

# G-TL

The first culture medium specifically designed for time-lapse.



# FOR TRULY UNDISTURBED TIME-LAPSE CULTURE

Time-lapse culture removes time limits and stresses from embryos during assessment while adding diagnostic power to classic morphology. G-TL is a new medium designed to optimise the use of time-lapse technology.

## A new approach

Time-lapse technology is changing the way we work and provides access to new tools for embryo monitoring and selection. Thanks to continuous monitoring, developmental analysis and stable environments, the new technology has the potential to minimise handling stress for embryos. As a result, time-lapse technology has placed new requirements on the culture media.

The success of in vitro fertilisation is strongly dependent on the embryo culture conditions that are related to the composition of the culture medium. Time-lapse minimises handling stress as it allows

continuous culture and assessment inside the incubator. G-TL takes full advantage of this, while easing some of the increased metabolic stress with an optimised formula of amino acids and energy substrates.

## Balancing stresses

In a sequential culture system, metabolic stress is minimised by providing nutrient gradients but handling stress may follow when changing the medium. Time-lapse monitoring using specialised culture media minimises handling stress but the media has to be optimised to reduce metabolic stress.



Metabolic stress is partly caused by ammonium excreted from the embryos and from the breakdown of amino acids in solution<sup>1, 2</sup>. The toxicity of ammonium to human embryos is well documented. Ammonium is known to retard embryo development and affects embryo metabolism, pH regulation, and gene expression<sup>1, 2, 3, 4</sup>.

G-TL provides uninterrupted culture conditions in an optimised culture solution to maximise embryo viability. The balanced mix of amino acids in G-TL is based on new knowledge about embryo metabolism and consumption of media constituents<sup>5</sup>. G-TL is designed to reduce ammonium load from breakdown products, while providing an optimised supply of amino acids for development.

### Use time-lapse with G-TL to balance handling and metabolic stresses.



## Load and let time-lapse work

Time-lapse systems offer the possibility to continuously monitor embryo development to make the best possible selections without disturbance.

By using G-TL culture medium embryos are exposed to the nutrients they need during time-lapse culture.

## In harmony with the G-Series

Any adaptation that gametes and embryos have to undertake due to changes in their environment come at a cost, which is ultimately paid in reduced viability.

As with all media in the G-Series, G-TL is founded on extensive studies<sup>5, 6, 7</sup> of physiology and developmental needs for optimal viability. The G-Series is designed to provide embryos with an environment as stable as possible, from aspiration to transfer.

## Realise the full potential of time-lapse technology



### Optimised for time-lapse culture

G-TL balances handling stress against metabolic stress. The optimised formulation of amino acids and energy substrates allows undisturbed time-lapse culture without excess build-up of ammonium.



### G-Series harmonised

G-TL is part of the G-Series. This means that it is optimised for viability and is compatible with handling and cryo-media to minimise stress.



### Hyaluronan for viability

Supports the preimplantation embryo development, facilitates embryo implantation and improves cryosurvivability.

# THE DEVELOPMENT OF G-TL

Time-lapse technology has become a valuable and integral part of many fertility clinics. Yet for truly reliable and undisturbed embryo culture, the technology needs a specialised culture medium. Vitrolife has drawn upon its years of experience in research and development to offer G-TL – the first medium specifically designed for time-lapse technology.

## Design phase

The G-Series was a natural starting point for the development of G-TL as the series is supported by studies of human physiology and the needs of embryos. The development process also applied new knowledge from metabolomics to alleviate metabolic stress and optimise the medium for continuous culture.

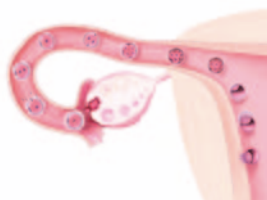
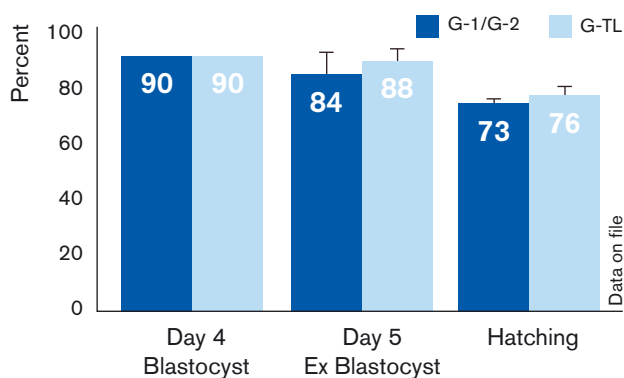


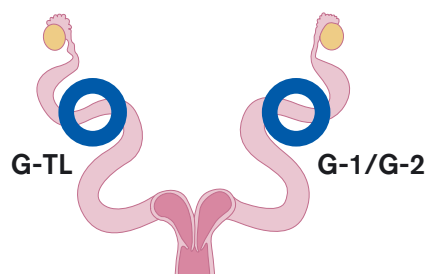
Fig 1. Embryo development



## Pre-clinical animal studies

G-TL has been compared to our current sequential culture system. The first study showed that G-TL gave comparable results on mouse embryo development (Fig 1). The project then progressed to transferring of mouse embryos and evaluating their viability (Fig 2). The results of implantation potential and foetal development showed no statistical difference when compared to our sequential media, G-1 & G-2 (Data on file).

Fig 2. Embryo transfer in mouse model



*A mouse uterus is bifurcated. Mouse embryos cultured in either G-TL or G-1/G-2 were transferred to the same uterus.*

### Design phase

Building on the successful G-Series, several compositions for a new culture medium were formulated and tested. The best composition was selected for further studies.

### Pre-clinical animal studies

The performance of G-TL was verified against G-1 and G-2 in three different laboratories. The parameters included embryo development, foetal development and placenta weight.

### Pre-clinical human studies

Study of embryo development with surplus human embryos donated to research.

## Pre-clinical human studies

With pre-clinical animal data showing equivalent results, the next step was to use surplus human embryos donated for research. When human embryos cultured in G-TL or our sequential system were compared we found no statistical differences in embryo development.

## Clinical study

The final step in the development of G-TL was to verify the performance in a clinical environment using time-lapse technology. This was performed in an international, prospective, controlled and randomised multicentre study.

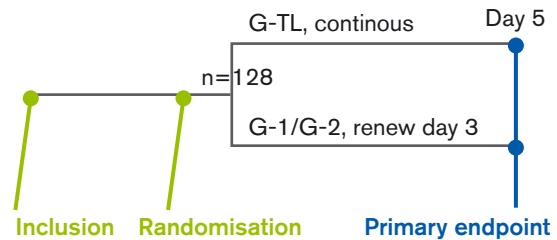
The study compared embryo siblings from 128 patients using a minimum of six 2PN/patient. The study aimed for blastocyst culture and single embryo transfer. The primary endpoint was number of good quality blastocysts on day 5 (Fig 3). The secondary endpoints were embryo quality on day 3 as well as the total blastocyst formation and blastocyst utilisation rates.

The results showed that G-TL when used for continuous culture in a time-lapse system gave the same levels of embryo development and utilisation as a sequential media system (Fig 4 and 5). Preliminary data show pregnancy rates similar to those obtained in G-1 and G-2, indicating that G-TL can function well as a part of the G-Series culture system.

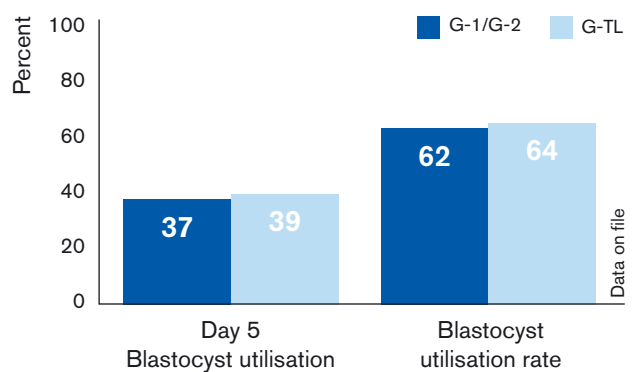
In conclusion, G-TL can be successfully used as a culture medium component in time-lapse systems resulting in good embryo viability. In the population receiving eSET only, outcome data showed that

both sequential media and G-TL gave comparable performance on a high level, with pregnancy rates around 50%.

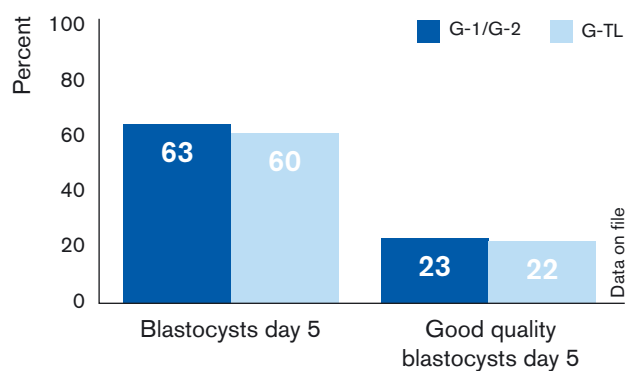
**Fig 3. Study design**



**Fig 4. Blastocyst utilisation rates per 2PN**



**Fig 5. Embryo development and quality**



## Clinical study

An international, prospective, randomised multicentre study to verify the performance of G-TL in a clinical environment using time-lapse technology.





# OPTIMISE ALL THE WAY

Increase the chances of success at each stage of IVF. Ensure optimal conditions before, during and after culture by using the whole G-Series.

## A smoother path

In vitro fertilisation takes oocytes and embryos on a journey outside of their natural habitat. Their fragility requires great care to be taken at each step, to avoid unnecessary in vitro stress. That is why G-TL is part of the G-Series media system. By using G-Series media you can be assured that at each stage of IVF, from aspiration to transfer, embryos will be surrounded by optimised conditions.

## Continuity throughout

All G-Series media share the same basic composition to secure viability and implantation potential. Osmolality, pH and supporting compounds are all kept constant. This foundation prevents intracellular stresses as the embryos progress through the IVF process.

Preparation	Retrieval	Handling		Culture	Transfer
G-RINSE	G-MOPS	OVOIL		G-TL	EmbryoGlue
		G-MOPS G-GAMETE	G-IVF		
Osmolality, pH and nutrients					
Consistency, QC and pre-testing					

*G-Series provides an optimised IVF pathway that minimises variation in environmental conditions.*

## The G-Series features



### Same basic composition

Same ionic composition, osmolality and pH to prevent intracellular stress.



### Embryo support closer to nature

Each product contains the appropriate nutrients for the development stage it is intended for.



### Hyaluronan for viability

Supports the preimplantation embryo development, facilitates embryo implantation and improves cryosurvivability.



### LOT-to-LOT consistency

High consistency means that reference values and scoring criteria can reveal true patient variation.



### Low reprotoxicity load

Extensively tested raw materials to minimise stress to maintain viability. Depending on the medium, endpoint tests such as Human Sperm Survival (HSSA), Mouse Embryo Assay (MEA) and endotoxin tests are used.



## Confidence at each step

Each product in the G-Series is developed to resemble conditions in the female reproductive tract and fulfil embryo requirements. For example, G-IVF helps you take the first step and is designed for sperm preparation and fertilisation of oocytes. During handling and manipulation outside the incubator G-MOPS gives oocytes and embryos the best possible physiological protection. Finally, EmbryoGlue promotes implantation with a proven formula that increases take-home baby rate<sup>8</sup>.

## Media that help you on the way

### G-RINSE

Prepare with G-Series from the start. Use it to test and rinse oocyte retrieval needles, wash the cervix prior to retrieval and transfer and for rinsing of contact materials. G-RINSE contains gentamicin, salts and a carbohydrate with the same osmolality as the other G-Series media. Rinsing with G-RINSE ensures that no dilution affects your culture.

### G-MOPS/G-MOPS PLUS

Handling media that allow you to perform all procedures outside of the CO<sub>2</sub> incubator, such as oocyte retrieval and ICSI, without worrying about a change in pH also in the most time consuming cases. The media contain amino acids and antibiotics and have the same osmolality and pH as Vitrolife culture media.

### G-GAMETE

Handling medium for oocytes and embryos that should be equilibrated in the incubator together with culture media. It has the same constituents as G-MOPS but with a different ratio of MOPS and bicarbonate to function after equilibration in the incubator.

### G-IVF

Optimised for fertilisation and to maintain gamete functionality. G-IVF contains glucose and fructose to support both cumulus cells and sperm functionality. Let the sperm begin its journey with the G-Series in G-IVF. The same medium can be used for all sperm preparation procedures including dilution of gradient solutions, washing, sperm counts and final dilution of sperm solution for fertilisation.

### EmbryoGlue

Implantation promoting transfer medium with a unique combination of hyaluronan<sup>9,10,11</sup> and recombinant albumin<sup>12</sup>. Over one million transfers have been made with EmbryoGlue and numerous studies have confirmed its ability to increase take-home baby rates without raising miscarriage rates<sup>8</sup>.

### OVOIL™

The gold standard of culture oil in IVF with excellent embryo development. OVOIL is 100% paraffin oil produced in a highly controlled process from extensively tested LOTs of raw materials. The combination of product integrity and testing secures your results and enhances control of your culture system.



"The G-Series has been used at the Conceptia Clinic in Canada since 2000 with good results, the clinical pregnancy rate in all age groups is 59%. – I find it beneficial to use the complete system with the same basic composition, reducing one parameter that the embryo has to adapt to, says Laboratory Director Tao Tao."



# TOGETHER. ALL THE WAY™

Product	Description	Size	REF
G-TL™	Medium for culture of embryos from fertilisation to the blastocyst stage.	30 mL	10145
G-RINSE™	Rinse solution	125 mL	10069
G-IVF™	Fertilisation medium	60 mL	10135
G-IVF™ PLUS	Fertilisation medium, containing HSA	60 mL	10136
G-MOPS™	Handling medium	125 mL	10129
G-MOPS™ PLUS	Handling medium, containing HSA	125 mL	10130
G-GAMETE™	Handling medium, containing HSA	30 mL	10126
G-MM™	Recombinant human albumin solution	10 mL	10038
HSA-solution™	Human serum albumin solution	10 mL	10064
EmbryoGlue®	Transfer medium	10 mL	10085
OVOIL™	Paraffin oil for oil overlay	100 mL	10029

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