Genea BIOMEDX

Gems®

DESIGNED BY EMBRYOLOGISTS WHO USE IT[1]

Gems®: A complete embryo medium suite, including the third generation of the world's first sequential media[1,2]

Gems®

For embryos cultured outside of the uterus, *in vivo* conditions must be recreated to stimulate embryo embryo development.[3] An **optimal culture environment** is vital to support the overall performance of the ART lab and is essential to minimise stress to gametes and embryos.[3-5]

In the 1990s, Genea IVF clinic in Australia (formerly Sydney IVF) developed one of the world's first sequential human embryo culture media suites.[1-2]

INTRODUCING Gems®

YOUR COMPLETE RANGE OF IVF AND VITRIFICATION MEDIA

Gems® is the third generation of this culture medium suite [1, 2] developed originally by Sydney IVF/Genea IVF clinic and further refined by Genea Biomedx in-house scientists. It has been conceived to support your needs at every stage of the ART process – from gamete collection right through to embryo transfer and cryopreservation.

OPTIMISED FOR EVERY STAGE:
Gems® Medium Suite includes gamete and embryo handling buffers and solutions for embryo culture and cryopreservation. [6, 7, 8]

ROBUST AND EFFECTIVE MEDIA:
A wide variety of amino acids, nutrients, vitamins, balanced salts and unique antioxidants to support embryo development in vitro. [6]

LONG HERITAGE:
Over 30-year history and experience in culture media development, aiming for optimum fertility outcomes.[1, 2]

ESTABLISHED SAFETY AND EFFICACY:
Gems® media has been in clinical use at Genea Fertility clinics in Australia since 2013, helping more than 200,000 embryos to be cultured and more than 16,000 babies born. [9]

CONSISTENTLY HIGH QUALITY BATCH-TO-BATCH:
Manufactured in state-of-the-art ISO13485-certified facilities in Sydney, Australia, undergoing extensive Quality Control testing before release. [6]

USER-FRIENDLY:
Gamete and Culture media are ready-to-use with clear labeling with distinctive colours and icons to aid ease of recognition in the lab.

DEVELOPED BY USERS FOR USERS

OVER 30 YEARS DEVELOPING CULTURE MEDIA

Experts from the fields of IVF and chemistry have contributed to the development of Gems® media suite.

1991

First in-house culture media (M91) developed at Sydney IVF. [1-2]

1997

1st Generation media in clinical use at Sydney IVF

1998

Media formulation licensed to Cook Medical

2006

2nd Generation media in clinical use at Sydney IVF

2008

2nd Generation media formulation licensed to Cook Medical

2011

Gems® clinical trial ran at Genea IVF clinics in 2011-2013

2013

3rd Generation media - Gems - in full clinical use at Genea IVF clinics.

2016

Gems® media manufacturing started at ISO13485 - certified facility in Sydney, Australia.

2016

Gems® media suite obtains CE Mark.

2017

Majority of Gems® media suite obtains FDA clearance.*

* Sperm solutions pending FDA clearance.

OPTIMISED FOR EVERY STEP

Gems® adapts to your laboratory practice and workload demands with a complete range of IVF and vitrification media with differing bottle sizes.

GAMETE HANDLING AND PREPARATION

Oocyte Retrieval Buffer

ORB-50 (50mL)
ORB-20 (20mL)

- HEPES-buffered, supplemented with gentamycin (0.01 mg/mL), not containing human serum albumin.

Sperm Wash Gradient Set

SWG-45P-50 (50mL)
SWG-90P-50 (50mL) (not for individual sale)

- Used for isolating motile sperm and removing seminal plasma from semen in preparation for insemination.
- HEPES-buffered, supplemented with gentamicin (0.01 mg/mL), human serum albumin (10 mg/mL) and coated silica.

Sperm Medium

SPM-50 (50mL)
SPM-20 (20mL)

- Used for washing sperm for IUI, IVF, ICSI and diagnostics.
- Bicarbonate-buffered, supplemented with gentamicin (0.01 mg/mL) and human serum albumin (10 mg/mL).

Sperm Buffer

SPM-50 (50mL)
SPM-20 (20mL)

- Used for washing sperm for IUI, IVF, ICSI and diagnostics.
- HEPES-buffered, supplemented with gentamicin (0.01 mg/mL) and human serum albumin (10 mg/mL).

VITRIFICATION & WARMING SOLUTIONS

Vitrification Set

VIT-SOL1-20 (20mL)
VIT-SOL2-20 (20mL)
VIT-SOL3-10 (10mL)
(not for individual sale)

- Used for vitrifying embryos.
- HEPES buffered, supplemented with Ethylene Glycol, Dimethyl Sulfoxide (DMSO), trehalose and human serum albumin (20mg/mL).

Warming Set

VRM-SOL1-20 (20mL)
WRM-SOL2-10 (10mL)
WRM-SOL3-10 (10mL)
(not for individual sale)

- Used for warming vitrified embryos.
- HEPES buffered, supplemented with trehalose and human serum albumin (20mg/mL).

OTHERS

VitBase

VBS-20 (20 mL)

- Used for maintaining embryos for a short period of time in a non-gassed environment.
- HEPES buffered, supplemented with human serum albumin (20mg/mL).

OPTIMISED FOR EVERY STEP

CULTURE MEDIA

Each Gems® culture medium has a tailored composition for optimal support of embryos, including amino acids, vitamins, nutrients, balanced salts and a pool of antioxidants, which are key for normal metabolism of gametes and embryos. [2,3]
Sequential media formulations are developed to adapt to developing embryos' needs, containing EDTA and low levels of glucose and essential amino acids for early stages, and no EDTA and higher levels of glucose and essential amino acids for later stages.
Geri Medium has been developed to support embryos throughout their in vitro development period for uninterrupted culture requiring no media change or replenishment [10]. It contains medium levels of EDTA, glucose and essential amino acids.
All Gems® culture media are optimised for use in a low oxygen (5%) environment. [2,3]

Fertilisation Medium
FEM-50 (50mL)
FEM-20 (20mL)

- Used for providing a suitable environment for fertilisation.
- Bicarbonate-buffered, supplemented with gentamicin (0.011mg/mL), human serum albumin (5 mg/mL) and high concentration of glucose.

Cleavage Medium
CLM-50 (50mL)
CLM-20 (20mL)

- Used for culturing embryos from fertilisation to Day 3.
- Bicarbonate-buffered, supplemented with gentamicin (0.011mg/mL), human serum albumin (5 mg/mL), antioxidants and low concentration of glucose.

Blastocyst Medium
BLM-50 (50mL)
BLM-20 (20mL)

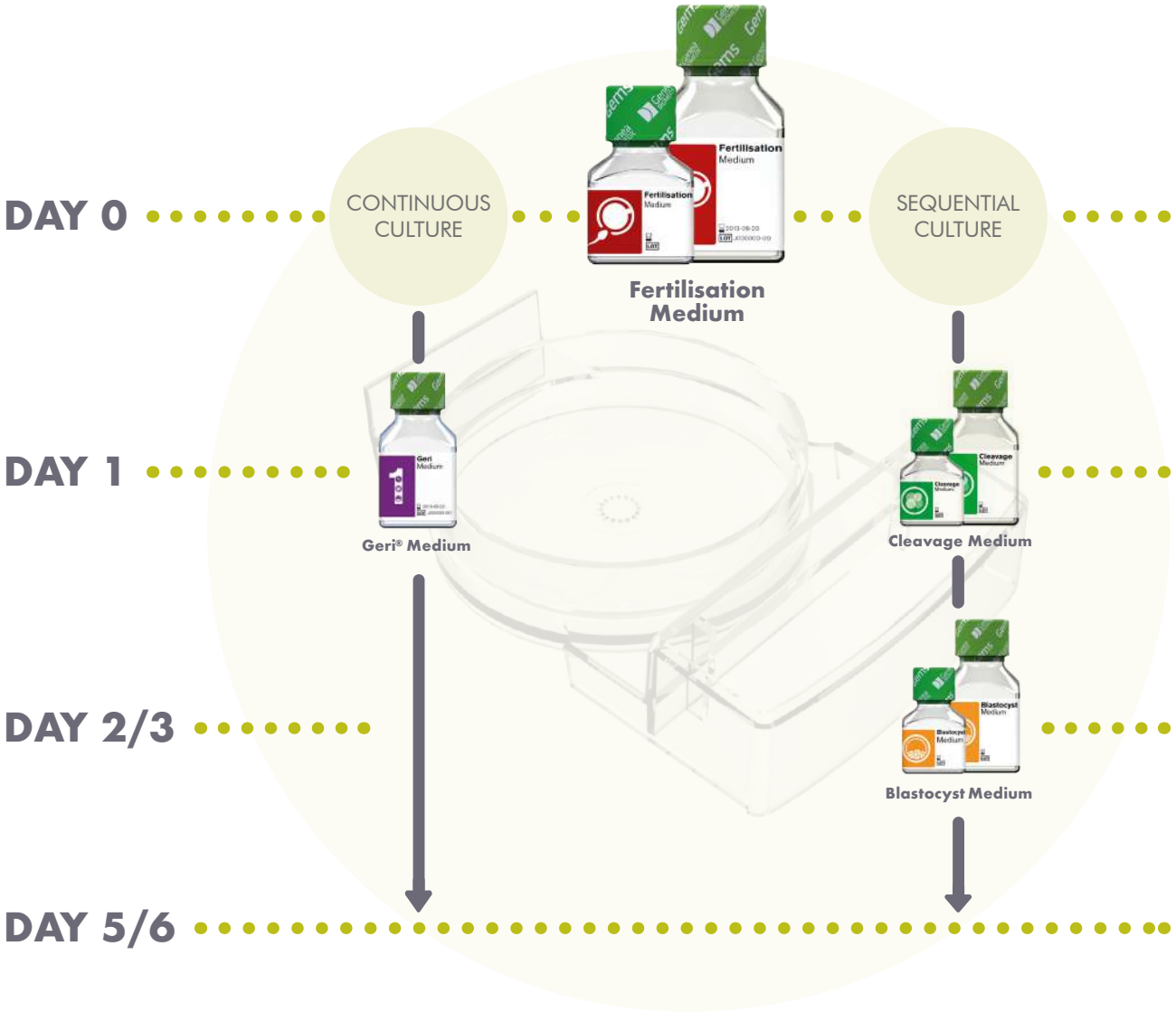
- Used for culturing embryos from Day 3 to blastocyst stage.
- Bicarbonate-buffered, supplemented with gentamicin (0.011mg/mL), human serum albumin (5 mg/mL), antioxidants and high concentration of glucose.

Geri® Medium
ONE-50 (50mL)
ONE-20 (20mL)

Used for culturing embryos uninterrupted from fertilisation to blastocyst stage.

- Bicarbonate-buffered, supplemented with gentamicin (0.011mg/mL), human serum albumin (5 mg/mL), antioxidants and medium concentration of glucose.
- Contains Glutamine in dipeptide form as Alanyl-Glutamine to prevent harmful ammonium build-up in medium.
- Helps simplify workflow and processes by eliminating the need for medium change or use of additional culture dishes during culture.

Whether your lab employs sequential or uninterrupted continuous embryo culture, with Gems® you have the flexibility to choose your preferred culture method.



CONSTITUENTS & DISTINGUISHING COMPONENTS

Gems® media contains key components to support embryo growth.

Gems ® medium suite products are buffered with bicarbonate or HEPES. They include gentamicin for microbial protection and varying levels of human serum albumin (HSA) as a protein source, depending on the product and its role in the IVF cycle.

There are many benefits to HSA in culture media[12-13]:

- Aiding embryo metabolism.
- Protecting against toxins.
- Assisting in pH buffering.
- Acting as a colloid osmotic regulator.
- Preventing embryos and gametes sticking to the device used to handle and culture them

Gems® culture media are advanced formulations including antioxidants to support embryo development.

- **L-carnitine:** An antioxidant that protects DNA and cell membranes from free radical damage and from apoptosis.[18]

L-carnitine supplementation has also been shown to have a positive effect in cryosurvival rates in bovine and porcine embryos.[16,17]

L-carnitine supplementation has been recently correlated with higher number of good quality embryos and improved clinical outcomes in human embryos.[18]

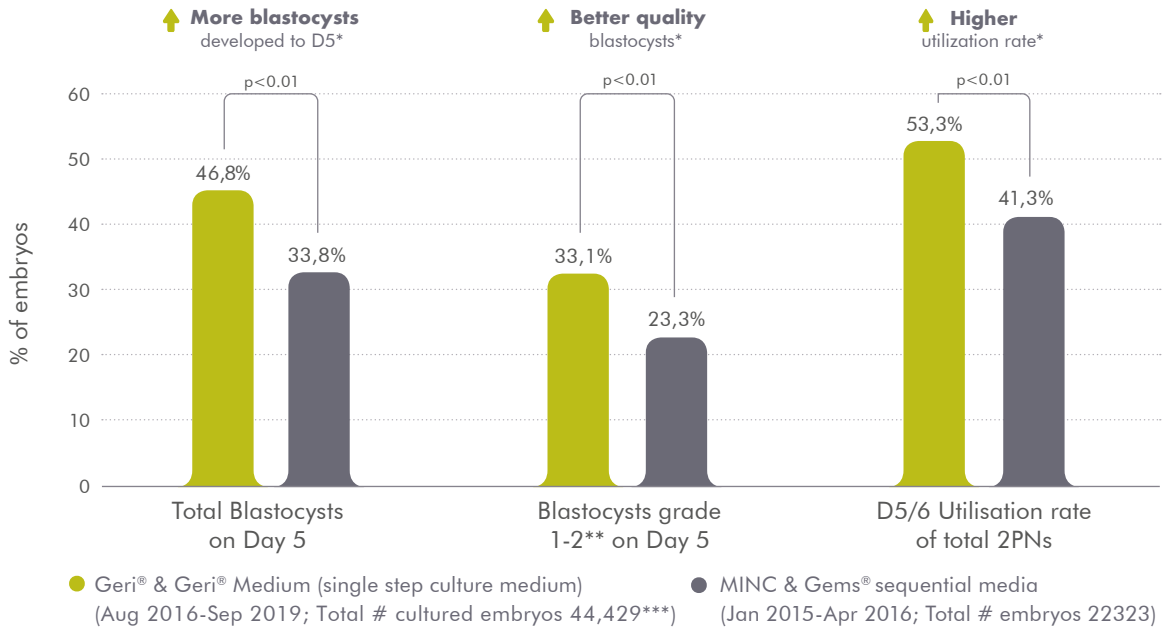
- **Cobalmin (vitaminB_{12}):** Important factor in methione synthase reaction, critical for maintaining normal DNA methylation[19] processes.
- **Folic acid (vitaminB_9):** An antioxidant that supports cell cleavage and growth. It is required for synthesis, repair and protection of DNA during methylation.[20,21,22]
- **Ascorbic acid (vitamin C):**An antioxidant that protects DNA and cell membranes from oxidative damage and apoptosis, reduces DNA fragmentation and abnormal gene expression, and when co-incubated with embryos, improves blastocyst development [23]

THE PROOF IS IN THE RESULTS

Gems® media have been in clinical use at Genea IVF clinics since 2013 across all cycle types and patient ages. Implementation of a fully undisturbed culture system using Geri® Medium alongside Geri® incubator resulted in an increase in blastocyst quality, embryo utilisation and pregnancy rates [24].
Over 200,000 embryos have been cultured and over 16,000 babies been born with the help of Gems media[9].

MAXIMISE THE POTENTIAL OF UNDISTURBED INCUBATION

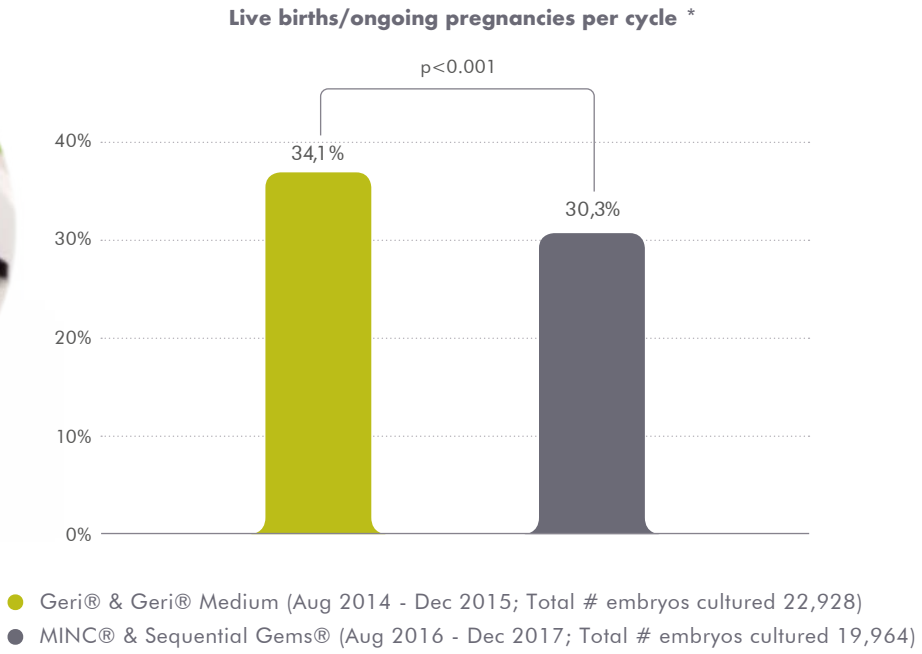
GENEA CLINICAL RESULTS : BLASTOCYSTS QUALITY AND UTILISATION RATES[24]
(All clinics, all cycles, combined ages)



* Statistically significant differences (p<0.01).
**Genea modified Gardner grading.
*** Zygotes utilised prior to Day 5 were removed from the total # of embryos cultured because their potential fate was unknown.

A statistically significant increase (p<0.001) in live births/ongoing pregnancies was seen when Genea IVF clinics changed culture system from benchtop incubator and sequential media to Geri® timelapse incubator and Geri® Medium. This shows that not only embryo development is improved by the optimised micro- environment of uninterrupted culture, but the practice translates to better clinical outcomes. [24]

GENEA IVF CLINICS' RESULTS OF ALL CYCLES, INCLUDING CUMULATIVE OUTCOMES FROM CYCLES FOLLOWED FOR UP TO 2 YEARS"



* Transition rate from foetal heart pregnancy approx 94% regardless of the culture system.

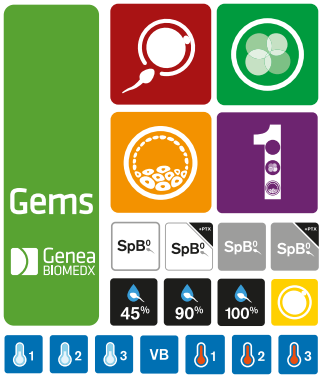
EASE OF USE

Pre-supplemented with human serum albumin (HSA) as a protein source [2, 13], Gems supports standardised laboratory practices.

Ready-to-use solutions to aid standardisation

Different bottle sizes adapt for different size labs and needs.

Clear symbols and colour coded labels aid recognition.



EXTENSIVE QUALITY AND REGULATORY CONTROL

Critical media ingredients and materials are screened before used for manufacturing. Finished products undergo applicable QC tests using analytical methods validated according to international pharmacopoeia and adhering to stringent acceptance criteria before product release to ensure their safety. [25.]

All Gems® media suite products have CE Mark, and most of them have FDA clearance*.Most media suite products are available in >40 countries.[35]

* Sperm solutions pending FDA clearance.

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26- Current BP (XVI A); Current Ph Eur (2.6.1); Current USP/NF <71> (External Lab)
27- Sterility: External Assay, Current BP (XVI A); Current Ph Eur (2.6.1); Current USP/NF <71>
28- pH: Inhouse validated method as per current BP, Ph Eur, USP/NF
29- Osmolality: Inhouse validated method as per current BP, Ph Eur, USP/NF
30- MEA: Inhouse validated 1-cell MEA method incl. positive and negative controls
31- SPTT: Inhouse validated method incl. two independent test samples and negative control
32- Gentamicin: Inhouse validated Gentamicin ELISA kit Assay
33- Endotoxin: Inhouse validated LAL (limulus amebocyte lysate) test as per Current BP, Ph Eur, USP/NF
34- HSA: Inhouse validated BCA Protein Assay
35- Genea Biomedx Data on File (QFRM89 Master Product List)

Genea BIOMEDX

For healthcare professionals only. Please refer to the instructions for use.

Gems® Culture medium suite complies with applicable medical device standards.

Gems® is manufactured by Genea Biomedx.

Gems Culture medium suite complies with applicable medical device standards.

www.geneabiomedx.com

CE 2797 Product complies with applicable European Union (EU) regulations

QRTM330-06