

Multifors 2

Parallel bioreactor for rapid and statistically accurate process data



May be subject to technical amendments.
Images examples only.

www.infors-ht.com

We bring life to your laboratory.

INFORS HT



Two worlds, one philosophy!
 INFORS HT supports the Masoala rain forest project in Zurich zoo. You can find detailed information at www.infors-ht.com.

Cultivating customer visions

INFORS HT is a company of international reputation in the field of biotechnology

Innovative thinking, quality and an understanding of the needs of our partners has secured INFORS HT an unrivalled place amongst manufacturers of bioreactor and shaker equipment. An enthusiasm for experiment and a creative mind has guided the company from its establishment in 1965 through its development to become firmly established as an important player in the field of biotechnology engineering. Independence, a distinctive character and a strong team spirit will continue to serve us well in the future. www.infors-ht.com



About our Quality Label

The Quality Label is INFORS HT's acknowledgment of Switzerland as a centre for research, development and manufacturing. Certified specialists stand for the first-class, tested quality of our shakers and bioreactors in terms of their materials, workmanship, safety and reliability. "Quality – Made in Switzerland" is also our customers' guarantee of straightforward, swift order processing, short delivery periods, and flexible, efficient service in administrative matters too. INFORS HT attaches great importance to fulfilling individual customer needs, as well as to long-term, close and trustful partnerships with purchasers and suppliers alike.

Quality Standards
 • ISO 9001

For process validation to cGMP
 • Documentation
 • IQ
 • OQ
 • FAT & SAT

Multifors 2 at a glance

KEY BENEFITS

- Faster results with optimised parallel handling
- Flexible and application-optimised configurations
- Space-saving, compact design
- OPC server for unlimited connection
- Precise control of your bioprocess
- 100 % aseptic sampling
- Clear path to scale-up

Touch screen controller with OPC server

Open-frame gas supply (massflow controller and/or rotameter)

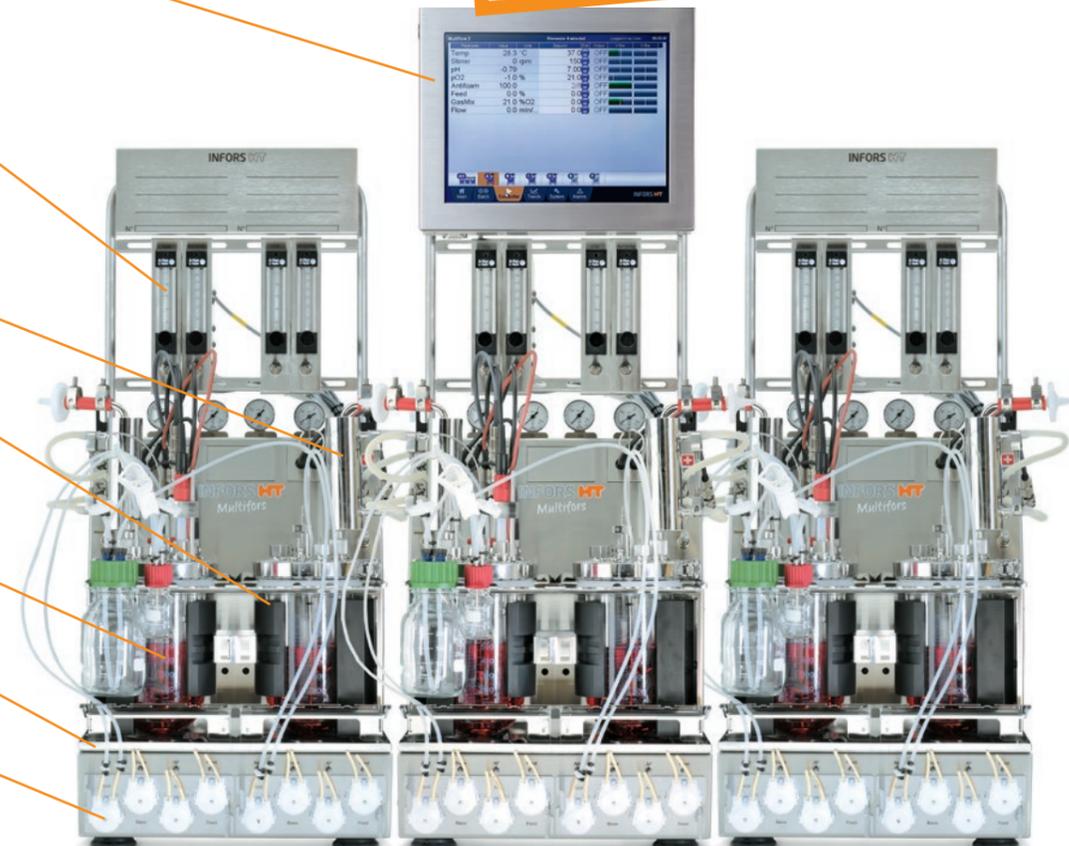
Thermodynamic exit gas cooler

Temperature control module

Fully equipped vessels

Magnetic drive system

High-precision pumps



Key technical data

Dimensions (W x D x H): 350 x 520 x ~960 mm
Working volumes: 100–250 mL / 180–500 mL / 320–1000 mL (bacterial system); 75–250 mL / 150–500 mL / 220–750 mL (cell culture), in pairs
Maximum expansion: 3 base units per operating panel, i.e., 6 vessels
Speed ranges: 100–1600 min⁻¹ for bacterial systems (depending on the vessel size), 30–300 min⁻¹ for cell cultures
Temperature range: 5 °C above coolant to 70 °C
Standard parameters: Stirrer speed, temperature, pH, pO₂, antifoam, feed

Applications

- Process development
- Process optimisation
- Scale-up
- Scale-down
- Statistical studies
- Process analytical technology (PAT)
- Media development
- Growth studies
- Toxicity testing
- High-throughput screening

What you get with Multifors 2

The INFORS HT Multifors 2 is especially designed for multiple, parallel bioprocesses in small volumes. Multifors 2 together with the parallel bioprocess software Iris offers the rapid and statistically accurate way to generate and understand process data. With a choice of preconfigured packages and an extensive list of options, Multifors 2 is always application optimised for your fermentation of microbes or your cell culture bioprocess. Different cultivation strategies such as culture in batch, fed-batch and continuous modes are possible. INFORS HT have been the pioneers in this technology for decades and our product and application specialists continuously improve and optimize the system for rapid parallel handling on the smallest possible space.



KEY FEATURES

Space-saving compact base unit

An extremely compact freestanding device, with two completely individual bioreactors located within a single base unit. Up to six bioreactors can be connected to one controller and require approx. 1.2 m of bench space. Groups can be built up two at a time and separated, moved and recombined as required. This gives more flexibility regarding location in a laboratory and the opportunity to add more base units and/or controllers to build the array you need.

Fully equipped vessels

The Multifors 2 has fully equipped vessels with working volumes from 75 mL up to 1 L with the characteristics of larger systems. The 316L stainless steel top plate includes many industry standard PG13.5 ports, enabling a wide array of sensors to be fitted (anti-foam, optical density, pH, pO₂, redox, capacitance, etc.).

Different vessel sizes are available. The vessel interior can be configured in a number of different ways with choices of impellers, spargers and special accessories, such as a draft tube or spin filter. A range of optional fittings are available to cover almost any possible application.

The construction and design of the vessels (with no welded parts) make Multifors 2 ideal for applications where GMP conditions have to be faithfully observed.

High-precision temperature control module



The aluminum heating block with integral cooling coil replaces the need for glass water jackets or heater pads. This aids easy handling, limits the weight of the vessel and allows a clear view to your bioprocess. Temperature ranges from approx. 5 °C above coolant to 70 °C.

100% aseptically designed stirring system

The Multifors 2 stirring system is a bottom drive system especially designed for aseptic small-volume parallel bioprocesses. It simplifies the removal of the vessel, reduces the risk of contamination and allows more space on the top plate. Optimised configurations are available for microbials and cell cultures. For details see pages 6/7.

Services requirements

- Electrical:** 230 V 5 A (option 120 V 10 A) supply, 50/60 Hz
- Air:** Clean, dry, oil-free air at 1 bar (reduced internally)
- Water:** Cold water at approx. 1 bar, <50 ppm suspended solids
- Drain:** Lower than unit, no back pressure

Multifors 2 can integrate with a house water supply, or with a chiller unit.

May be subject to technical amendments.

Open-frame gas supply with up to 4 mass flow controllers

The open frame gas supply is highly flexible and allows a free choice of mass flow controllers, rotameters and gas mixing for up to 4 gases (air, N₂, O₂ and CO₂, each with integrated pressure control) in virtually any combination between the sparger and the headspace. Optimised configurations are available for microbials and cell cultures. For details see pages 6/7.

More reproducible and accurate results thanks to the innovative thermodynamic exit gas cooler

Excessive loss of liquid from a bioreactor vessel as water vapour can be serious at any scale but is even more critical when small volumes are used. The internal structure of the INFORS HT exit gas cooler condenses moisture leaving in the exit gas stream with maximum efficiency.



Time-saving, high-precision pumps

Four high-precision pumps per vessel are included for feed, acid, base and antifoam as standard. This makes the Multifors 2 ready for applications such as fed-batch or continuous culture out of the box.

The pump heads can be removed on a single plate in groups of 4 and autoclaved with the vessel. This reduces handling time considerably as tubing does not need to be threaded around the pump heads and adjusted before use. Handling errors due to misplaced pumps and tubing are completely eliminated with this unique construction. Set-up simply involves relocating the plate back into position. Automatic emptying, filling of tubing and calibration of the pumps makes the task even easier.

Super Safe Sampler – 100 % aseptic and absolutely hygienic sampling



The INFORS HT Super Safe Sampler allows you to take smallest samples without wasting any culture. This helps to get more precise results especially in small-scale bioprocesses due to minimum loss of culture volume. The truly aseptic design makes contamination during sampling impossible.

Vessel specifications

700/750 mL total volume (inner diameter 70 mm)
 4 x 12 mm/PG13.5 for sensors, exit gas cooler and inoculation
 4 x 10 mm for Pt100, sparger, sample/harvest and antifoam/level
 4 x 7 mm for corrective reagents, feed etc.

1000/1400 mL total volume (inner diameter 90 mm)
 5 x 12 mm/PG13.5 for sensors, exit gas cooler and inoculation
 Other sizes as 500 mL working volume (see above)

Maximum dimensions for two vessels in vessel holder
 400 ml working volume: 395 mm high x 385 mm diameter
 500 mL working volume: 409 mm high x 385 mm diameter
 750/1000 mL working volume: 435 mm high x 385 mm diameter

May be subject to technical amendments.

HIGHLIGHT

Get faster results with optimised parallel handling

A support frame carries both culture vessels, 4 reagent bottles and 8 pump heads all together for autoclaving. This reduces handling time considerably.

3 easy steps and you're ready to go

1) Replace vessel holder on base unit



2) Fit plates with pump heads



3) Synchronised start of all bioreactors



Individual configuration for your application

Multifors 2 Fermentation



INFORS HT has over 45 years experience in designing bioreactors to provide powerful mixing, good temperature control plus flexible oxygenation and feeding strategies. All this know-how has been transferred into the Multifors 2.

SPECIAL FEATURES

High cell density and process understanding

The Multifors 2 stirring system is especially designed for aseptic small-volume parallel bioprocesses. It reduces the risk of contamination and allows more space on the top plate for many sensors. Together with the parallel bioprocess control software Iris there are no limits for your cultivation strategy and more process understanding.

The bottom drive stirring system is powerful and reliable, with stirring speed up to 1200 min⁻¹ to set no limits to high cell density cultures. Rushton impellers and a ring sparger for high gas flow rates are included as standard. The mixing and mass transfer characteristics are scalable with standard bench-scale stirred tank reactors.

A simple test demonstrates the power of the magnetic coupling: Pure Glycerol can be stirred continuously at 1100 min⁻¹ (at room temperature, no gassing) without slipping of the coupling or overload of the motor.

Customised gas strategy

The INFORS HT open-frame gassing system offers very precise gas mixing and gas flow control for highly accurate pO₂ control. The whole system offers a very high k_La that is comparable to larger system to make scale-up as easy as possible. Any combination of air, O₂, N₂ or any other single gas can be directed into the sparger or head space.

As standard for microbial cultivation we recommend:

- pO₂ control: Air and O₂ to sparger via mass flow controller

Multifors 2 Cell



For culture of suspended mammalian cells (CHO, HEK, etc.) and insect cells (Sf9, HiFive, etc.), as well as adherent cells on microcarriers. All equipment is fully optimised for sterile and reproducible parallel bioprocesses, which allows advanced cell cultivation to your wishes.

SPECIAL FEATURES

100 % aseptically designed low-speed stirring system

The open axial magnetically coupled stirring system uses a slow-speed bottom drive motor (30 up to 300 min⁻¹) for gentle and reliable mixing. A pitched blade stirrer is included as standard, which allows a shear-stress-free movement and mixing of the cells. The magnetic coupling is easy to clean and 100 % aseptically designed without compromises.

Customised gas strategy

The INFORS HT open-frame gassing system offers very precise gas mixing and gas flow control for highly accurate pO₂ and pH control. This is especially important for optimal cultivation of sensitive cell cultures. Any combination of air, O₂, N₂ or CO₂ as single gas or gas mix can be directed into the sparger or head space.

As standard for cell culture we recommend:

- pO₂ control: Air, O₂ and N₂ to sparger via mass flow controller
- pH control: CO₂ to sparger via mass flow controller
- Antifoam: Headspace aeration with air as mechanical anti-foam device

Perfusion

A spin filter is often used for both immobilised cell cultures and those in suspension because of its easiness to scale-up. A rotating filter keeps cells outside, creating a pool of cell-free medium inside the filter cup. Cell-free medium can be removed and replenished with fresh medium, continuously or in batches. Multifors 2 Cell can also be set up with other perfusion systems, e.g., hollow-fibre module for tangential flow filtration (TFF), alternating tangential filtration (ATF) or ultrasonic resonance system.

May be subject to technical amendments.

Cultivation of adherent cells

Adherent cell types (e.g., Vero, HeLa, BHK, etc.) are anchorage dependent and have to be cultured on suitable surfaces. For cultivation in stirred cell bioreactors adherent cells can be immobilised on micro carriers, disks or beads of silica, glass, dextran or similar materials. An optimal process control and gentle stirring of the Multifors 2 Cell system allows adherent cells to be cultured without the need for lengthy cell line adaptation to suspension culture.

Cultivation of stem cells

Cultivation of hematopoietic or embryonal stem cells, in suspension or on immobilised materials needs not only specialised cultivation media for expansion and proliferation. A precisely controlled cultivation system with accurate pO₂ and pH control, as well as shear-stress-sensitive mixing and sparging systems makes Multifors 2 Cell the ideal choice for parallel stem cell cultivation.



Packages Multifors 2

| | Microbial Package | Cell Culture Package |
|--|---|---|
| Compact base unit | | x |
| Fully equipped vessels | | x |
| – Total volume per vessel | 400 mL / 750 mL / 1400 mL | 400 mL / 700 mL / 1000 mL |
| – Working volume per vessel | 100–250 mL / 180–500 mL / 320–1000 mL | 75–250 mL / 150–500 mL / 220–750 mL |
| – Vessel type | Flat bottom | Round bottom |
| – Stirrer type | 2 Rushton impellers | 1 Pitched blade impeller |
| – Sparger type | Ring sparger for microbials | Ring sparger for cell culture |
| – Baffles | Only in 1400 ml vessel | No baffles |
| Temperature control module | | x |
| Magnetically coupled stirrer system | | x |
| – Stirrer speed | 100–1600 min ⁻¹ (depending on the vessel size) | 30–300 min ⁻¹ |
| Open-frame gas supply | | x |
| – Gas mix | Air/O ₂ for pO ₂ control Options for other gas mix | Air/O ₂ /N ₂ gas mix for pO ₂ control CO ₂ for pH control Options for other gas mix |
| – Submerge gassing | Gas mix to sparger (approx. 0.02–2 vvm) | Gas mix to sparger (approx. 0.001–0.1 vvm) |
| – Headspace gassing | Optional | Air to headspace (approx. 1 vvm) |
| – Gas flow control | | Mass flow control or rotameter |
| Thermodynamic exit gas cooler | | x |
| 4 High-precision pumps (1 analog + 3 digital) | | 0.0034–3.46 mL/min (standard) 0.017–17.16 mL/min (option) 0.0012–1.24 mL/min (option) |
| Super Safe Sampler | | x |
| Touch screen controller with OPC server | | x |

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Touch screen with OPC server

Bioprocess control begins with the quality and flexibility of the local controller. The Multifors 2 touch screen controller provides accurate and reliable measurement, control and communication with supervisory software. The touch screen controller is able to provide individual control for up to 6 bioreactors. Key parameters for all six vessels are shown in an overview main screen but control of each unit is fully independent.

Unlimited connection with external devices

As a standard the Multifors 2 has an integrated OPC server. Connecting external devices such as HPLC, MS, glucose analyser, etc., is possible via analogue in/out signals, Modbus or OPC XML DA. The integrated OPC server also provides a link to SCADA software via a network.

Very flexible cascade control

All measured parameters can be cascaded to another parameter to provide control without any limitation. Parameter configurations can be saved and reused.

Faster setup with the INFORS HT ALL functions

The ALL functions make emptying and priming of pumps easy even if a full system with 24 pumps is used. Each set of pumps can be defined separately, e.g., all the acid pumps for duration of the filling or emptying operation.

- Calibration of pH and pO₂ probes with one push of a button
- Start ALL/Stop ALL capability for ease of handling with multiple vessels

Easy to use

The user interface has been optimised after detailed testing by users, psychologists and usability experts and features simple and intuitive operation. A tabbed menu system makes it easy to find associated items together and move between options. Password protection and different user levels allows personnel with varying degrees of knowledge and experience to safely use the bioreactor.

Simple connection of peripheral equipment

A connector is provided as standard for additional analogue inputs and outputs (from sensors and pumps typically). Additional parameters can be added quickly and without the additional expense of extensive reprogramming.

Up to 24 parameters per vessel

- Temperature
- Stirrer speed
- pH
- pO₂
- Antifoam
- Feed
- + 16 free channels



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Accessories

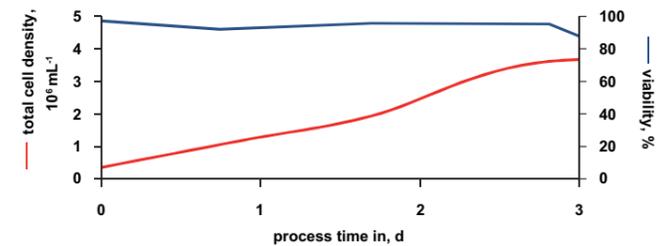
Integration of external sensors or analysers

With several freely programmable channels and the integrated OPC XML DA server as standard, the integration of sensors and external analysers is very easy.

External sensors or analysers such as HPLC, MS, glucose measurement devices, etc., can be integrated via analogue signals, Modbus or OPC XML DA. With the Iris bioprocess software, all parameters can be combined and cascaded individually.

Online cell density and biomass

INFORS HT provides solutions for the online detection of cell densities and biomass. You'll get a better understanding of your processes without manually taking a sample, which reduces your process time significantly.



As a standard, we provide the Optek ASD12-N sensors for automated detection of both total cell density and biomass during the cultivation of cells or microorganisms. The ideal sensors will be chosen for your application.

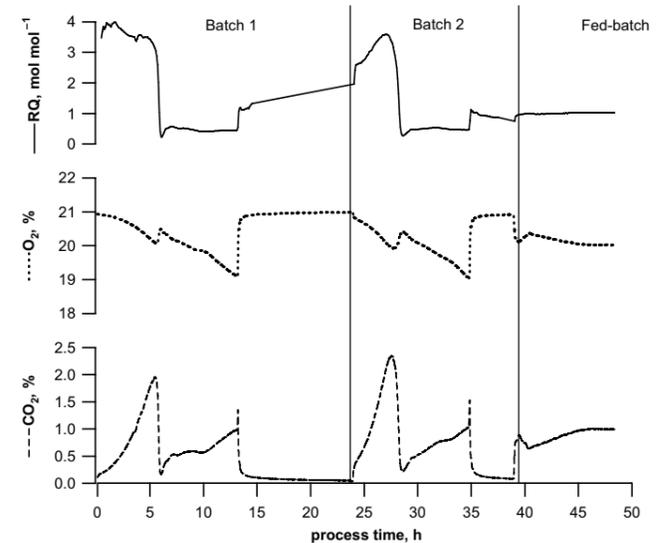
For determining the viable cell density, sensors from ABER Instruments can also easily be operated with the INFORS HT Multifors 2.

RQ measurement and control

INFORS HT offers you professional solutions for O₂ and CO₂ analysis for metabolic studies and bioprocess control: the INFORS HT Gas Analyser or BlueSens gas sensors.

The O₂ or CO₂ analysis can be seamlessly integrated into your bioreactor, thus enabling you to make direct estimations as to the condition of the culture during the actual bioprocess. The Iris software allows the calculation of parameters such as the CO₂ evolution rate (CER), the O₂ uptake rate (OUR) and the resulting respiratory quotient (RQ).

This in turn makes it possible to adopt a systematic approach to bioprocess control, to maintain specific metabolic states and to prevent O₂ limitations or substrate limitations.



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Qualification

Compliance with regulatory requirements is becoming a critical issue for more users each year. INFORS HT provides a full qualification service with standard or customised packages to meet this need, e.g., cGMP compliance.

What is available?

The process starts with the Design Qualification and then planning of the production for qualification. Testing occurs at many points in the process and usually ends with a Factory Acceptance Test (FAT).



A package of comprehensive documentation is prepared and shipped with the bioreactor. Tests for IQ (Installation Qualification) and OQ (Operational Qualification) can then be made using this information. Site Acceptance Test (SAT) is typically carried out to show the equipment meets all necessary requirements.



Our Iris software is compliant with international standards such as FDA 21 CFR Part 11.

An important point to note is that ALL our bioreactors are manufactured to exactly the same high standards, it is only the amount of testing and documentation which varies.

Service and support



At INFORS HT, we are committed to providing the very highest level of customer support and service, based on our principles of customer proximity, expertise and efficiency.

- Close and direct contact with our specialists
- Technical and scientific experts
- Fast responses when you need it

Our high-quality service sets INFORS HT ahead and makes a real difference for our customers. Key services enable our users to get the most from their equipment, quickly and easily.

- Customer support (email, phone, on site)
- Technical solutions for special requests
- Installation and commissioning
- Equipment and application training
- Preventative maintenance

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As unique as your bioprocess!



Multitron Cell



Labfors 5



Techfors

INFORS HT equipment is individually adapted to meet the needs of your bioprocess. Our designers and application experts take the time to configure an optimised solution to your needs in partnership with you. Combined with the INFORS HT Iris bioprocess software, the full potential productivity of your cell culture or microbial fermentation can be successfully unlocked.

From laboratory-scale shaker to pilot-scale bioreactor

As different as these devices are, you will find they have a lot in common:

- Individual configuration for your application
- Simplified handling
- Common operation and control
- Turnkey equipment which is usable "out of the box"
- Exceptional Swiss quality
- Outstanding service and support from day 1

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