

Expression

Sequencing

OR

Clone outgrowth

Expansion

Titer measurements

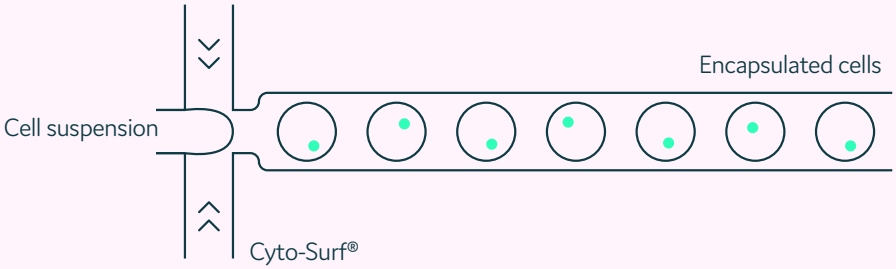
Less than one working day

sphere FLUIDICS work small, think big.

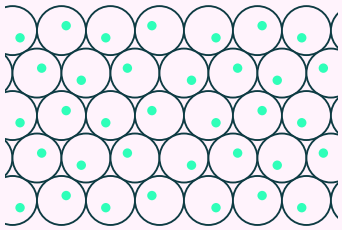
Cell Selection, Sorted

The Cyto-Mine® workflow is a fully integrated microfluidic process including single cell screening, sorting, verification, and isolation.

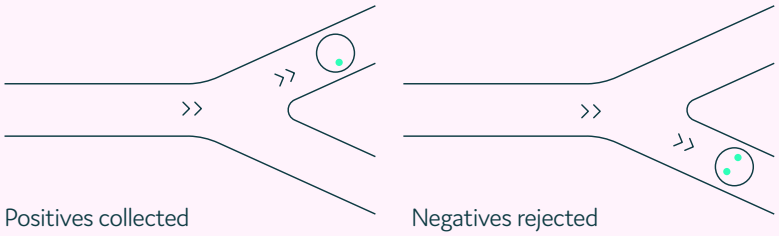
1 Cells encapsulated at high dilution so that the probability of 2 or more cells per picodroplet is ~0.1%



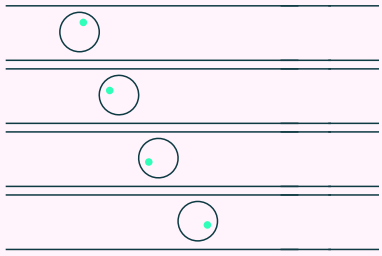
2 Cells incubated or stored



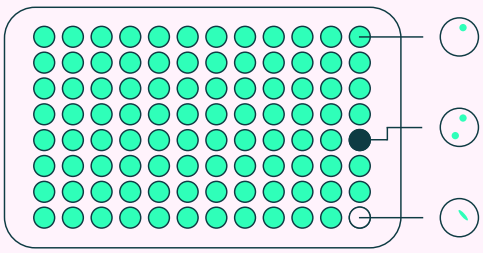
3 Cells sorted to divert all empty picodroplets to waste



4 Visual verification by ultra-high speed, multi-frame optical imaging immediately prior to dispense confirms the presence of a single cell per picodroplet



5 Cells gently dispensed to pre-filled 96- or 384-well microplates, and detected cell number annotated on interactive well map in Cyto-Mine® Studio Data Analysis software.



Key Applications

- Antibody Discovery
- Cell Line Development
- Cell Therapy Research
- Synthetic Biology
- Genome Editing
- Cell Engineering

sphere FLUIDICS work small, think big.

Benefits

Simplify and accelerate workflows
Combine cell isolation, assay, sorting, imaging, and dispensing into an automated workflow with real-time interactive tracking.

Significantly improve throughput
Increase screening capabilities and analyze up to 200,000 single cells or 40 million cells (in pools) in 1 day.

Screen and select high-value clones
Picodroplets provide miniaturized compartments to assay for target proteins or productivity titer.

Improve cell viability and cell outgrowth
Leverage single cell encapsulation in picodroplets to protect cells from shear stress.

Ensure proof of monoclonality

Collect visual evidence of monoclonality and gain confidence in a single cell progenitor.

REALLY User-friendly software
Simple-to-use with no need for specialized users so you can get up and running with experiments from day one. It's also FDA 21 CFR Part 11-compliant.

sphere FLUIDICS
work small, think big.

Cyto-Surf® A and B

Cyto-Surf® A and B are the two droplet-forming and dispensing reagents needed to operate our Cyto-Mine® platform.

They have been optimized to provide reliable, consistent, and robust Cyto-Mine® operation over long periods of time and are fully biocompatible. They're manufactured in-house to the highest quality standards under our registered ISO 9001 quality management system.

Features

- Fully optimized for Cyto-Mine®
- Ensures reliable, robust operation
- Fully biocompatible
- Made in house to the highest quality standards

Cyto-Surf® A is a high-performance oil used in Cyto-Mine® workflows to ensure reliable and precise dispensing.

Cyto-Surf® B provides the critical surfactant needed to create long-term-stable water droplets within the oil phase. It provides the optimum conditions for cell viability.

sphere FLUIDICS work small, think big.

Cyto-Cartridge®

Cyto-Cartridge® is the core of the Cyto-Mine® platform that provides all the necessary microfluidic functions for implementing picodroplet workflows. This single-use device is designed to be easy to use, and it includes encapsulation, incubation, sorting, and dispensing functions in one place.

Cyto-Cartridge® is manufactured to the highest quality standards under our ISO 9001 quality management system. It is made from fully biocompatible materials in a clean environment and is optimized to work seamlessly with the Cyto-Mine® platform and Cyto-Surf® reagents.

Each Cyto-Cartridge® is barcoded to enhance quality control and data tracking during experiments. Its disposable feature ensures zero cross-contamination between runs, maintaining the integrity and quality of your cells for each experiment.

Features

- Optimized for Cyto-Mine® to provide all necessary workflow functions in one device.
- Easy to use – add cells, insert into Cyto-Mine®, and go.
- Single-use and fully disposable to ensure zero cross-contamination.
- Fully biocompatible and made to the highest quality standards.
- Barcoded to enhance quality control and data tracking.

Cyto-Cellect® Human IgGκ Detection Kit

Our Cyto-Cellect® Human IgGκ Detection Kit is a FRET assay that detects the presence of IgG with a kappa light chain. It is an easy-to-use assay to quantify clone cell productivity accurately and with high sensitivity. When picodroplets are formed during the Cyto-Mine® workflow, our Human IgGκ Detection probes are co-encapsulated with the cells. As the encapsulated cells are incubated and start to secrete IgG kappa antibody the probes bind to the target in close proximity and allow energy transfer when excited by the Cyto-Mine® laser.

Each kit includes 5 vials, each containing the donor-acceptor pair of Human IgGκ Detection probes, manufactured without the use of animal- or human-derived materials. Our Detection Kit is workflow-ready and compatible with CHO cell culture medium to get you up and running with minimum effort.

Features

- Animal-origin free
- Free of Human-derived materials
- Sensitive and robust
- Easy-to-use FRET-based assay

sphere FLUIDICS work small, think big.

Case study: Fujifilm Diosynth Biotechnologies

As conventional manual screening techniques, such as colony picking and limiting dilution cloning, are slow and laborious. Fujifilm Diosynth Biotechnologies sought to overcome bottlenecks in the cell development process through developing a single-step cloning process using novel technologies.

Scientists at Fujifilm Diosynth Biotechnologies have transformed their cell line development processes using Cyto-Mine®. Multiple procedures and assays within the cell line development pathway are miniaturized and integrated within Cyto-Mine®, allowing tasks that would previously have taken weeks to complete to be undertaken within one day. In turn, projects can swiftly transition from the initial transfection phase to developing highly productive cell lines, reducing timelines from around 25 weeks to approximately 10 weeks.

Approximately 200,000 individual cells can be screened in a matter of hours using this approach, compared to, at best, 10,000 cells over a few weeks using semi-automated or manual analysis techniques. Additionally, single cells may be visualized using Cyto-Mine®, and accurate monoclonality data can be provided to support biopharmaceutical regulatory submissions.

Overall, scientists spend less time conducting laborious manual procedures and can complete more projects within a given timeframe. So, motivated by the possibilities for Cyto-Mine® in enhancing their research, scientists at Fujifilm Diosynth Biotechnologies are now exploring further applications of this novel technology platform.

"Our workflows are considerably more efficient as cellular screening is conducted early in the process, allowing the best-performing cells to be selected and taken forward for development."

Dr Fay Saunders

FUJIFILM Diosynth Biotechnologies

sphere FLUIDICS work small, think big.

Pico-Mine®

Pico-Mine® is our semi-automated platform designed to support earlier-stage research using picodroplet technology. It provides ultra-flexibility for workflows and assays to help you find your valuable and rare biological variants among large cell populations. Pico-Mine® radically increases throughput and reduces cost across a wide range of applications helping you save on resources and boosting your chances of success.

Benefits

- **Flexible but simple**
  Pico-Mine® lets you mix and match functions to build the workflow you need for every project. It is also simple to use without needing microfluidics expertise so you can focus on your science
- **High-throughput low cost**
  Picodroplet technology allows both cell-by cell assessment and rapid, low stress processing of cells – all at tiny volumes. You get the best of all worlds – precise measurements of large libraries in hours at low cost.
- **Complex workflows**
  Pico-Mine® biochips allow a wide range of functions to be combined to execute the most complex workflows. And we can provide custom biochips too if you need something slightly different.

Selected applications

- **Strain engineering/Enzyme evolution**
  Analyze and direct enzyme evolution to find the optimum structure
- **Drug resistance**
  Screen billions of bacteria a day to identify those developing resistance to your drug of interest
- **Cell engineering**
  Engineer your cells one-by-one using either transduction or transfection methods
- **Cell therapy**
  Co-encapsulate CAR-T and target cells and enrich your population based on activity
- **Antibody discovery**
  Screen the entire repertoire of native B cells to find the rare cells you want - fast
- **Synthetic biology**
  Profile biosynthetic metabolic pathway libraries and find the best cells easily

sphere FLUIDICS
work small, think big.

Case study: VIB (Vlaams Instituut Voor Biotechnologie)

The VIB Tech Watch initiative aims to drive scientific progress by facilitating access to the latest platforms and emerging technologies. The initiative involves ongoing research into new methods and techniques and partnerships with companies to become early adopters of emerging technologies.

This led VIB to the platforms and microfluidic-based technologies from Sphere Fluidics. Sphere Fluidics' flexible Pico-Mine® provides semi-automated capabilities for the microfluidic picodroplet encapsulation and isolation of cells along with the ability to process, assay, and sort the encapsulated cells to help find highly valuable and rare biological variants among vast cell populations. Additionally, and most importantly, researchers don't need experience in microfluidics to use the instrument, making it assessable for VIB to integrate into their workflows and projects.

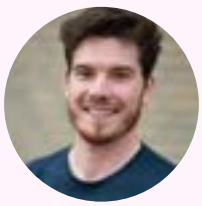
Key areas of implementation include; studies into antibiotic-resistance, overcoming limitations posed by mammalian cell lines in biologics production, and nanobody screening and selection.

By integrating Pico-Mine®, VIB is now equipped with enhanced single cell analysis capabilities, without extensive training in microfluidics, to overcome the limitations of screening 24-well plates and flow cytometry.

Pico-Mine® offers microfluidic technology in an easy-to-use, semi-automated system, allowing researchers with no experience in microfluidics to run experiments in a matter of a few weeks. In addition to its ease of use, there are many different experiments VIB can do with the setup to expand their research capabilities and stay at the forefront of single-cell research.

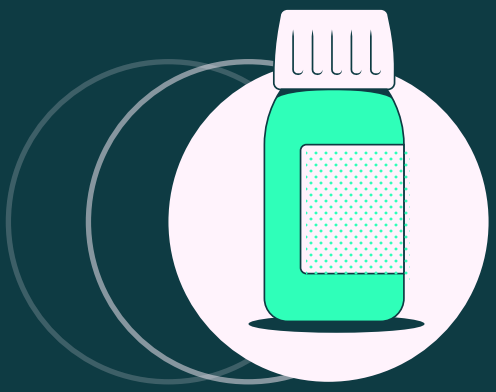
For example, one project focused on the identification of the better secretors of IgG molecules in yeast. VIB uses the device to screen mutant libraries of yeast to isolate the highest secreting yeast cells for biologics production. From this screening, VIB aims to find new mutations that enhance protein secretion.

"Pico-Mine® provides a platform to develop custom assays specifically for our research, and it does an excellent job."



Michiel Bontinck | VIB

sphere FLUIDICS work small, think big.



Droplet Microfluidics Chemicals

We develop and manufacture a range of surfactants and other chemicals to enable the more effective use of picodroplet-based microfluidic devices for numerous applications such as cell line development, antibody discovery, synthetic biology, enzyme evolution, and even mass spectrometry. You can rely on their quality and reliability to get reproducible results, every time. We should have you covered, but, if you do need something more unique, our highly skilled teams are on hand to discuss novel solutions.

sphere FLUIDICS work small, think big.

Pico-Surf®

Pico-Surf® is a patented range of biocompatible surfactants that are used in a variety of microdroplet and picodroplet applications. They act to stabilise picodroplets and their cellular or molecular contents. Picodroplets are highly stable over a wide range of temperatures and biological conditions, ensuring reliability and reproducibility.

Pico-Surf® is commonly used in research programs focusing on monoclonal antibody discovery, cell line development, synthetic biology, stem cell engineering, isolation and analysis, single cell genome editing (CRISPR-Cas9), single cell disease research, diagnostics, prognostics and more.

Applications

Pico-Surf® surfactants are used in a variety of microdroplet and picodroplet applications, including but not limited to:

- Cell and molecular biology assays
- Cell growth studies
- ESI-MS
- Cell secretion assays
- Single cell analysis
- Single cell isolation

Benefits

- **Biocompatibility**
  High gas exchange rates support high viability and proliferation
- **Highest picodroplet stability**
  Best in class picodroplet stability with consistent formation and stabilization of picodroplets from 8pL to 700pL (diameter)
- **Stability at high temperature**
  demonstrated by the low level of picodroplet fusion
- **Low voltage for picodroplet sorting**
  purity and quality of the surfactants enables a more efficient picodroplet sorting process
- **Excellent batch to batch reproducibility**
  all products undergo rigorous QC and QA testing to ensure batch consistency
- **Patented molecular structure**
  patent freedom to operate in a wide range of application areas

sphere FLUIDICS work small, think big.

Pico-Break™ Emulsion Breaking Solution

Pico-Break™ is used to gently reduce the stability of picodroplets in order to release cellular or molecular contents into an aqueous medium for subsequent processing.

Features

- Gently breaks picodroplets by phase separation via chemically-induced coalescence
- Compatible with picodroplets stabilized by Pico-Surf® surfactants
- Contains a dye to visually confirm recovery of sample material

Pico-Wave™ Diluent

Pico-Wave™ is a diluent comprising a fluorinated oil which is well suited for diluting Pico-Surf® for use with your specific applications.

Features

- Optimized for use with Pico-Surf® and our other specialist chemicals
- Compatible with our range of Pico-Gen™ microfluidic biochips
- High purity and long shelf life
- Animal Origin Free

sphere FLUIDICS work small, think big.

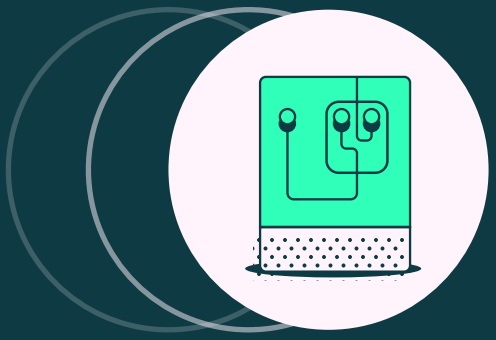
Pico-Glide™ Biochip Coating Agent

Pico-Glide™ is a microfluidic biochip coating agent designed for users who manufacture their own microfluidic biochips using plasma etched glass or polydimethyl siloxane (PDMS).

Features

- Promotes consistent in-house manufacture of microfluidic biochips
- Minimizes non-specific binding interactions
- Improves picodroplet performance and stability

sphere FLUIDICS work small, think big.



Microfluidic Biochips

Our range of polydimethyl siloxane (PDMS) biochips are specially designed to help customers reproducibly generate or sort picodroplets, with a range of volumes from around 35 pL - 1,000 pL.

We design our biochips to work seamlessly with our Pico-Mine® platform but can also be used with other droplet microfluidics systems. They are also compatible with a wide range of cell types (e.g., bacteria, yeast, CHO cells, hybridomas, B-cells) and molecules.

We have a variety of Pico-Gen™, Pico-Sort™ and Pico-Mix™ Biochips available to purchase but if you can't find the right biochip for your application, our scientists can potentially design one for you.

Features

- High picodroplet production rate
- Highly mono-dispersed picodroplet generation
- Straightforward 'Plug & Play' fluidic interface
- Long residence time on biochip for easy visualization
- Fluorophilic channel surface coating for high performance

sphere FLUIDICS work small, think big.

Pico-Gen™

Pico-Gen™ biochips are designed for generating picodroplets from a single aqueous source. With a wide range of sizes and designs available they enable reliable and consistent picodroplet formation, with volumes ranging from 35 pL to more than 1,000 pL.

Nozzle options

40 x 40 µm
60 x 60 µm
80 x 80 µm

Product code	C101	C102	C103	C104	C112
Slide Size (Length x Width x Thickness, mm)	75 x 25 x 1				
PDMS Block Size (Length x Width x Thickness, mm)	15 x 16 x 4				
Inlet/Outlet Diameter	1000 µm				
Flow Focus Nozzle (a x b, µm)	40 x 40	60 x 60	80 x 80	40 x 40	60 x 60
Picodroplet Diameter Range	Ø 40 - 75 µm	Ø 65 - 100 µm	Ø 95 - 125 µm	Ø 40 - 75 µm	Ø 65 - 100 µm
Picodroplet Volume Range	35 - 220 pL	150 - 550 pL	500 – 1,000 pL	35 - 220 pL	150 - 550 pL
Channel Surface Property	Fluorophilic				
Biochip Format	1 oil inlet, 1 aqueous inlet, 1 picodroplet outlet				2 aqueous inlets
In-line Filter	1 filter at oil inlet			2 inlet filters	3 inlet filters

Pico-Mix™

Pico-Mix™ enables the reliable addition of a liquid reagent into picodroplets and promotes the rapid mixing of reagents within the picodroplet. The optimal output picodroplet volume ranges from 350 - 400 pL.

sphere FLUIDICS
work small, think big.

Pico-Sort™ Generation/Sorting Biochip

The Pico-Sort™ Generation / Sorting Biochip is developed for sorting and isolation of “hit” picodroplets from the starting cell population based on a user-defined optical readout with volumes

Pico-Sort™ Reinjection/Sorting Biochip

The Pico-Sort™ Reinjection / Sorting Biochip is created for picodroplet reinjection, sorting and isolation of “hit” picodroplets from the starting cell population based on a user-defined optical readout.

Generation / Sorting

Reinjection / Sorting

work small, think big.

Ordering Info

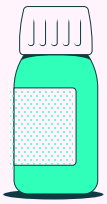
Cyto-Mine® and Pico-Mine® Platforms

Our platforms are developed in close collaboration with key opinion leaders to fit seamlessly into your lab workflows. We focus on ease-of-use, speed, and reducing hands-on time while delivering high-quality outputs. They are all complemented by software, consumables, support, and training designed to help you advance, quickly.

Product name	Product code
Cyto-Mine®	S003
Cyto-Mine® Data Analysis Software	R302
Cyto-Mine® Consumables Bundle Includes: Cyto-Mine® Cartridge, Pack of 5 Cyto-Surf® A (250ml bottle) Cyto-Surf® B (250ml bottle)	C301
Cyto-Cartridge® Pack of 5	C302
Cyto-Surf® A (250ml)	C303
Cyto-Surf® B (250ml)	C304
Cyto-Cellect® Human IgG_K Detection Kit	C310
Pico-Mine® System	S002
Pico-Safe™ Laser and Electrical Safety Box	B201

sphere FLUIDICS work small, think big.

Ordering Info



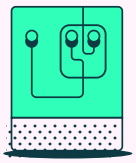
Droplet Microfluidics Chemicals

- **PICO-Surf®** is a range of biocompatible surfactants that act to stabilise picodroplets and their cellular or molecular contents.
- **PICO-Break™** is used to release the contents of a picodroplet emulsion.
- **PICO-Glide™** is a coating agent used on microfluidic biochips and other devices to minimise non-specific binding interactions, improving picodroplet stability and reproducibility.
- **PICO-Wave™** is a diluent for routine use with picodroplets.

Product name	Volume	Product type	Product code
Pico-Surf®(2% (w/w) in Novec™ 7500)	10 mL	Surfactant	C021
Pico-Surf® (5% (w/w) in Novec™ 7500)	10 mL	Surfactant	C022
Pico-Surf® (2% (w/w) in Novec™ 7500)	50 mL	Surfactant	C023
Pico-Surf® (5% (w/w) in Novec™ 7500)	50 mL	Surfactant	C024
Pico-Break™ 1	10 mL	Emulsion Breaking Solution	C081
Pico-Break™ 1	50 mL	Emulsion Breaking Solution	C082
Pico-Glide™ 1	5 mL	Microfluidic Biochip Coating Agent	C071
Pico-Glide™ 1	10 mL	Microfluidic Biochip Coating Agent	C072
Pico-Glide™ 1	25 mL	Microfluidic Biochip Coating Agent	C073
Pico-Wave™ 7500	100 mL	Diluent	C094
Pico-Wave™ 7500	250 mL	Diluent	C095
Pico-Wave™ 7500	500 mL	Diluent	C096

sphere FLUIDICS work small, think big.

Ordering Info



Microfluidic Biochips

Choose from our range of Pico-Gen™, Pico-Mix™ and Pico-Sort™ biochips, or if you can't find one quite right for your application, we can design one for you.

Product name	Volume	Product type	Product code
Pico-Gen™ single aqueous, oil inlet filter biochip	35 - 220 pL	40 x 40	C101
Pico-Gen™ single aqueous, oil inlet filter biochip	150 - 550 pL	60 x 60	C102
Pico-Gen™ single aqueous, oil inlet filter biochip	500 – 1,000 pL	80 x 80	C103
Pico-Gen™ single aqueous, two inlet filters biochip	35 - 220 pL	40 x 40	C104
Pico-Mix™ biochip	350 pL - 400 pL	n/a	C401
Pico-Sort™ generation / sorting biochip	400 - 700 pL	n/a	C201
Pico-Sort™ reinjection / sorting biochip	400 - 700 pL	n/a	C202

sphere FLUIDICS work small, think big.

sphere FLUIDICS

work small, think big.

Info@spherefluidics.com
spherefluidics.com

Sphere Fluidics Ltd is an ISO 9001:2015 accredited company.

All Sphere Fluidics' supplied chemicals and bioreagents are Animal Origin Free and GLP-compliant.