



Automate your Multi-Organ-Chip Assays







TISSUSE
Emulating Human Biology



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Automation is key

With the approval of the **FDA Modernization Act 2.0**, the requirement to use animal testing for drug development has finally been eliminated – paving the way for innovative animal-free technologies like **Multi-Organ-Chips***. The next step towards regulatory acceptance and industry adoption is the development and validation of standardized assays

for safety & efficacy testing. We are convinced that **automation** is the key to this. But how does it work? In this brochure we will explain the features of our automated solution and how you can benefit from it!

* For a brief introduction to our technology and our **HUMIMIC Chips** have a look at our technology brochure:



Introducing: The HUMIMIC AutoLab

The **HUMIMIC** AutoLab is a small research lab that allows for the **automatic operation and observation** of up to **24 Multi-Organ-Chips** in parallel. It is compatible with the **HUMIMIC** Chip2, Chip3 and Chip4. The automation results in:



Increased throughput & assay complexity – with minimal manual effort!



Physiological & consistent culture conditions for higher reproducibility.



High-content data & AI based optimization of future assays.



Let's have a look at an ordinary **Multi-Organ-Chip assay**. It usually consists of the four steps shown on the right. All of these steps can be supported or even fully automated by the **HUMIMIC AutoLab**, as you will discover on the following pages.





1 Planning

With the **HUMIMIC LabOS**, we developed a software dedicated to the **HUMIMIC AutoLab**. It enables you to plan the execution of your individual automated assays – whether they are simple or complex. Schedule your **liquid handling processes**, such as medium exchanges and substance applications, as well as automated **microscopic imaging**. The modern and user-friendly interface is guiding you through the planning process step-by-step:

1

Create a new **assay** or load a pre-planned one.

2

Define the **pump settings** (e.g. pressure and frequency) for the medium circulation.

3

Create **conditions** by entering the characteristics of your Chips, such as organ models and medium type.

4
Choose & specify what the robot should do, such as "put liquid in" or "take liquid out".

5

Define **sequences** by assigning the tasks to your Chip compartments.

6

Schedule your sequences in **time blocks** (time of day & frequency).


7

Verify that your schedule is free from conflicts and your assay ready to go!

+

tasks that you perform, such as "take a picture".



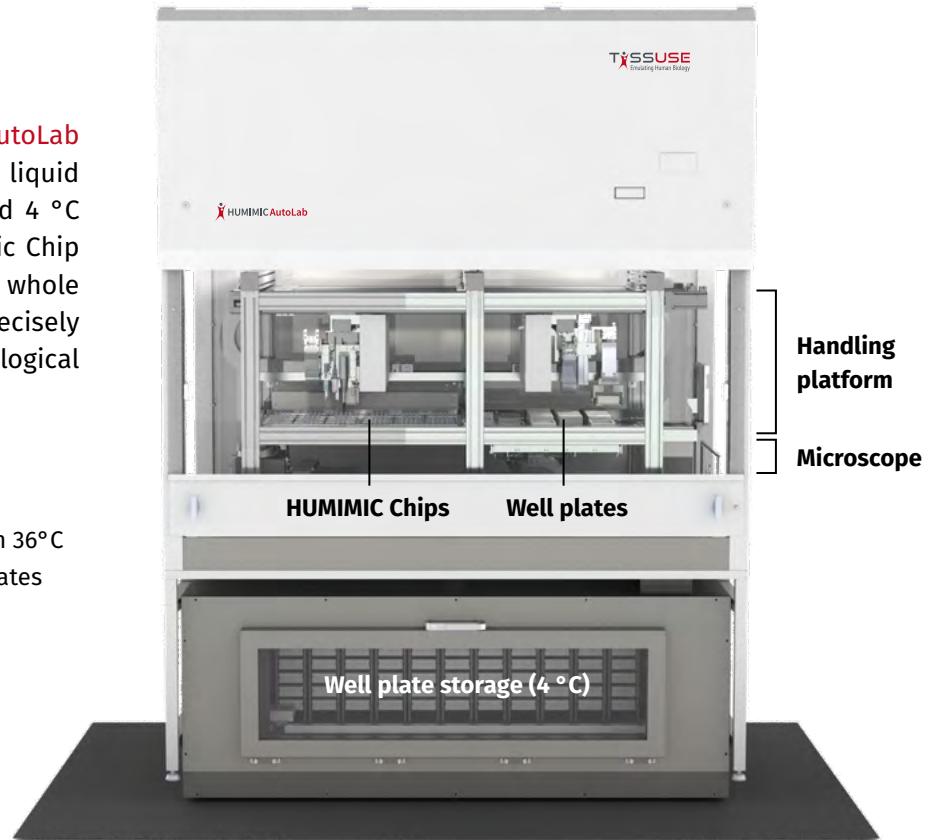


It's getting serious: Pipette tip boxes are placed on the platform before the start of the experiment.

2 Execution

The unique design of the **HUMIMIC AutoLab** – with its combination of Chip and liquid handling platform, microscope, and 4 °C storage unit – enables an automatic Chip operation for several weeks! The whole experiment takes place under precisely regulated, consistent, and physiological conditions:

- Sterile class II safety cabinet
- Temperature regulation: Separate incubation of Chips (adjustable from 36°C to 40°C) and pre-warming of well plates
- No interruption of cell-culture conditions
- Tubeless on-chip micropumps for medium flow regulation



A handling platform ...

Dispenser with a high repeat accuracy of pipetting steps and a pipetting range of <math><1</math> to 350 μl



**Multi-Organ-Chip
lid opener**

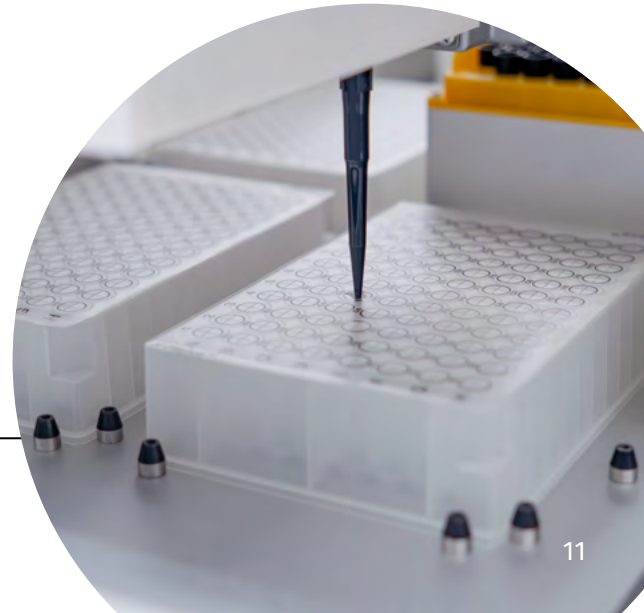


...with no time limitations

24/7 operating hours of the robot enable a **physiological dosing and feeding regimen**, which could otherwise only be achieved by shift and weekend work. Even frequent substance applications for PB/PK profiling are no longer a problem (see p. 20)!

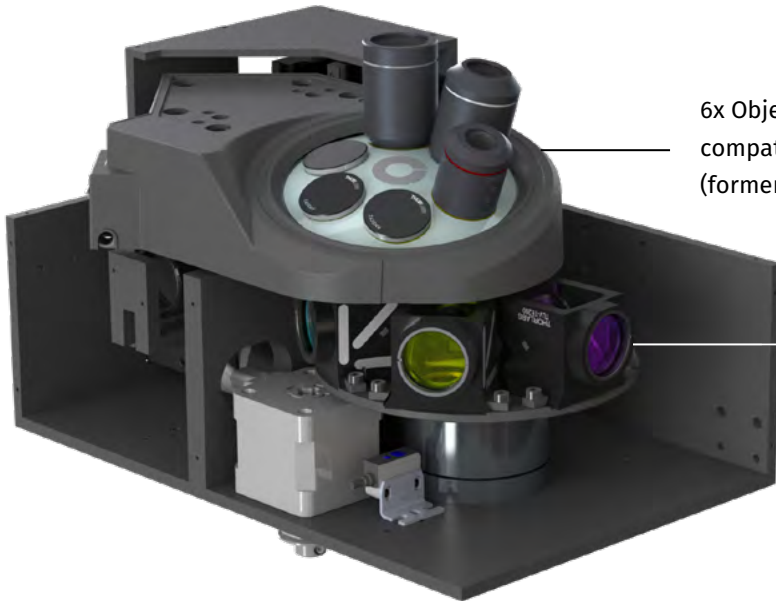


3 well plate positions
& automated transport



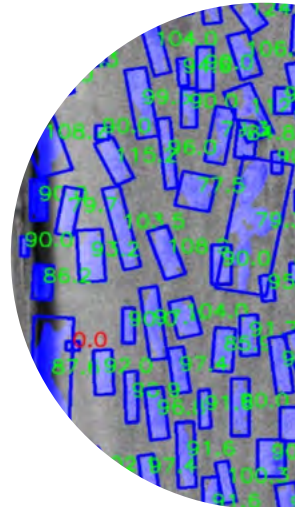
Observe your experiment – at all times

The **integrated Brightfield & Fluorescence microscope** can be operated manually and automatically.

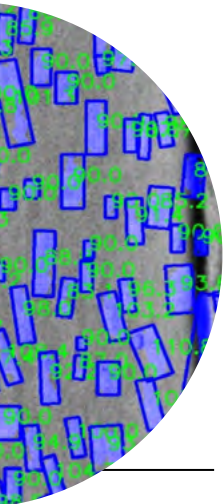


6x Objective turret,
compatible with *Evident*
(formerly *Olympus*) objectives

5x Fluorescence
filter changer



Spheroid tracking



AI based detection
of endothelialization



Microscopic observation and in-process analysis (e.g. spheroid tracking, CO₂ or pH heat maps, AI-based endothelial cell detection) and additional **direct measurements** (e.g. temperature, pressure) allow continuous monitoring of the experiment and thus **in-process quality control**. Detect potential assay outcomes ahead of time with the option to adjust the treatment!



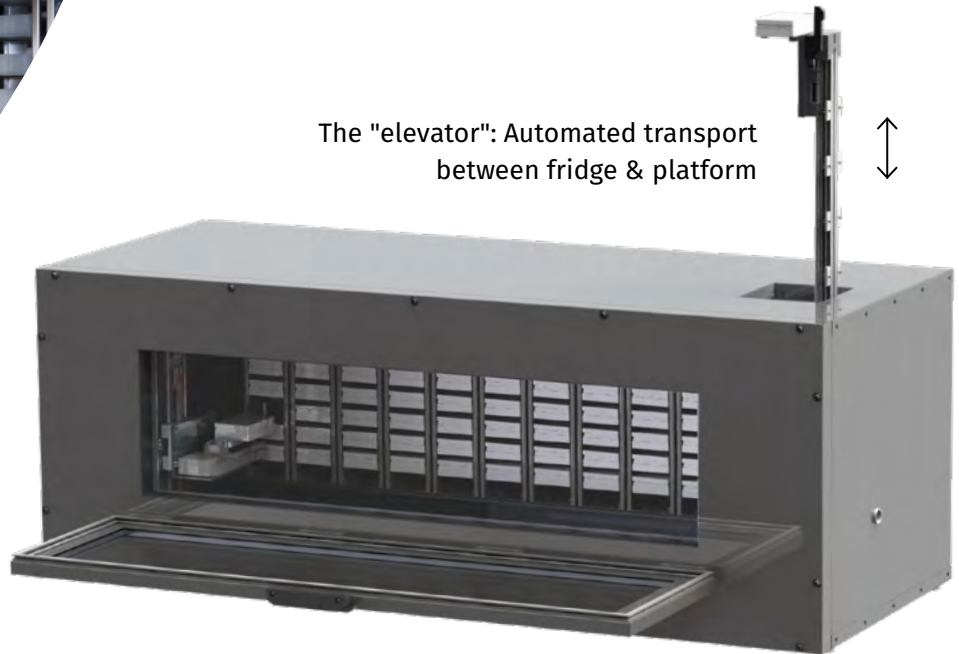
Keep it cool – at 4 °C to be exact

Store **samples, substances, and media** in the integrated refrigerator.

The "elevator": Automated transport between fridge & platform

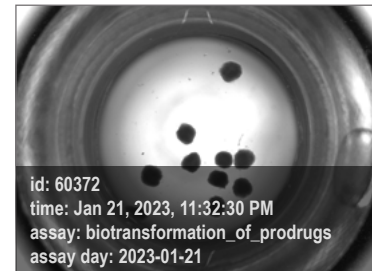
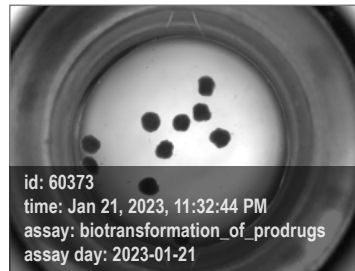
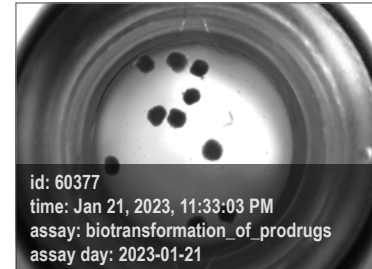
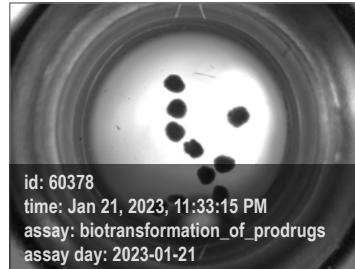
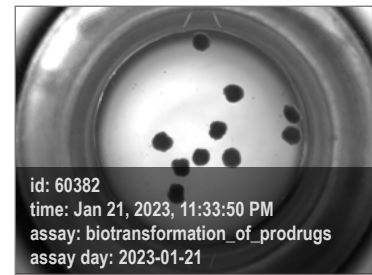
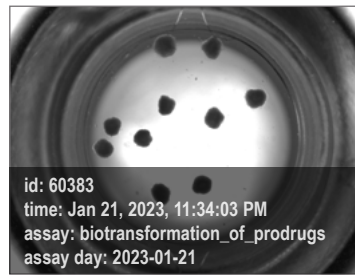


Room for up to 66 well plates



3 Evaluation & Documentation

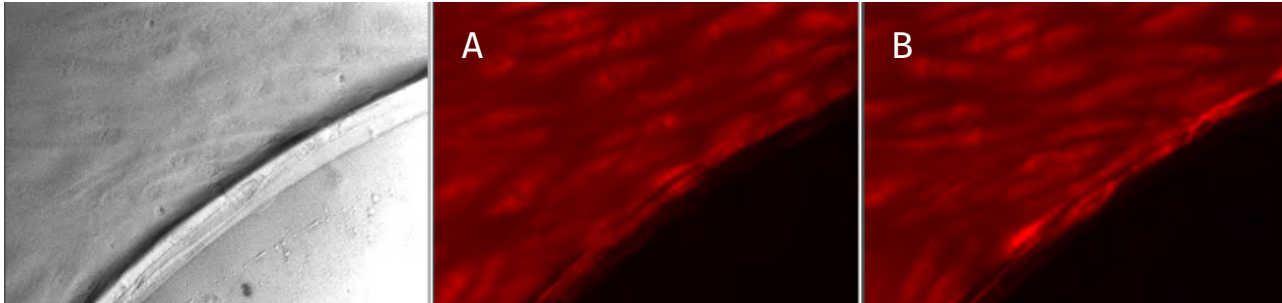
As shown on pages 12 and 13, you can already analyze and evaluate a lot of the recorded data while the experiment is still running. When it is time for the endpoint analysis, the tissue models can be retrieved from the Chips as usual. The **HUMIMIC AutoLab** can support you by automatically keeping a record of the sample plates. Another time saver is the automatic documentation: All images & metadata are saved and assorted directly in the **HUMIMIC LabOS**.



AI & Machine learning

With the **HUMIMIC AutoLab** you will not only gain **high-content data** (e.g. hundreds of microscopic images & associated metadata) but will also be provided the tools to transform these into usable readouts. Together with us, the possibilities to use and further develop **Machine learning & AI methods** are almost endless.

One example of this is virtual staining: After feeding the AI with a significant amount of data in the "learning phase" it is then able to generate virtual stainings – out of brightfield images alone. The results look remarkably similar to real stainings. Can you tell the difference?



Brightfield image

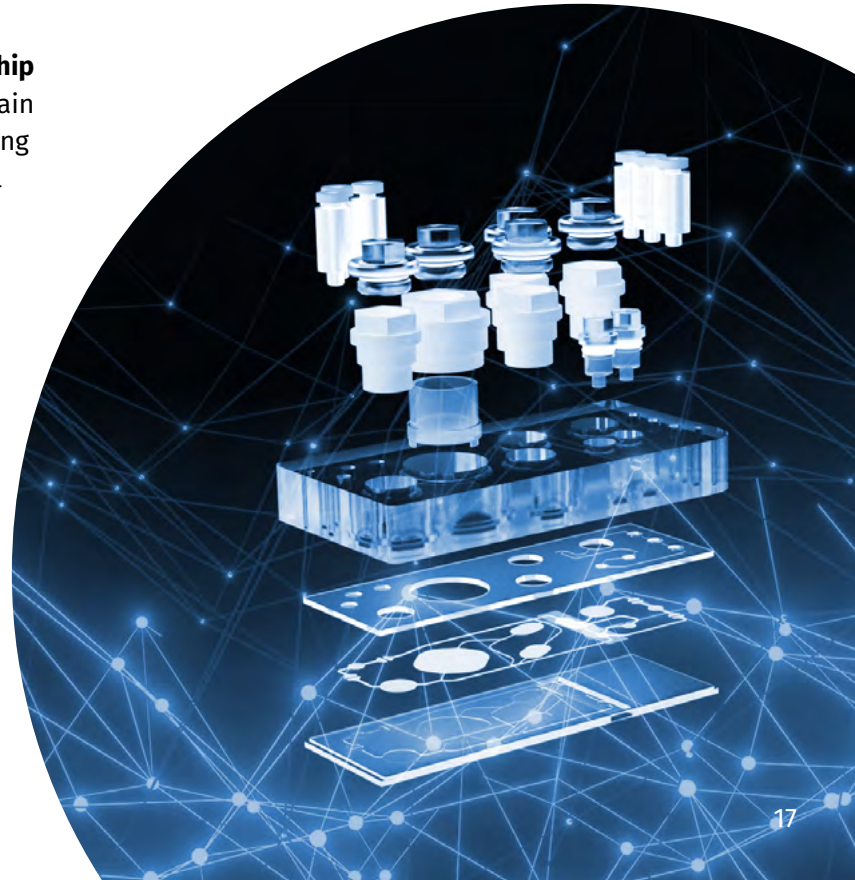
Real or AI? Find the solution on the next page.

4 Prediction & Optimization

We are convinced: **The future of Multi-Organ-Chip technology is digital.** With every assay, you gain more and more data – combined with existing theoretical models and AI methods, we will eventually be able to simulate and predict future assays even before they are executed.

Work with us and be a part of the digital revolution of Multi-Organ-Chips!

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Enough with the theory!

After we have gone through the four phases of a Multi-Organ-Chip assay in theory now, on these last pages you will find a few **practical examples** and real-life experiences.



Hands-on: Placing the Chips on the platform at the beginning of your experiment is one of the few manual activities left. Other than that you can sit back and focus on your other scientific tasks!

Overview of established assays

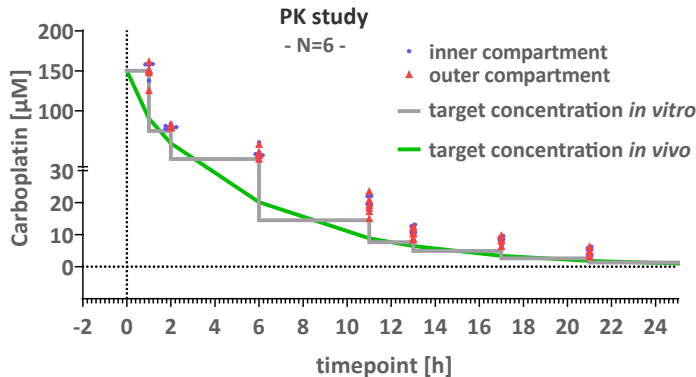
Organs	Objective	Duration
Liver	Feasibility assay adaptation on liver toxicity	7 days
Intestine & Liver	Industry assay on liver toxicity	14 days
Skin & Liver	Industry assay on liver toxicity	6 days
Bone marrow	Industry assay on hematotoxicity	35 days
Gastric cancer & Liver	Biotransformation of chemotherapeutic prodrugs	5 days
DLBCL* & Liver	Biotransformation of chemotherapeutic prodrugs	7 days
Neurospheres & Liver	Biotransformation of neurite growth inhibitors	7 days
Bone marrow	PB/PK assay	24 hours

* Diffuse large B-cell lymphoma

Bone marrow assay with PB/PK approach

As already mentioned, one of the main advantages of automated assay execution is the possibility of particularly elaborate or complex assays. Such as **PB/PK assays**: To recreate the known degradation curve of the substances, small-scale and very frequent dilution steps are necessary. During manual

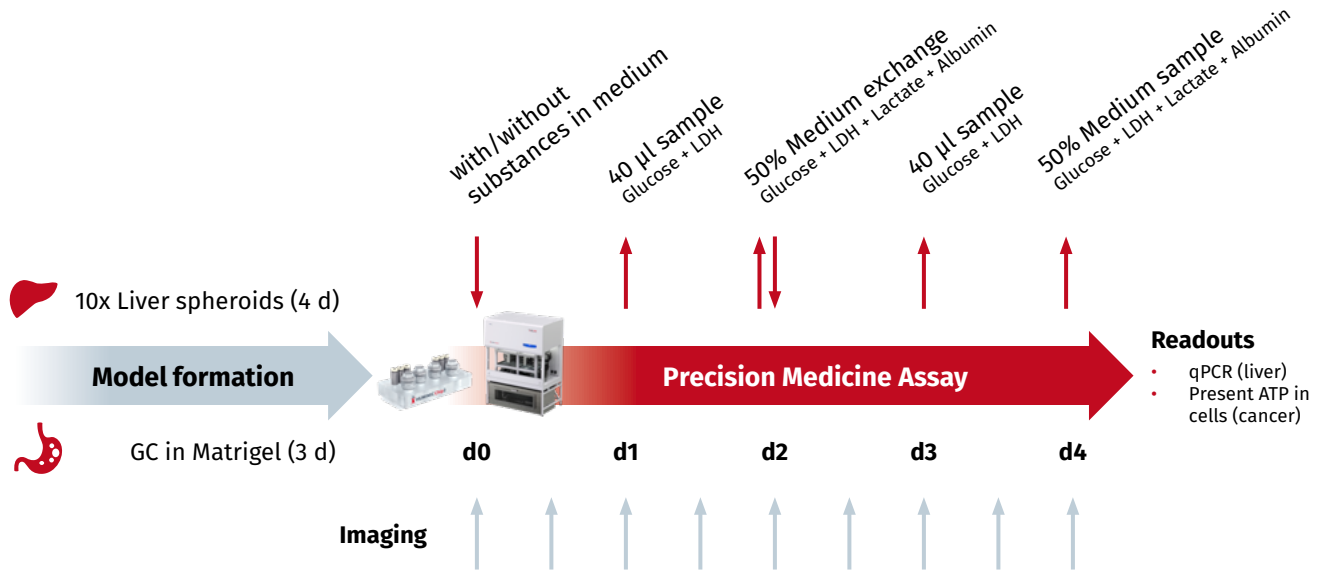
execution, this is either very time-consuming or not physiological enough, due to the reduction of the dilution steps. A problem that can easily be solved with the **HUMIMIC AutoLab!** These are the results of our automated 24h PB/PK assay:



- **Sampling and dilution every 1-4 h**
- **Theoretical concentration matches the concentration in the medium compartment**
- **ADME-like substance concentrations**

Gastric cancer & Liver

What could the planning of an automated assay look like? This is an exemplary experiment set-up of an assay where Gastric cancer (patient material) and Liver (HepaRG + HHStEC) were combined.



How was your experience working with the HUMIMIC AutoLab?



"The HUMIMIC AutoLab is a powerful automatization tool, which dramatically reduces my manual workload for larger experiments. While usually needing a helping hand for daily routines like medium exchanges, imaging and substance application, the 24/7 highly standardized handling of 24 Multi-Organ-Chips offers the possibility for even more complex regimes of experiments."

Ricky Bayer
PhD student, TU Berlin

Up to 85% time savings with a standard two-organ assay

48 circuits



Medium preparation
Every fourth day

0.5 h

0.5 h

0.5 h

...

0.5 h

Medium analysis
Every fourth day

0.25 h

0.25 h

...

0.25 h

Automated medium exchange

- up to several times a day
- 24/7 operation time

-3 h

-3 h

-3 h

-3 h

-3 h

-3 h

-3 h

-3 h

...

-3 h



Microscopy (Brightfield, Fluorescence)
Regular | Continuous

-1 h

-1 h

-1 h

-1 h

-1 h

-1 h

-1 h

-1 h

...

-1 h

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