Integrated Culture Solutions

Creating the optimal environment for human embryos

ORIGIO • SAGE • Humagen • TPC • K-Systems • RI • Wallace • LifeGlobal • CooperGenomics



Fertility and Genomic Solutions

Creating the optimal culture environment

The primary role of a culture system is to provide an environment that minimizes damage and stress to gametes and embryos *in vitro*.

Culture media plays an integral role in optimizing the culture system. They deliver a balance of ions, energy substrates and nutrients to support the developing embryo. They also provide protection from extra- and intracellular stressors, and help maintain homeostasis, which is essential for successful culture.



Culture media

There are two main approaches to embryo culture: sequential and single-step. Evidence from published literature¹ show outcomes are comparable in the two systems.

Sequential

- Uses stage-specific formulations to mimic the *in vivo* environment
- Components reflect the metabolic needs of the embryo at different stages

Single-step

- Composition is not tailored to stage-specific demands; all components are provided, and the embryo uses these as and when needed
- Careful design means optimal development is still supported



Ulture

Storage, handling and use of media

The way culture media are handled and stored can have a significant impact on their quality and may affect clinical results.²

- Store media at 2–8°C out of direct light and tightly capped
- Follow aseptic techniques and limit the number of times a single bottle is opened and closed
- Consider time taken, workstation airflow, temperature and micro drop size or well culture when preparing dishes
- Fully equilibrate CO₂ and temperature before use. Time for equilibration will depend on drop size, thickness of the oil overlay and whether the bottle has previously been opened







Plastic and hardware

All the careful work in establishing excellent culture conditions can be undone if the plasticware and equipment used are poor quality.

- Use culture dishes and plasticware (pipettes, tips, etc.) that are appropriate for use within ART, e.g. are CE-marked, have been MEA-tested and/or are subjected to a sensitive sperm survival assay before use
- Use validated equipment that ensures optimal pH and temperature for gametes and embryos is maintained

Oil overlay

When culturing under oil, the handling and use of the oil is just as important as your culture medium

- Use oil that is specifically approved and quality tested for use within ART
- Store in dark conditions at 2-8°C
- Equilibrate to 37°C in an atmosphere of 5-6% CO₂ before use

- 1. Sfontouris IA, et al. Blastocyst culture using single versus sequential media in clinical IVF: a systematic review and meta-analysis of randomized controlled trials. J Assist Reprod Genet. 2016;33:1261–1272
- 2. Smith GD, et al. (eds.), Embryo Culture: Methods and Protocols, Methods in Molecular Biology. 2012. Vol 912, chapter 21, pp 371

Optimizing the incubator environment

The primary function of an incubator in the ART lab is to provide stable conditions for the embryo, and create an environment where pH, temperature and air quality are tightly controlled.



Gas phase and pH

Culturing gametes and embryos in the right pH is crucial. As CO_2 concentration helps regulate the pH of the culture medium, it is essential that the level of CO_2 in the incubator is known and consistent.

- Ensure that the CO₂ level in each incubator is independently validated
- Do not rely on the CO₂ setting in the incubator; the relationship between CO₂ and pH is dependent on the bicarbonate level of the media, as well as the lab's altitude¹

Temperature control

Maintaining a constant temperature of 37°C is a top priority during all stages of culture.

- Cooling oocytes causes spindles to depolymerize.²
 Once re-warmed, there is a risk of reformation failure, wrongful reattachment of the chromosomes and subsequent aneuploidy of the embryo
- Exposing early embryos to temperature changes may upset cellular metabolism, membrane stability and transport processes³
- Strictly monitor the incubator temperature, which can be more easily controlled in incubators with chambers for individual patients

Humidity and osmolality

Many incubators regulate humidity to avoid media evaporation during culture, which may cause harmful rises in medium osmolality. However, culture in a nonhumidified environment is possible if the culture dishes are covered with adequate amounts of oil overlay.⁴



Air quality

Embryos are sensitive to environmental toxicants, particularly to volatile organic compounds (VOCs). Establishing good air quality, ideally via chemical air filtration, is essential to have an optimal culture system.⁵⁻⁷

- Ensure incubators are fitted with an in-line HEPA gas filter; enclosed incubator environments may have concentrated VOC levels several times higher than the ambient air
- Ensure cleanliness of the lab air by either installing HEPA filters or using mobile air filtration units

Oxygen (O_2) concentration

Lowering the O₂ concentration in the culture environment has repeatedly been found beneficial for embryo development and outcomes,⁸ most notably when reduced throughout the entire culture period (i.e. to the blastocyst stage).⁹⁻¹¹

Monitor and regulate incubator O₂ concentrations for optimal embryo development

- 1. Elder K, et al. In-Vitro Fertilization. 3rd edn. Cambridge: Cambridge University Press. 2010. doi:10.1017/CBO9780511984761
- 2. Pickering S, et al. Transient cooling to room temperature can cause irreversible disruption of the meiotic spindle in the human oocyte. Fertility and Sterility. 1990;54:102–108
- 3. Fawzy M, et al. Comparing 36.5°C with 37°C for human embryo culture: a prospective randomized controlled trial. Reprod Biomed Online. 2018;36:620–626
- 4. Swain JE. Decisions for the IVF laboratory: comparative analysis of embryo culture incubators. Reproductive BioMedicine Online. 2014;28:535-547
- 5. Morbeck D. Air quality in the assisted reproduction laboratory: a mini review. J assist Reprod Genet. 2015;32:1019–1024
- 6. Mortimer D, et al. Cairo consensus on the IVF laboratory environment and air quality: report of an expert meeting. Reprod Biomed Online. 2018;36:658-674
- 7. Munch EM, et al. Lack of carbon air filtration impacts early embryo development. J Assist Reprod Genet. 2015;32:1009–1017
- 8. Bontekoe S, et al. Low oxygen concentrations for embryo culture in assisted reproductive technologies. Cochrane Database of Systematic Reviews. 2012;7:CD008950

- 10. Meintjes M, et al. A controlled randomized trial evaluating the effect of lowered incubator oxygen tension on live births in a predominantly blastocyst transfer program. Human Reproduction. 2009;24:300–307
- 11. Waldenstrom U, et al. Low-oxygen compared with high-oxygen atmosphere in blastocyst culture, a prospective randomized study. 2009;91:2461-2465

Kovacic B and Vlaisavljević V. Influence of atmospheric versus reduced oxygen concentration on development of human blastocysts in vitro: a prospective study on sibling oocytes. Reprod Biomed Online. 2008;17:229–236

An integrated solution for embryo culture

CooperSurgical Fertility and Genomic Solutions offers a broad range of products and services designed to work in harmony with your culture protocol. Along with clinical support from our expert embryology team, we are able to offer a complete culture system – including equipment, consumables and scientific knowledge – to give your embryos the optimal environment for development.





Partnering beyond products

We collaborate with clinics and experts worldwide to create a global network of scientific leaders, embryologists and clinical training experts. By partnering with us you become part of this network, and benefit from the knowledge, training and product solutions our leading specialists provide.

Our team of experienced embryologists assists customers with the establishment of clinics (turn-key projects), laboratory design and clinic audits to optimize lab performance. In addition, they give lectures, run seminars and workshops, and support the research and development of new products.

Partnering with CooperSurgical, you benefit from:

- Unique solutions at every step of the ART cycle
- Training and knowledge to drive clinical efficiency and improve outcomes
- Access to a global network of scientific leaders, embryologists and clinical training experts
- Industry-leading ART innovation

Working together, we can advance your clinical workflow and productivity, helping you improve outcomes in your clinic.



Train with us

CooperSurgical Fertility and Genomic Solutions provides global hands-on training courses for a comprehensive range of genomic and assisted reproductive technologies.

Our training centers are fully equipped to support expert tuition, laboratory demonstrations, peer-to-peer discussions, and the sharing of best practice in a professional yet relaxed atmosphere. Our courses focus on providing evidence-based training by skilled, experienced embryologists in specific topics, including embryo culture, vitrification, sperm selection, biopsy and genetic testing.

If you or your staff could benefit from training, see our website fertility.coopersurgical.com/training-lab for more information, course schedule and bookings.

As well as our training lab courses, we run regular hands-on workshops around the globe. To find out about events coming up in your region, contact your local CooperSurgical representative.

Our Experts



Toni di Bernadino Director, Clinical and Technical Support



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Inger Britt Carlsson, PhD Global Director (Genomics), Medical Affairs



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Rachel Chin, MSc Technical Support Manager



Kelly Ketterson, PhD Vice President, Center of Excellence



David Morroll, PhD Director of Clinical Support



Olga Razina, MSc Embryology Advisor

Clinical Application Specialists

Our new clinical application service allows you to partner with experts from the CooperSurgical Medical Affairs team. As Reproductive Science Specialists, our expert team can provide support with:

- Lab audits
- pH testing
- Setting up media evaluations

- Troubleshooting
- Advice on laboratory design
- In-clinic training





ORIGIO, SAGE & LifeGlobal culture media

High-quality culture media for every protocol and preference. Manufactured in a purpose built, ISO 13485 and ISO 9001 certified state-of-the-art production facility to maintain the highest standards for product quality and reliability. CE-marked and FDA cleared.



High-quality oils specifically designed to meet United States Pharmacopeia's (USP) and European Pharmacopoeia (PhEur) requirements. Atomic fingerprint, POV, sterility, endotoxin level (< 0.1 EU/mL) and 1-cell MEA tested. Available pre-washed or unwashed.



G210 InviCell long-term incubator

Ambient humidity incubator designed with intelligent software to maintain optimum environmental conditions. CE marked, FDA cleared and Australia TGA.



Humidified incubator designed to maintain consistent culture environments. CE marked, FDA cleared and Australia TGA.





Specifically developed for IVF and made from a non-toxic medical grade, non-pyrogenic polystyrene material. 1-cell MEA, endotoxin (LAL), and sterility tested. CE-marked and FDA cleared.

Product range

K-Systems stacking system

| Stacking system 110V | |
|----------------------|--|
| Stacking system 220V | |
| | |

Long-term incubator

| K-Systems G210 InviCell Plus Standard Model | |
|---------------------------------------------|--|
| ORIGIO/PLANER BT37 Benchtop Incubator | |

G210 dish inserts

| ifeGlobal | |
|--------------|--|
| Falcon | |
| NUNC | |
| /itrolife | |
| ifeGlobal pH | |
| Falcon pH | |
| NUNC pH | |
| /itrolife pH | |

LifeGlobal dishes

| embryo corral® |
|------------------------|
| 4-Well GPS® |
| Universal GPS® |
| embryo GPS® |
| μDrop GPS [®] |
| Mini GPS® 38 |
| 38Special GPS® |
| |

Handling devices

| RI EZ-Grip® |
|----------------------------|
| RI EZ-Squeeze [™] |
| RI EZ-Strip® |
| RI EZ-Tip [®] |
| ORIGIO STRIPPER® |

Collection and manipulation media

| Quinn's Advantage Medium w/ HEPES |
|-----------------------------------|
| global® Collect® |
| global ® w/ HEPES |
| global® total® LP w/ HEPES |
| ORIGIO® Handling |
| global® total w/HEPES |

Fertilization media

| ORIGIO [®] Sequential Fert [™] | | |
|-----------------------------------------------------------|--|--|
| Quinn's Advantage [™] Protein Plus Fert Medium | | |
| Quinn's Advantage [™] Fertilization (HTF) Medium | | |
| global® for Fertilization | | |
| global® total® for Fertilization | | |
| global® total® LP for Fertilization | | |

Culture media

| SAGE 1-Step [™] | | |
|---------------------------------------------------------------|--|--|
| global® | | |
| global® total® | | |
| global® total® LP | | |
| ORIGIO [®] Sequential Cleav [™] | | |
| Quinn's Advantage Protein Plus [™] Cleavage Medium | | |
| ORIGIO [®] Sequential Blast [™] | | |
| Quinn's Advantage Protein Plus [™] Blastocyst Medium | | |
| EmbryoGen® | | |
| BlastGen™ | | |
| SAGE HSA | | |
| SAGE 1-Step GM-CSF | | |
| LifeGlobal HSA | | |
| | | |

Oil

| ORIGIO Liquid Paraffin | |
|------------------------------|---|
| SAGE Oil for Tissue Culture | |
| LifeGlobal LifeGuard® Oil | |
| LifeGlobal Paraffin Oil P.G. | • |
| LifeGlobal LiteOil® | |



A solution as unique as your business

At CooperSurgical, we partner with you to drive clinical efficiency

When you partner with CooperSurgical you become part of a truly global network of clinical experts ready to support you with highly specialized solutions, both for individual clinics and across large organizations. By providing you with optimal products, services and training our aim is to offer you the best possible support to drive the efficency of your clinic – and achieve the best results.

*Day-to-day delivery may vary according to geographical location

