

Evaluation of MIRI[®] M IVF Incubator as a Culture System

Validated Performance and Future-Ready Flexibility for Modern IVF Labs



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MIRI® M multiroom IVF incubator

Executive Summary

The MIRI® M multiroom IVF Incubator represents a next-generation solution in assisted reproductive technology, combining validated performance, exceptional environmental stability, and unprecedented workflow flexibility. Independently evaluated under GLP conditions by Embryotools®, the MIRI® M multiroom IVF incubator has been proven to provide embryo culture conditions equivalent to gold standard benchtop incubators while introducing a modular design with 18 independent chambers, integrated backup power, and consistent developmental outcomes [1]. This white paper summarizes the scientific validation, key performance indicators (KPIs), including cleavage rate, blastocyst formation, embryo quality, and clinical implications of MIRI® M multiroom IVF incubator for modern IVF laboratories.

Introduction

Redefining Embryo Culture in the Modern Lab

Optimizing embryo culture conditions is one of the most critical determinants of success in assisted reproduction, as even small fluctuations in environmental parameters can significantly affect fertilization, cleavage, and implantation outcomes [2]. Studies have demonstrated that stable temperature, pH, humidity, and gas concentration are fundamental to maintaining embryo viability and genomic integrity during *in vitro* culture [3].

Modern IVF laboratories require incubators that deliver not only stable and controlled environments but also operational flexibility to support evolving clinical workflows. Traditional benchtop incubators, while effective, are limited in their adaptability to dynamic laboratory conditions, and interruptions such as frequent lid openings or manipulations can disturb critical microenvironmental stability and alter embryo morphokinetics [4].

The MIRI® M multiroom IVF incubator addresses this need by offering precise environmental control combined with modular functionality that enables uninterrupted, continuous embryo culture. Its innovative design allows each independent chamber to be undocked and transported without compromising the controlled environment, delivering reliable performance validated under rigorous laboratory conditions.

Validated Performance Under Independent Lab Conditions

Embryotools®, a leading independent laboratory specializing in assisted reproduction research, quality control, and device validation, conducted a comprehensive validation study to assess the performance of the MIRI® M multiroom IVF incubator.

A total of 438 mouse embryos were cultured, whereas 378 were cultured in the MIRI® M multiroom IVF incubator and 60 in standard benchtop incubator (MIRI® multiroom IVF incubator) serving as control. Across all incubator’s performance indicators (cleavage rate, blastocyst formation, blastocyst quality, and total cell counts) MIRI® M multiroom IVF incubator showed no statistically significant difference compared with the control group.

These findings confirm that MIRI® M multiroom IVF incubator maintains embryo viability and morphology equivalent to industry benchmark system, demonstrating that its design and environmental control capabilities effectively sustain optimal conditions for embryo development.

Measurements of Device Performance and Effectiveness

Key performance indicators (KPIs) are critical for evaluating the effectiveness of IVF incubators. Following the Vienna Consensus, routine monitoring of cleavage, embryo development and blastocyst formation enables early identification of environmental deviations and supports the maintenance of optimal culture conditions [5]. The Embryotools® validation study assessed multiple KPIs, demonstrating that MIRI® M multiroom IVF incubator consistently meets or exceeds international benchmark standards [1]. A summary of these results is presented in **Table 1**.

Table 1. Embryo Culture KPIs – Comparison of MIRI® M Performance and ESHRE Standards.

KPI	ESHRE Competency	ESHRE Benchmark	MIRI® M Result	Interpretation
Cleavage Rate (Day 2)	>95%	>99%	99.5%	Meets benchmark, excellent early development support
Blastocyst Development Rate (Day 5/6)	≥40%*	≥60%*	95–96%	Exceeds benchmark, robust extended development
Good Quality Blastocyst Development rate (Day 5/6)	≥30%**	≥40%**	~90%	Exceeds blastocyst quality standards, aligned with consensus criteria

***Note:** The additional 10 – 15% blastocyst formation by Day 6 is considered a supplementary **performance indicator** according to ESHRE guidelines.

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- **Cleavage rate:** This KPI is defined as the proportion of zygotes that cleave to become embryos on Day 2 (44 ± 1 h post-insemination). It provides an indication of the ability of the culture system to support cleavage of fertilized oocytes (i.e. with occurrence of cellular division), and of embryo viability, so a low cleavage rate could be a warning that the culture system has been impacted by an extrinsic factor. Monitoring cleavage rates helps ensure that the incubators provide a stable environment for early embryo development. The reference values: **competency >95%; benchmark >99%** [5].

Embryo culture in the MIRI® M multiroom IVF incubator achieved a cleavage rate of 99.5% (Table 1 and Figure 1), meeting the ESHRE benchmark and demonstrating excellent support for early embryo development.

- **Blastocyst formation rate:** This KPI is defined as the proportion of blastocysts observed at 116 ± 2 hours post-insemination as a function of the number of normally fertilised oocytes. It estimates the ability of the culture system to support blastocyst formation from fertilised oocytes and provides an indication of embryo viability. The reference values: **competency $\geq 40\%$; benchmark $\geq 60\%$ (Day 5)**. An additional performance indicator might be the development of an **additional 10 – 15% blastocysts by 140 ± 2 hours post-insemination (i.e., by Day 6)** [5]. Monitoring blastocyst development rates helps ensure that the incubators provide optimal conditions for later stages of embryo development.

Embryo culture in the MIRI® M multiroom IVF incubator achieved a blastocyst formation rate of 95.8% by Day 5 and 96% by Day 6 (Table 1 and Figure 1), exceeding ESHRE benchmark thresholds and confirming the incubator's ability to support extended embryo development.

- **Good quality blastocyst rate:** This performance indicator is defined as the number of good-quality blastocysts as a function of the number of normally fertilised oocytes. Blastocyst quality is defined in the Istanbul consensus [6]. This indicator estimates the ability of the culture system to support the formation of high-grade blastocysts from fertilised oocytes and provides an indication of embryo viability. The reference values: **competency $\geq 30\%$; benchmark $\geq 40\%$ (Day 5)**. An additional performance indicator might be the development of an **additional 5 – 15% blastocysts by 140 ± 2 hours post-insemination (i.e., by Day 6)**, depending upon the culture system [5]. Ensuring high-quality blastocyst development is crucial for successful embryo transfer and implantation.

Embryo culture in the MIRI® M multiroom IVF incubator demonstrated a good quality blastocyst rate of 89.8% by Day 6 (Table 1 and Figure 1), far surpassing ESHRE standards and highlighting its effectiveness in supporting the development of high-grade embryos with strong implantation potential.

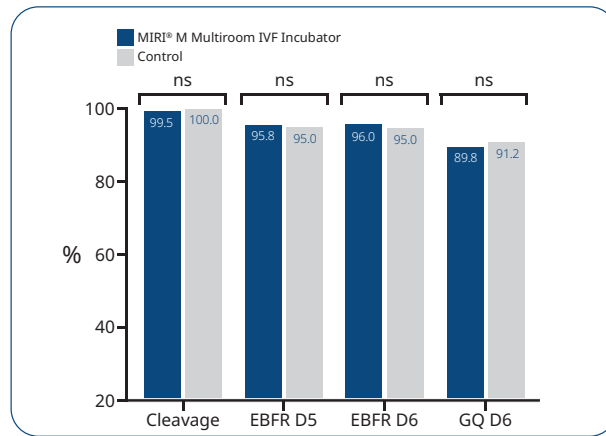


Figure 1. *In vitro* assessment of cleavage rate, expanded blastocyst formation rate (EBFR) on Day 5 and Day 6 and good quality blastocyst rate (GQ) on Day 6. The parameters studied are compared between the MIRI® M multiroom IVF incubator and the control. Results show no statistically significant differences (ns, $p > 0.05$) between groups across all parameters measured, indicating comparable performance in supporting embryo development.

- **Total cell counts:** This performance indicator represents the total number of cells within a blastocyst, reflecting the cumulative outcome of cellular division throughout preimplantation development. Because cellular division is considered the single most important indicator of embryo viability, total cell count provides valuable quantitative information on the embryo's proliferative capacity and development competence [7]. Higher total cell numbers are generally associated with improved implantation potential and better clinical outcomes. Monitoring this parameter therefore complements traditional morphological and morphokinetic assessments by offering deeper insight into the culture system's ability to sustain optimal growth conditions.

The total cell counts consistency were comparable across all 18 the MIRI® M multiroom IVF incubator chambers and the control system ($p > 0.05$), as shown in Figure 2, confirming that the incubator effectively maintains a stable microenvironment that supports normal cellular proliferation throughout development.

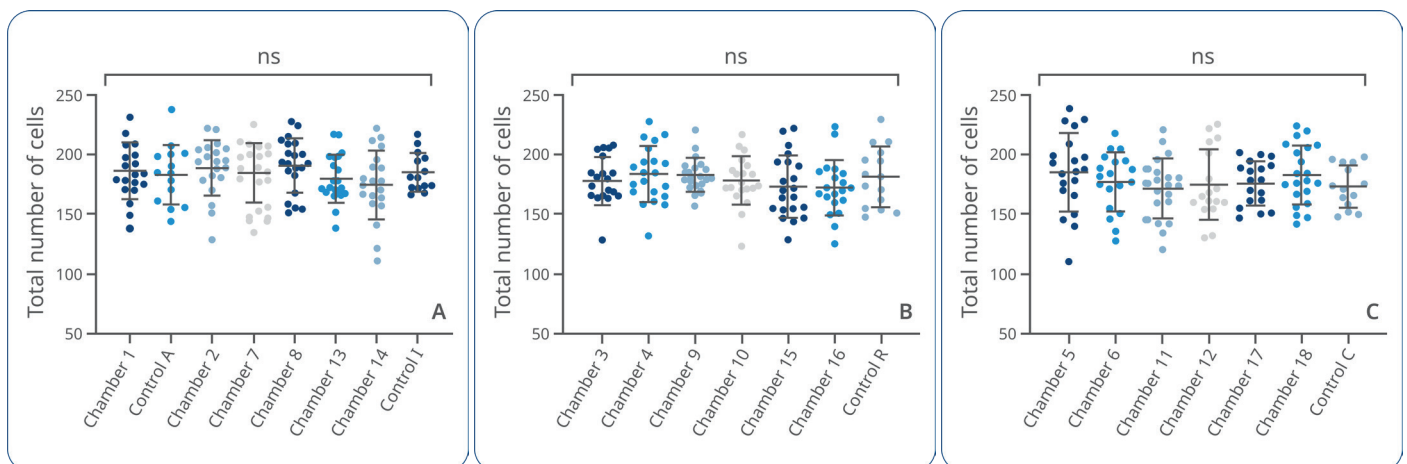


Figure 2. *In vitro* assessment of total cell number per blastocyst across all 18 chambers of the MIRI® M multiroom IVF incubator and the control system. The total cell counts showed no statistically significant difference (ns, $p > 0.05$) between groups, indicating consistent culture conditions across all 18 chambers and confirming the incubator's ability to maintain a stable microenvironment that supports normal cellular proliferation throughout preimplantation development.

Importance of Environmental Control and System Resilience in IVF Labs

Maintaining a stable and controlled environment is fundamental to the success of *in vitro* embryo culture in IVF. The goal of *in vitro* embryo culture is to provide conditions that will lead to the production of embryos that have the same developmental potential as the embryos that develop *in vivo* [2]. Precise regulation of key parameters such as temperature, gas composition, pH, humidity, and osmolality directly influences embryo viability, genomic stability, and developmental potential. At the same time, system resilience, the ability of IVF incubator to maintain optimal conditions despite external fluctuations or operational disturbances, is critical to ensuring uninterrupted embryo culture.

Factors influencing stability of the culture environment

Temperature Stability

Using and maintaining a stable and physiologically appropriate temperature throughout the embryo culture process is one of the most critical determinants of optimizing IVF culture system because abnormal temperatures may lead to increased embryonic fragmentation, delayed cell division, and even chromosomal abnormalities and thus compromise IVF outcome. *In vitro* handling of gametes or embryos generally goes through three cycles with temperature differences: from a 37.0 °C incubator to room temperature; from room temperature to a heating microscope stage; and from the microscope stage to a 37.0 °C incubator [8].

Physiologically, the reproductive tract presents a dynamic temperature gradient, with regions being 0.2 – 2.3 °C cooler than core body temperature, suggesting that the *in vivo* embryonic microenvironment is not uniform [8, 9]. Despite this variability, numerous studies indicate that a culture temperature close to 37.0 °C remains optimal for human embryo development [2, 3]. Even minor deviations from optimal thermal conditions can compromise embryo quality, as both hypothermic and hyperthermic conditions, with gradual variation from 35.0 to 37.5 °C, significantly affect blastocyst formation rates and mitotic cell division timing [9], although a slightly lower temperature might be safer than higher temperature [2].

Experimental validation of the MIRI® M multiroom IVF incubator confirmed excellent temperature stability across all 18 chambers under normal laboratory conditions, as shown in the temperature profiles of Figure 3.

When the chambers were docked in the MIRI® M Docking Station, the average temperature over a 24-hour period ranged from 36.92 °C to 37.06 °C, with a minimal standard deviation of 0.01–0.03 °C, indicating highly consistent thermal conditions.

Even after removal of the chambers from the docking station and placement under a standard laminar flow hood, the maximum observed temperature decrease was only $\leq 0.15\text{ }^{\circ}\text{C}$ after one hour, despite a 30-minute battery limit, demonstrating the system's capacity to maintain thermal stability during routine handling and manipulations.

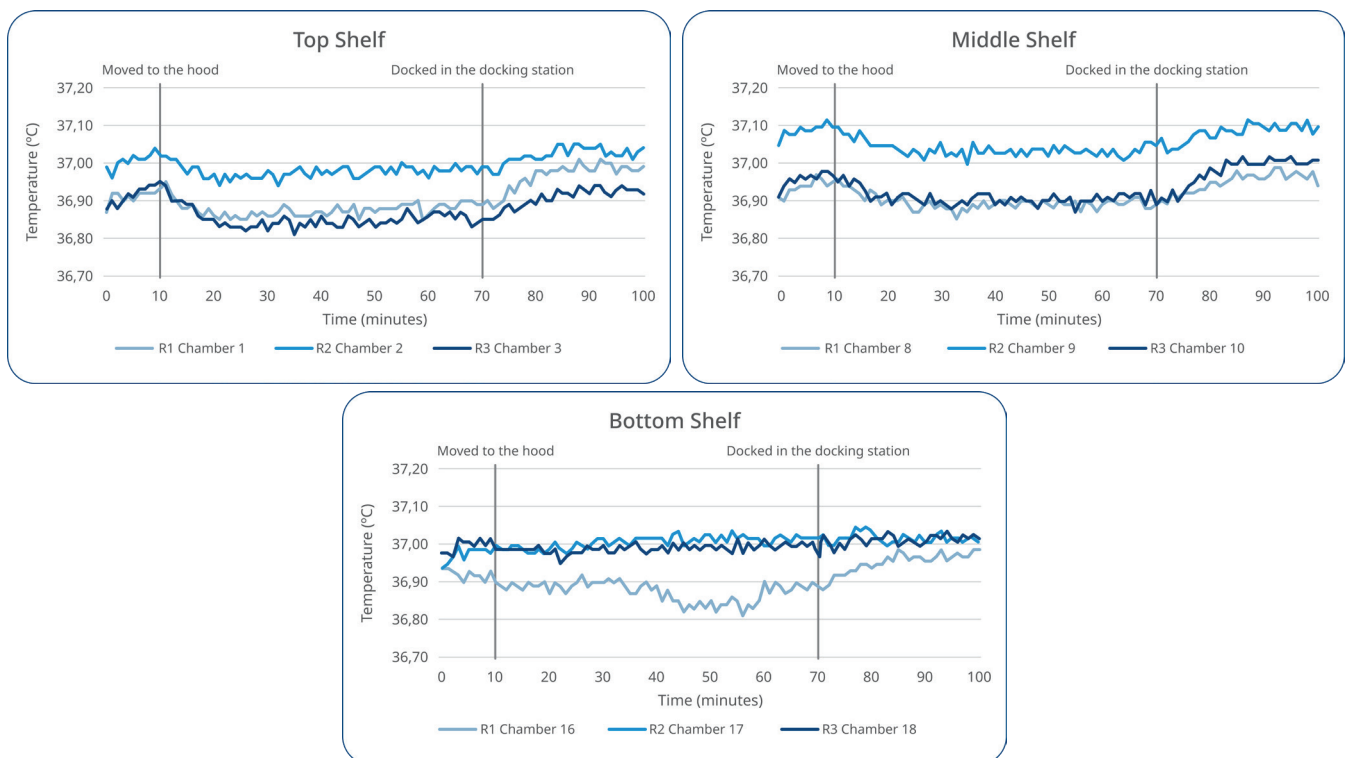


Figure 3. *In vitro* assessment of temperature stability in the MIRI® M multiroom IVF incubator, showing consistent conditions (36.92 – 37.06 °C, SD 0.01 – 0.03 °C) and minimal deviation ($\leq 0.15\text{ }^{\circ}\text{C}$) after chamber relocation.

Another critical aspect affecting the integrity of the culture environment is the frequency of opening and closing the incubator lid, which should be minimized to preserve optimal conditions for embryo development. In a comparative study, the temperature inside a small benchtop incubator recovered to 37.0 °C within about 5 minutes after a 5-second door opening [10]. It is also crucial that only one patient's gametes or embryos should be cultured in each incubator compartment [2], to avoid affecting others when the lid is opened and to keep the incubation environment as stable as possible [8].

However, this is unrealistic for fertility centers with an annual cycle volume exceeding one thousand. One of the reasons the MIRI® M multi-chamber benchtop incubator was developed is its movable chamber design, which enhances flexibility and stability during continuous embryo culture, while also ensuring a more stable incubation environment and reducing the risk of cross-influence between patients. By using multiple chambers simultaneously, this system allows embryos to be cultured in separate, individually controlled, movable chambers, making it possible for each patient to have an individual incubation compartment. Each chamber remains continuously assigned to a specific patient, allowing it to be repositioned on the docking station without compromising traceability.

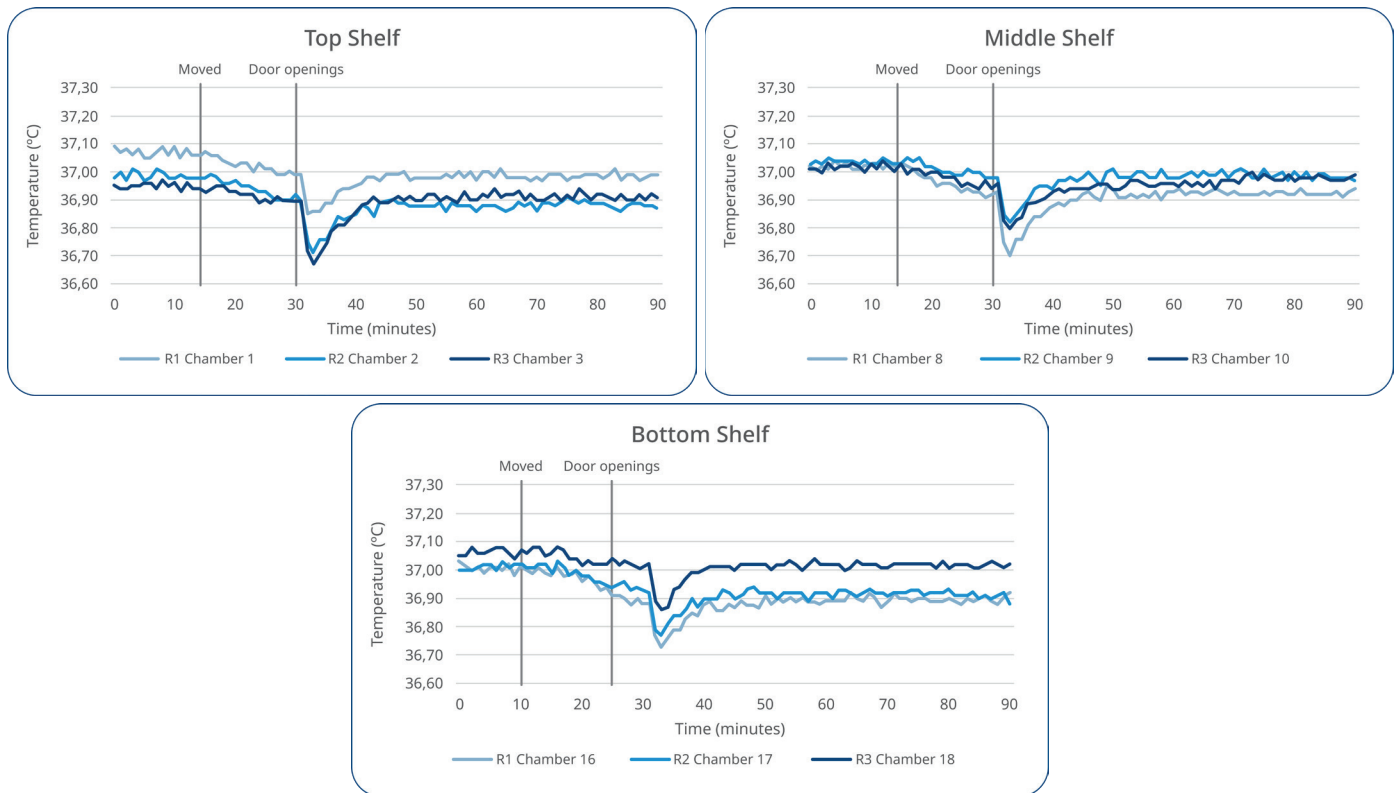


Figure 4. Temperature recovery in the MIRI® M multiroom IVF incubator occurred within approximately 5 minutes following lid opening or movement, with deviations remaining within ± 0.5 °C.

Following two consecutive 5-second lid openings, the MIRI® M multiroom IVF incubator demonstrated a rapid and efficient recovery of temperature conditions, as shown in Figure 4.

Despite multiple interruptions, the temperature inside the MIRI® M multiroom IVF incubator chambers returned to the target level within approximately 5 minutes, maintaining fluctuations well within the acceptable range (± 0.5 °C) [2].

Incubators can only operate effectively within a certain ambient temperature range. Fluctuations in ambient temperature can impact the internal temperature of incubators, potentially altering the microenvironment for embryos [8].

The response of the MIRI® M multiroom IVF incubator to temperature fluctuations in the external environment was investigated. The MIRI® M multiroom IVF incubator demonstrated outstanding temperature stability even under extreme conditions.

During an overnight air conditioning failure, with the room temperature rising by nearly 6.0 °C to reach 30.0 °C, the average chamber temperature changed by only 0.12 °C, and a 30-minute power outage showed no appreciable impact on chamber temperature, with deviation remaining within the ± 0.1 °C setpoint range and stabilizing to nominal values within one hour, as shown in Figure 5 and Figure 6.

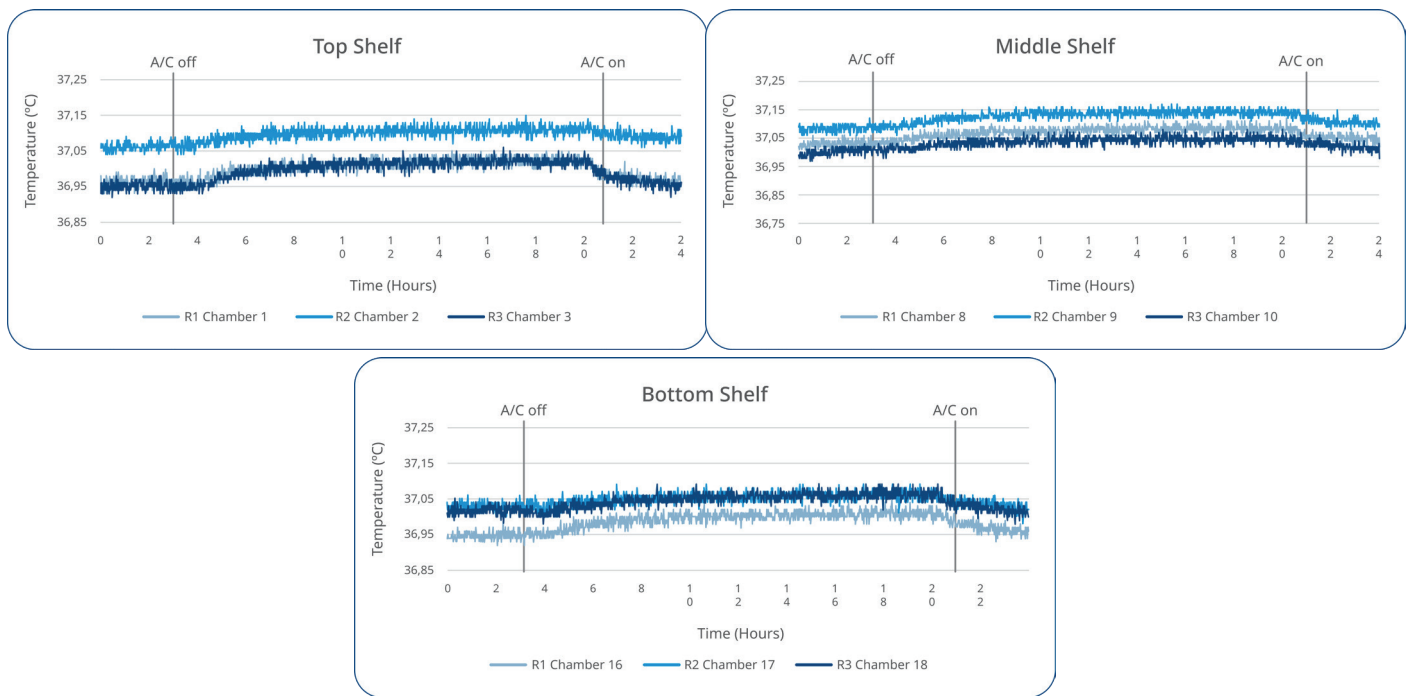


Figure 5. Temperature resilience of the MIRI® M multiroom IVF incubator chambers during an overnight air conditioning failure, showing only minimal average internal temperature increase (0.12 °C) despite an approximately 6.0 °C rise in room temperature.

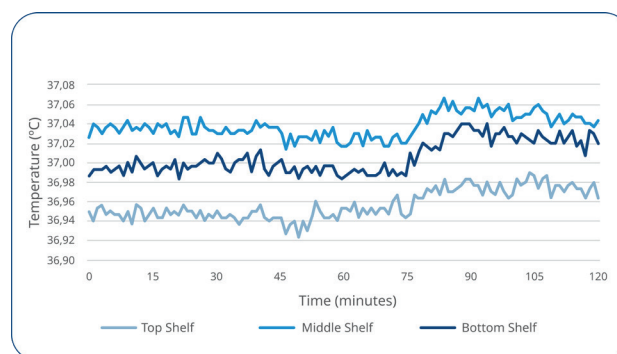


Figure 6. Temperature resilience of the chambers during a 30-minute power failure, showing minimal deviation within ± 0.1 °C setpoint range and stabilization to nominal temperature within approximately one hour after reactivation.

Modern multiroom incubators, such as the MIRI® M multiroom IVF incubator, help mitigate the risks associated with temperature fluctuations by ensuring highly precise temperature control (with deviations within ± 0.1 °C from the setpoints), both throughout culture process and during manipulations. This exceptional stability preserves embryo developmental potential, minimizes cellular stress and ultimately improves clinical outcomes.

pH Stability

Stabilization of pH during IVF is critical to avoid environmental stress that can compromise embryo development [2]. The stability of culture medium pH is influenced by multiple factors, such as its pH buffer system, CO₂ concentration in the incubator, preparation protocol of the culture system, culture method, and altitude. Commercial culture media generally recommend a pH range of 7.2 – 7.4 for embryo culture. Although embryos seem to tolerate a wide range of pH, variations outside of physiological ranges negatively affect embryo metabolism and development and viability [3].

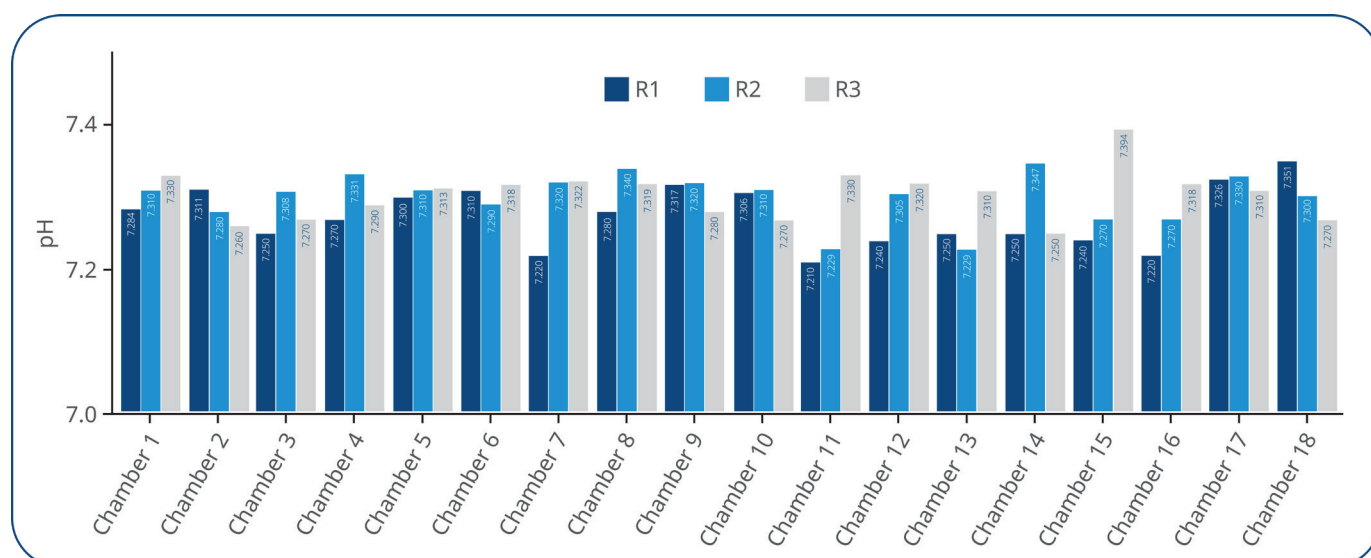


Figure 7. pH stability across all 18 chambers of MIRI® M multiroom IVF incubator. Values remained within the physiological range (7.2 – 7.4) under all test conditions. R1 – R3 represent three replicates in each chamber.

Across all 18 chambers of the MIRI® M multiroom IVF incubator, pH levels remained firmly within the physiological range (7.2 – 7.4) during standard operating conditions, with minimal variation between shelves or chambers, as shown in Figure 7. Even when chambers were undocked for 30 minutes, gas-phase control remained effective, and no significant changes in pH were observed. Following two consecutive lid openings (5-second each), the pH values showed no meaningful deviation from baseline, indicating robust gas regulation and minimal CO₂ diffusion loss.

Osmolality Stability

Any fluctuation in culture media osmolality may adversely stress the embryos and obstruct their growth and development. It has been demonstrated that optimal osmolality range of *in vitro* media for human embryos is approximately 250 – 290 mOsm/kg [3, 8], whereas osmolality greater than 300 mOsm/kg can induce stress and negatively influence embryo development, although this threshold may vary depending on the initial osmolality of the medium used [11].

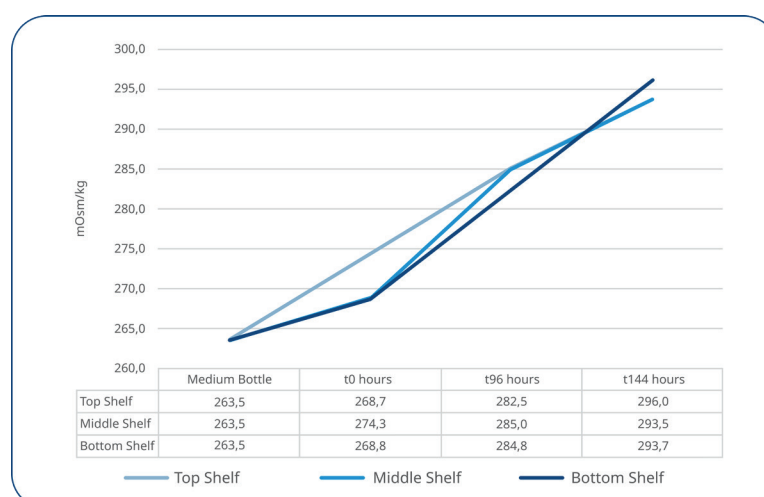


Figure 8. Osmolality profile across top, middle and bottom shelves of MIRI® M multiroom IVF incubator over a 144-hour culture period, showing gradual increase from the baseline and stable values within approximately 280 – 296 mOsm/kg.

The MIRI® M multiroom IVF incubator maintained osmolality stability, with values consistently within a narrow range of 280 – 296 mOsm/kg across all chambers over a 7-day culture period, as shown in Figure 8. Over the 144-hour culture period, a mean increase of approximately 11.7% was observed compared with the baseline, and this increase did not appear to be detrimental for embryo culture, as demonstrated by the outcomes of the MEA tests performed.

This stable osmolality profile reflects effective humidity and gas regulation within the incubator, minimizing medium evaporation and helping to preserve the physiological environment essential for embryo development.

Humidity Stability

Unfortunately, osmolality may inadvertently be affected by many factors in the lab. Humidity levels inside the incubators, play an important role in osmolality stabilization [11]. However, excessive humidity can also create a favourable environment for microbial overgrowth, which may compromise embryo development and culture conditions [2]. To mitigate evaporation without relying solely in high humidity and preserve proper pH and osmotic pressure, an oil overlay in culture dishes is used as an effective barrier, helping to maintain medium volume and osmolality [12].

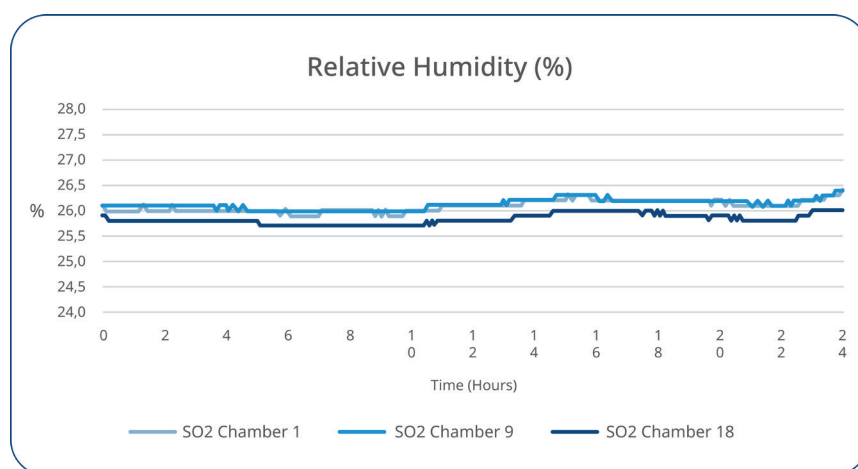


Figure 9. Relative humidity profile over a 24-hour period, showing stable humidity control (25.5 – 26.5%) across all chambers of the MIRI M® multiroom IVF incubator.

The MIRI® M multiroom IVF incubator demonstrated stable humidity control throughout continuous culture conditions. However, as this is a dry gas incubator, the use of high volumes of oil and large culture medium drops is recommended to minimize evaporation [3].

Relative humidity was monitored every 5 minutes over 24-hour period and remained within a narrow range of approximately 25.5 – 26.5% across all chambers, as shown in Figure 9. This uniformity indicates consistent environmental regulation, ensuring stable culture conditions and minimizing the risk of medium evaporation during embryo development.

Conclusion

Based on the test results, MIRI® M is future-ready for IVF laboratories for these reasons:

- Achieves benchmark embryonic developmental outcomes.
- Provides unique flexibility, exceptional environmental stability, and operational reliability.
- Meets international guidelines for key performance indicators (KPIs) and environmental control in IVF labs.
- Delivers consistent results in both routine and challenging laboratory conditions.
- Maintains an optimal microenvironment and adapts to evolving clinical needs.
- Features a modular design that supports uninterrupted workflows, contributing to improved clinical outcomes.
- Serves as more than an incubator – it is a future-ready partner for modern IVF laboratories.



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Infertility is a problem that has a significant social, psychological, and economic impact on afflicted individuals and couples. It is a global concern that knows no race or creed. It has been estimated that 1 in 6 couples struggle with infertility at least once in their lifetime.

Esco Medical is one of the divisions of the Esco Lifesciences Group. We provide innovative technological solutions for fertility clinics and laboratories. We aim to become the leading manufacturer of high-quality equipment such as long-term embryo incubators, ART workstations, anti-vibration tables, and time-lapse incubators.

Our products are designed with the Silent Embryo Hypothesis as a guiding principle. The Silent Embryo Hypothesis states that the less disturbed an embryo can remain, the better its developmental potential will be. Most of our products are designed in Denmark and made in the EU. Our primary focus is to increase pregnancy success rates and patient satisfaction.

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