



Gavi

FOR STANDARDISED VITRIFICATION WITH HIGH-QUALITY RESULTS¹⁻⁵

Gavi®: World's first technology⁶ to automate the critical equilibration steps in the vitrification process^{1,2}



Gavi

CURRENT CHALLENGES IN VITRIFICATION

Cryopreservation is an essential part of any ART program. Embryos that have been cryopreserved, and subsequently thawed, account for 37.8% of all embryo transfers in Europe.¹

Vitrification uses a flash-freezing process that **reduces the risk of critical ice formation** and provides a **higher post-thawing embryo survival rate** compared to slow-freezing.^{2,3}

However, currently vitrification is a complex manual process:⁴

- **Many equilibration variables:** Success is dependent on the precise volume and timing of embryos' exposure to cryoprotectant solutions.^{4,5}
- **Manual handling:** Currently, embryologists must manually move embryos between vitrification solutions, potentially causing critical stress.⁴
- **Inconsistent results:** As a labor-intensive process, results can vary between clinics and embryologists.^{4,5}
- **Requires highly skilled practitioners:** With so many critical variables, the process requires extensive training and experience.^{4,5}



INTRODUCING Gavi®

THE WORLD'S FIRST AUTOMATED VITRIFICATION INSTRUMENT⁶

Created after four years of intensive development, Gavi® is the first technology⁶ to automate the critical equilibration step, helping to standardize the complex vitrification process.⁴ Gavi® approaches vitrification in an entirely new way, helping to achieve consistent high quality results every time.⁴



CONSISTENT AND REPRODUCIBLE PROCESS:

A process that happens the same way every time^{4,7}, helping to reduce outcome variation across users.



UNIQUE Gavi®POD:

Innovatively designed to hold oocytes, zygotes, cleavage and blastocyst stage embryos throughout the full vitrification process and storage.⁸



PRECISE EQUILIBRATION PROCESS:

Gavi® automates and controls critical parameters of temperature, time of exposure, volume and flow rate during the equilibration.^{4,8-9}



HIGH-QUALITY RESULTS:

Blastocyst survival rates exceed competency values defined in the ESHRE/ALPHA Vienna consensus publication on lab performance indicators.¹⁰⁻¹¹



A CONTROLLED, CLOSED-SYSTEM ENVIRONMENT

That prevents direct contact between the embryo and liquid nitrogen (LN₂).⁸



SHORT LEARNING CURVE:

Gavi® requires low technical skills and short time to achieve competency.^{4,10}

1. DeGeyter, C. et al. (EIM) 2018 HR, 33 (9) 1586–1601. 2. Valojerdi MR. et al. Vitrification versus slow freezing gives excellent survival, post warming embryo morphology and pregnancy outcomes for human cleaved embryos. J Assist. Reprod. Genet. 2009;26(6):347-354. 3. Rienzi, L. et al. "Oocyte, embryo and blastocyst cryopreservation in ART: systematic review and meta-analysis comparing slow-freezing versus vitrification to produce evidence for the development of global guidance." Human reproduction update 23.2 (2017): 139-155. 4. Roy, TK. et al. Embryo vitrification using a novel semi-automated closed system yields *in vitro* outcomes equivalent to the manual Cryotop® method. Human Reproduction. 2014;19(11):2431–2438. 5. Gosden, R. "Cryopreservation: a cold look at technology for fertility preservation." Fertility and sterility 96.2 (2011): 264-268. 6. US Patent No:8,859,283. 7. Hobson, N. et al. PP-041-A pilot study evaluating clinical outcomes of the semi-automated Gavi® vitrification system. Reproductive BioMedicine Online 32 (2016): S19. 8. QFRM168 Gavi® user manual. 9. QRTF273_02 Gavi® Vitrification Equilibration Protocols Summary. 10. QRTV224 Human Embryo Vitrification on Gavi®. 11. ESHRE Special Interest Group Embryology and Alpha Scientists in Reproductive Medicine, RBM Online, 2017.

THE Gavi® FAMILY

Gavi® comes with a range of supplied accessories including:



• Gavi® LN₂ Bucket:

• Holds liquid nitrogen
• for the final stage of the
• vitrification process.¹



Gavi® Operating ••••• Tray:

Holds the Gavi®
Medium Cartridge,
Cassette and Tip & Seal
Cartridge.¹

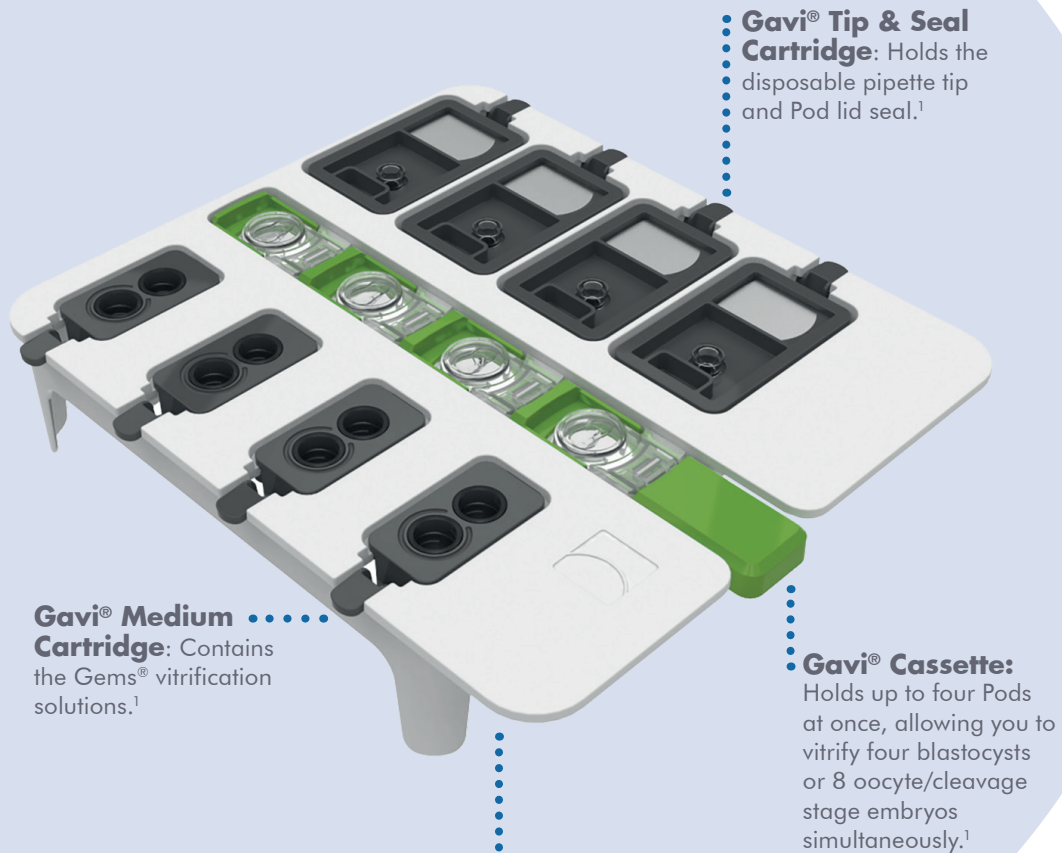


••• Gavi® Tweezers:

For a secure grasp of
the Gavi® Cassette
when dunked into
Gavi® LN₂ Bucket.¹

1. QFRM168 Gavi® user manual.

CONSUMABLES USED WITH Gavi®*



1.QFRM168 Gavi® user manual.

*Gavi® Pod, Gavi® Cassette, Gavi® Medium Cartridge, Gavi® Tip & Seal, Gavi® Working station and Gavi® storage dividers are sold separately from Gavi® instrument.

OPTIMAL CONDITIONS FOR VITRIFICATION

There are **many critical variables within the vitrification process** that can impact embryos' survival post-thawing – from achieving the right balance between the cryoprotectant concentrations and flow rates¹ to reducing manual handling.

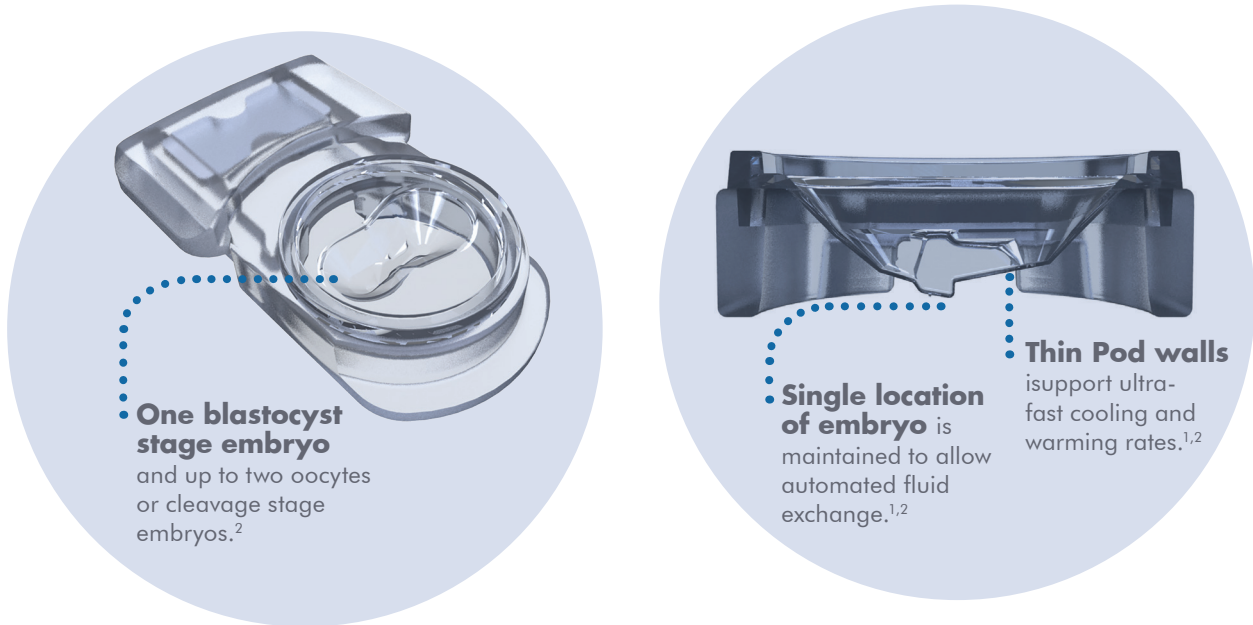
Gavi® HELPS YOU TO ACHIEVE OPTIMAL VITRIFICATION CONDITIONS WITH:

- **Automated solution dispensing:** A robotic liquid-handling unit dispenses the necessary solutions with a precision difficult to achieve by hand, and eliminating the need to manually move embryos between fluids.¹
- **Gavi® Pod design:** Designed to secure embryos in place during fluid exchange and liquid nitrogen (LN₂) storage¹, and to allow for rapid cooling and warming rates.
- **Control of exposure:** The time of exposure to cryoprotectant solutions is carefully controlled to avoid toxic over-exposure.¹⁻³
- **Temperature control:** The Peltier Module maintains and controls a precise, defined temperature.¹⁻⁴
- **Reduces the risk of cross-contamination:** After equilibration, the Pod is automatically heat-sealed so it can be placed directly into LN₂.^{1,2}



SMART INNOVATION: THE Gavi® POD

The key to Gavi®'s automated vitrification process is the Pod that holds the embryo in place during processing and LN₂ storage.



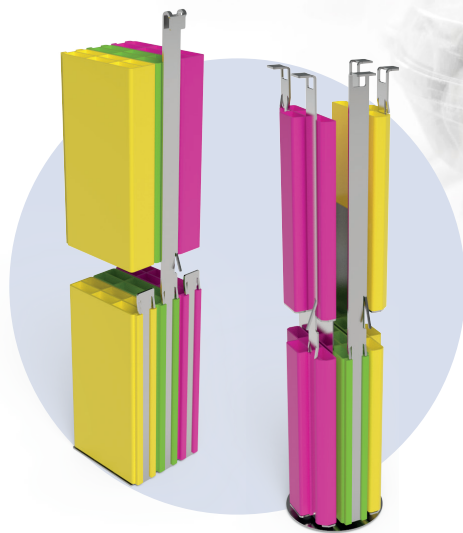
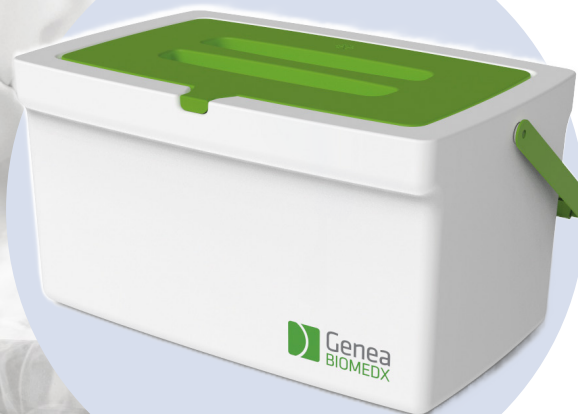
- The Gavi® Pod's unique design minimises embryo handling and stress compared to the manual process, thereby reducing the potential for adverse events like embryo loss.^{1,5}
- Gavi® helps to eliminate the risk of cross-contamination.^{1,5}
 - Provides a **closed system**: Automated heat-sealing ensures no contact with liquid N₂.
 - Each embryo/oocyte is processed with its own dedicated set of consumables.
- Gavi® Warming Solution 1 can be **added directly to the Pod** during thawing.²

1. Roy, TK. et al. Embryo vitrification using a novel semi-automated closed system yields *in vitro* outcomes equivalent to the manual Cryotop® method. Human Reproduction. 2014;19(11):2431–2438. 2. QFRM168 Gavi® user manual. 3. QFRM430_06_ Gavi® Service Manual. 4. QRTF273_02 Gavi® Equilibration Protocols Summary. 5. Wale, P. & Gardner, D. Hum Reprod Update 2016; 22, (1) 1–22.

ACCESSORIES USED WITH Gavi®*

For further ease, we offer:

Gavi® Working station: Holds the Gavi® cassette within LN₂ to facilitate the removal of single Pods for thawing.¹



..... **Gavi® Storage Dividers:** For use with cryogenic storage canisters, to provide orderly organization of Cassette and Pods by patient.¹ Available in round or rectangular form.

*Gavi® Pod, Gavi® Cassette, Gavi® Medium Cartridge, Gavi® Tip & Seal, Gavi® Working station and Gavi® storage dividers are sold separately from Gavi® instrument.

GREATER CONSISTENCY OF RESULTS COMPARED TO MANUAL METHODS²

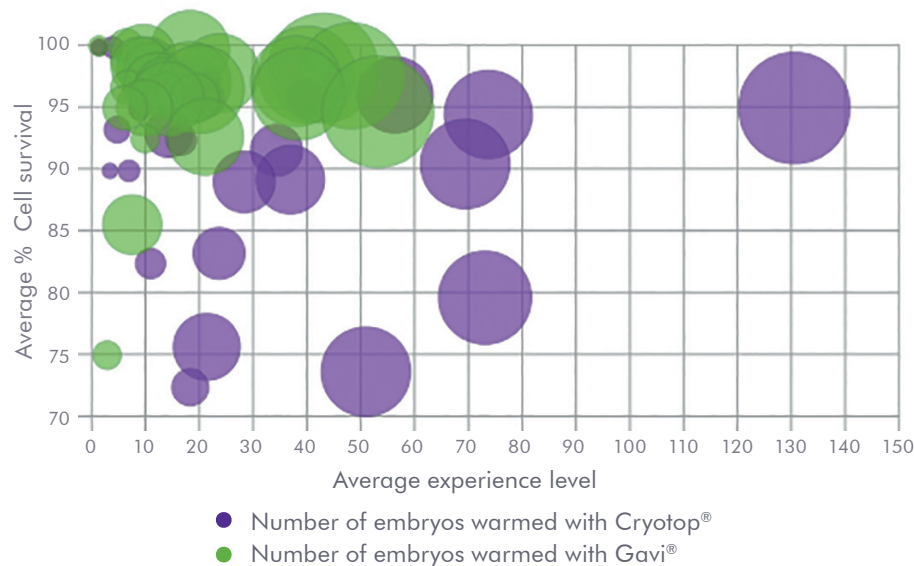
To evaluate the potential improvements from a training and standardisation perspective, survival results across freeze scientists for the early stages of implementation at all Genea labs of Gavi® (2015–2017) and Cryotop® (2009–2010) were retrospectively analysed.

When comparing blastocyst survival, Gavi® **reduces the variability of results among embryologists** of different experience levels with a particular device.^{2,3}

Gavi® requires reduced technical skill compared to manual vitrification methods, with shorter learning curves, and a reduced time to achieve vitrification competency.²⁻⁴

RECOVERED EMBRYO SURVIVAL BY EMBRYOLOGIST PERFORMING VITRIFICATION - Gavi® VS Cryotop®

(Adapted from Tumurbaatar. et al, ESHRE 2017²)



* Experience level was calculated using the embryo freeze order per scientist on that device. For example, if a scientist had frozen 10 embryos, three of which were warmed being the second, third and seventh frozen, then the average device experience level for this scientist = $(2 + 3 + 7)/3 = 4$.

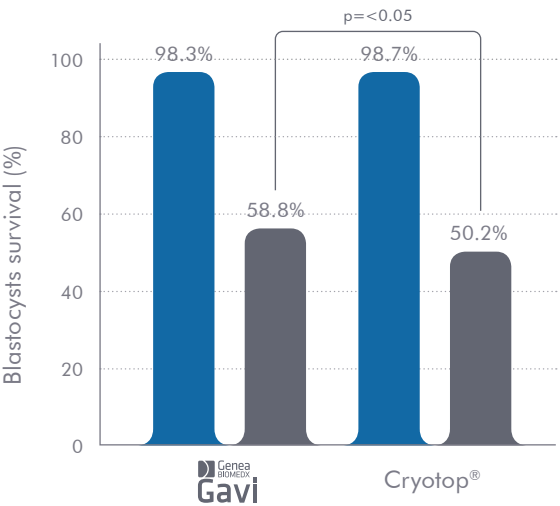
1. QFRM168 Gavi® user manual.
2. Tumurbaatar, U. et al. Genea, Oral 073 presented at ESHRE 2017.
3. QRTV224 Human Embryo Vitrification on Gavi®.
4. Roy et al, Hum Reprod 2014; 29 (11) 2431-2438.

DELIVERS COMPARABLE LABORATORY AND CLINICAL OUTCOMES

EVALUATION OF LABORATORY AND CLINICAL OUTCOMES OF HUMAN EUPLOID EMBRYOS VITRIFIED AT GENEART CLINICS

Improved blastocyst survival¹

Significantly more blastocysts from the Gavi[®] group that survived at 100% than from the Cryotop[®] group.



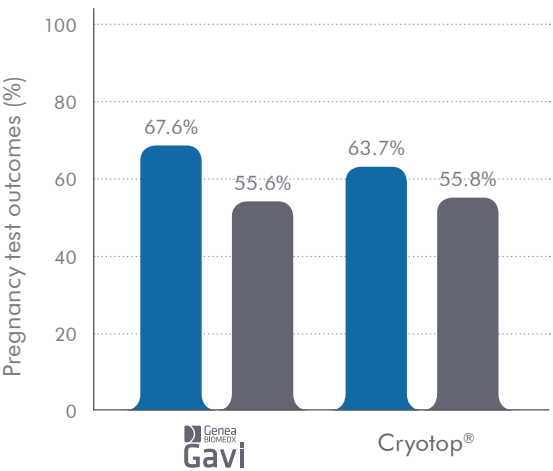
● Mean initial survival >75% ● Mean initial survival 100%

	Warmed (for ET) #	Mean Initial survival >75%	Mean Initial survival 100%
Gavi [®]	264	98.3%	58.8*
Cryotop [®]	276	98.7%	50.2*

*p<0.05, Fisher's Exact test

Comparable outcomes¹

Summary of embryo transfers and pregnancy tests outcomes.



● % + βhCG ● % FH Pregnancies

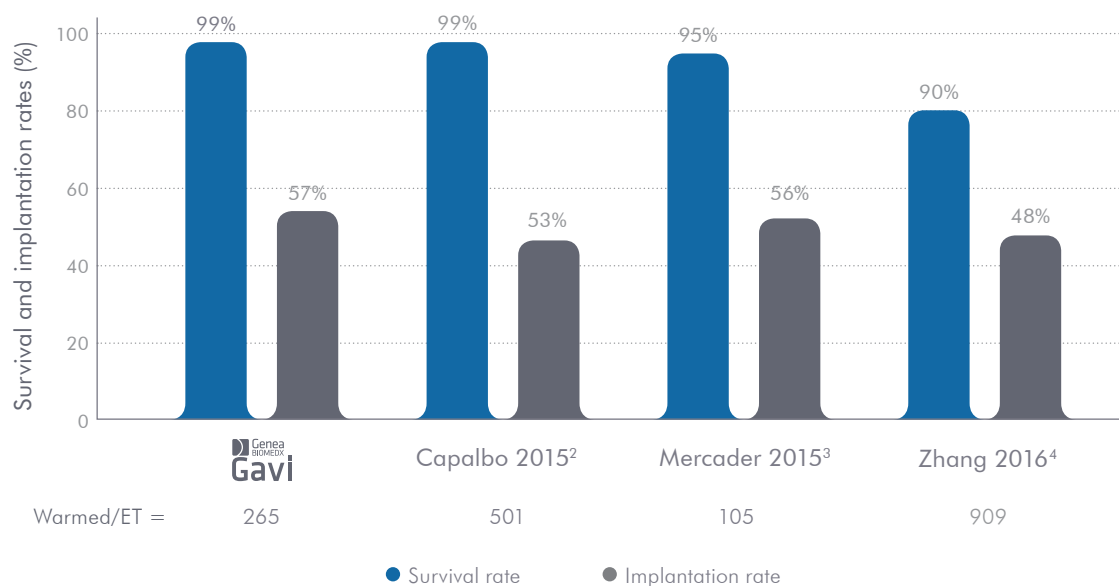
	#ETs	%+βhCG	% FH Pregnancies
Gavi [®]	259	67.6%	55.6%**
Cryotop [®]	273	63.7%	55.8%**

**No significant difference

ET = Embryo Tranfer. + βhCG = Positive chemical pregnancy. FH pregnancy = Foetal Heart pregnancy.



COMPARABLE CLINICAL OUTCOMES¹⁻⁴ OF Gavi® WITH EXTERNAL PUBLICATIONS USING Cryotop®, TRANSFERRING EUPLOID BLASTOCYSTS



A review was carried out of the published literature, reporting vitrification survival and clinical outcomes (implantation rates) of euploid blastocysts vitrified using a Cryotop® system following biopsy for PGS/PGD (PGT-A/PGT-M), to compare both survival and implantation rate. All studies, including Gavi® Genea study, reported a cryo-survival competency level >90% and comparable implantation rates.

1. Data on file QRTV224_08 Human Embryo Vitrification on Gavi®. 2. Capalbo, A. et al. "Consistent and reproducible outcomes of blastocyst biopsy and aneuploidy screening across different biopsy practitioners: a multicentre study involving 2586 embryo biopsies" Hum Reprod 31.1 (2016): 199-208. 3. Mercader, A. et al. Abstract presented at COGEN, Paris 2015- data on file IVI, Valencia, Spain. 4. Zhang, S. et al. "Number of biopsied trophectoderm cells is likely to affect the implantation potential of blastocysts with poor trophectoderm quality." Fertil Steril 105.5 (2016): 1222-1227.
PGS = Preimplantation Genetic Screening. PGD = Preimplantation Genetic Diagnosis. PGT-A = Preimplantation Genetic Testing for Aneuploidies. PGT-M = Preimplantation Genetic Testing for monogenic/single gene disorders.



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

Gavi® is manufactured by Genea Biomedx.

For further information, please contact your Service Representative or visit:

www.geneabiomedx.com



Product complies with applicable
European Union (EU) regulations



QRTM332-02

