

Summary of safety and clinical performance

EmbryoGlue™

This summary of safety and clinical performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions for Use (IFUs) as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

1 Device identification and general information

1.1	Device trade name	EmbryoGlue
1.2	Manufacturer's name and address	Vitrolife Sweden AB, Gustaf Werners gata 2, SE-421 32 Västra Frölunda, Sweden
1.3	Manufacturer's single registration number (SRN)	SE-MF-000002389
1.4	Basic UDI-DI	735002591AABDC
1.5	Medical device nomenclature description/text	A solution that provides a physiological environment for the retrieval, culture, maintenance, transfer, and/or storage of human sperm, harvested oocytes (eggs), and/or resulting embryos associated with the method of in vitro fertilization (IVF). The solution typically contains various combinations of salts, carbohydrates, amino acids, enzymes, hormones, albumin, vitamins, and/or drugs (e.g., antibiotics). This is a single-use device.
1.6	Class of device	Class III
1.7	Year when the first certificate (CE) was issued covering the device	MDD: REF 10085 in 2006, REF 10168 in 2019 MDR: 2024 (both REF 10085 and REF 10168)
1.8	Authorized representative if applicable; name and SRN	Not applicable
1.9	NB's name (the NB that will validate the SSCP) and the NB's single identification number	DNV Product Assurance AS Veritasveien 1, 1363 Høvik, Norway 2460

2 Intended use of the device

2.1 Intended purpose

EmbryoGlue is a medical device intended for use in Assisted Reproductive Technology (ART) as a medium for embryo transfer.

2.2 Indication and target population

The Indication for use of EmbryoGlue is "medium for embryo transfer". The target patient population is an adult or reproductive-age population that undergoes *in vitro* fertilization (IVF) treatment.

2.3 Contraindications and/or limitations

EmbryoGlue contains recombinant human albumin (rHA) (produced in yeast) and gentamicin. Do not use in patients with known hypersensitivity/allergy to any of the components.

3 Device description

3.1 Description of the device

EmbryoGlue is a bicarbonate buffered, physiological salt medium containing rHA, hyaluronan and gentamicin. The composition of EmbryoGlue has been developed to support implantation during embryo transfer. It is ready to use after equilibration at +37°C and 6% CO₂ atmosphere. Based on its Indication for Use, EmbryoGlue has patient contact.

EmbryoGlue is available in a 10 mL bottle (REF 10085) and as a patient pack, which contains 5 × 1.5 mL vials (REF 10168) (Figure 1). The device has a shelf life of 24 weeks (REF 10085) or 30 weeks (REF 10168) from the date of manufacture with storage at +2 to +8 °C and is stable until the expiry date shown on the container labels and the LOT-specific Certificate of Analysis. The medium is sterile filtered using aseptic technique and is sold in PETG bottles or polypropylene copolymer vials (pre-sterilized using gamma irradiation). EmbryoGlue 10mL bottles (REF 10085) can be used for up to two weeks after first opening while 1.5mL vials (REF 10168) should not be stored after opening.

Based on regulatory guidelines, the medicinal components present in EmbryoGlue are rHA and gentamicin.



Figure 1. EmbryoGlue in 10mL bottle (left) or 5x1.5 mLvials (right)

3.2 A reference to previous generation (s) or variants if such exists, and a description of the differences

Previous version of EmbryoGlue was EmbryoGlue version 3, as a part of Vitrolife GIII Series media. EmbryoGlue version 3 had penicillin G as an antibiotic. In 2007, Vitrolife replaced penicillin G with gentamicin due to its longer stability. EmbryoGlue version 3 is no longer available on the market.

Currently, EmbryoGlue is sold in two different volumes*:

- EmbryoGlue 10 mL (REF 10085) – Packed in PETG bottle with tamper evident seal.
- EmbryoGlue 5 × 1.5 mL (REF 10168) – Packed in USP Class VI Micro packaging vial with closure.

**All data presented in this document are related to the current version of EmbryoGlue sold on the market, unless otherwise specified.*

3.3 Description of any accessories which are intended to be used in combination with the device

Not applicable.

3.4 Description of any other devices and products which are intended to be used in combination with the device

General equipment and sterile non-toxic disposables for the IVF lab.

4 Risks and warnings

4.1 Residual risks and undesirable effects

The potential risks that could affect the patient or end user during the clinical use of EmbryoGlue are listed as below.

Effect	Hazardous situation
Patient	Patient exposed to gentamicin
	Patient exposed to rHA
	Patient exposed to non-biocompatible product
	Patient exposed to high level of endotoxins
	Patient exposed to microbial contamination or contaminated media
	Patient exposed to traces of yeast from rHA
	Patient exposed to unintended product
	Allergic patient exposed to gentamicin
	Allergic patient exposed to yeast
End user	User exposed to gentamicin
	User exposed to rHA
	User exposed to traces of yeast from rHA
	Allergic user exposed to gentamicin
	Allergic User exposed to yeast

For EmbryoGlue, all identified risks were deemed acceptable following the implementation of appropriate risk control measures. Regarding risks associated with rHA, the benefit-risk analysis concluded that the benefits of using rHA outweigh the potential risks of hypersensitivity. A systematic literature review conducted as part of the clinical evaluation did not identify any case reports of allergic reactions or hypersensitivity linked to the use of rHA in IVF settings.

No adverse events or undesirable side effects have been reported for the device throughout its time on the market. To manage risks associated with the use of EmbryoGlue, all raw materials are subject to stringent quality control (QC) procedures. Each batch (LOT) of the final product undergoes QC testing for sterility, bacterial endotoxins, and embryo toxicity prior to market release.

Biological evaluation supports the safe use of EmbryoGlue in clinical applications. None of the device components are classified as carcinogenic, mutagenic, or toxic to reproduction (CMR), and the primary packaging does not contain any hazardous substances or Substances of Very High Concern (SVHCs). All materials have been thoroughly tested to ensure device safety.

Stability studies have confirmed that the product maintains its specified properties throughout its shelf life. Additionally, end users are informed of the contraindications, and precautions through comprehensive labeling and the Instructions for Use (IFU).

4.2 Warnings and precautions

Contraindications

EmbryoGlue® contains recombinant human albumin (produced in yeast) and gentamicin. Do not use in patients with known hypersensitivity/allergy to any of the components.

Precautions

Precautions related to the use of EmbryoGlue REF 10085, and REF 10168 are listed.

- Discard product if bottle integrity is compromised. Do not use EmbryoGlue if it appears cloudy.
- To avoid contamination Vitrolife strongly recommends that media should be opened and used only with aseptic technique.
- The risk of reproductive toxicity and developmental toxicity for IVF media, including Vitrolife's IVF media, have not been determined and are uncertain.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established.
- Not for injection.
- Discard product according to standard clinical practice for medical hazardous waste when the procedure is finished.
- Federal (US) law restricts this device to sale by or on the order of a physician or practitioner trained in its use (Rx only).

An additional precaution related to the use of EmbryoGlue REF 10168 is listed.

- Re-use may result in microbiological contamination and/or property changes in the product.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

No field safety corrective actions have been taken for EmbryoGlue during its lifetime.

5 Summary of clinical evaluation and post-market clinical follow-up

5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable.

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

There is no clinical investigation conducted for EmbryoGlue before its CE-marking.

5.3 Summary of clinical data from other sources, if applicable

A recent systematic literature search was conducted to identify clinical data on the safety and performance of EmbryoGlue. An overview of clinical pregnancy rates (CPRs) and live birth rates (LBRs) including the use of EmbryoGlue reported by scientific literature from 2023 was summarized in

Table 1. The CPRs and LBRs from treatment cycles including the use of EmbryoGlue aligned with the yearly European results published by ESHRE [1].

Table 1. Clinical pregnancy rates (CPRs) and live birth rates (LBRs) after the use of EmbryoGlue reported by literature

Reference	CPR (%)	LBR (%)
[2] Horiuchi, 2023	31.7	NR
[3] Le, 2023*	53.2	NR
[4] Nakagawa, 2023	47.4	NR
[5] Ferrandiz, 2023 *	34.3	NR
[6] Koch, 2023 *	55.9	47.1
[7] Yan, 2023	39.6	34.2
[8] Lee, 2023	71.4	NR
[9] Bhoi, 2024	69.5	60.6
[10] Mizobe, 2024*	68.8	58.6
[11] Sorak, 2024	42	NR
[12] Illingworth, 2024*	47.4	41.7
[13] Kozinszky, 2024	35.2	NR
[14] Shi, 2024*	62.2	51.6
[15] Georgiou, 2025*	42.3	36.6

Note: NR: Not reported. * The clinical outcomes reported in the articles are stratified by groups, and outcomes are combined when all groups used EmbryoGlue as the embryo transfer medium.

5.4 An overall summary of the clinical performance and safety

According to the Indication for Use, EmbryoGlue is intended to support implantation following embryo transfer. Since implantation is the first step in the establishment of pregnancy, clinical pregnancy is considered relevant to confirm the safety and performance of EmbryoGlue. The CPRs reported after the use of EmbryoGlue aligns with the yearly European results published by ESHRE[1].

The high-level clinical evidence available from systematic review and meta-analysis [16-21] indicates that the addition of functional levels of hyaluronan to an embryo transfer medium is clinically beneficial. Bontekoe et al. 2014 [16] evaluated 16 RCTs and showed improved CPRs and LBRs with the use of functional concentrations of hyaluronan as an adherence compound in ART cycles. The meta-analysis by Heymann et al. 2020 [17] evaluated 26 RCTs and found that functional hyaluronan concentrations (0.5mg/ml) in the transfer media improved CPRs and LBRs. Tyler et al. 2022 [19] showed that performing ET with hyaluronan versus routine care (n = 9, RR 1.457, 95% CI 1.197-1.261, I² = 46.48%) led to higher CPRs. The best available evidence summarized by Heymann et al. 2022 [18] indicates that the addition of functional levels of HA to embryo transfer medium is clinically beneficial in cycles with autologous oocytes. There is moderate evidence to conclude that the addition of functional levels of hyaluronan to a transfer medium may increase the chance of live birth from 32% to 39%, with an additional live birth for every 14 embryos transferred. Hyaluronan addition improves CPRs from 42% to 47% and multiple pregnancy rates from 16% to 23%. He et al. 2023 [20] investigated the effectiveness and safety of 36 different therapies for patients with recurrent implantation failure (RIF) and concluded that embryo medium enriched with hyaluronan could significantly improve pregnancy outcomes in these patients.

According to recent good practice recommendations from the ESHRE Add-ons working group, the addition of hyaluronan to a transfer medium is recommended. Current data indicate that the addition of hyaluronan as an adherence compound in embryo transfer media in IVF treatment increases LBR following fresh transfers, without a significant effect on adverse outcomes. No effect was seen following frozen-thawed embryo transfers. The higher multiple pregnancy rates after the use of a hyaluronan-supplemented transfer medium should be further investigated [21].

Data from biological evaluation, post market surveillance (PMS) and risks management also add support to the safety and performance of EmbryoGlue. No undesirable side-effects have been identified for EmbryoGlue during its lifecycle and the benefit-risk profile is acceptable.

Together, these data confirm safety and performance of EmbryoGlue for its Indication for Use and clinical claims.

5.5 Ongoing or planned post-market clinical follow-up

There are no ongoing or planned PMCF studies for EmbryoGlue. However, PMS will continuously monitor the device throughout its lifetime and general PMCF procedures such as an end user survey, screening of scientific literature and AE databases will be conducted to identify any emerging risks, AEs/Incidents/complications, or performance issues.

6 Possible diagnostic or therapeutic alternatives

ART is a treatment option for patients failing to conceive naturally as well as patients who have tried other treatments such as medications and surgical procedures without success. There are no therapeutic alternatives for patients at this stage.

For embryo transfer, Vitrolife has four products with embryo transfer as an intended use: EmbryoGlue, G2 PLUS, G-TL and Gx-TL. EmbryoGlue has a high concentration of hyaluronan, whereas the others have lower concentrations.

Meta-analysis and systematic reviews indicate that the addition of a high concentration of hyaluronan to embryo transfer medium is clinically beneficial, reporting improved CPRs and LBRs with the use of EmbryoGlue. ESHRE Add-ons working group recommend the addition of HA to transfer media based on the current evidence [21].

7 Suggested profile and training for users

The end user (IVF professional) is expected to follow good practice in IVF laboratories (2015) and use the device according to its IFU. As no special design feature or safety concerns were identified for EmbryoGlue, no specific training is required for end-users.

8 Reference to any harmonized standards and common specifications applied

- Regulation (EU) 2017/745 (MDR)
- EN ISO 14971:2019/A11:2021. Medical Devices. Application of risk management to medical devices. December 2021.
- ISO/TR 20416:2020. Medical devices — Post-market surveillance for manufacturers. July 2020
- EN ISO 20417:2021. Medical devices — Information to be supplied by the manufacturer. December 2021
- MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies. April 2020
- MDCG 2019-9 Rev.1. Summary of safety and clinical performance. A guide for manufacturers and notified bodies. March 2022

The conformity assessment procedure follows Annex IX in the MDR.

9 Revision history

Version	Date issued	Description	Revision validated by the Notified Body
v.1.0	2020-10-13	Initial version of Draft SSCP for EmbryoGlue (REP-2379)	
v.2.0	2021-09-16	Annual update of SSCP for EmbryoGlue (REP-2379)	
v.3.0	2022-06-30	Annual update of SSCP for EmbryoGlue (REP-2379)	
v.4.0	2022-09-07	Edits according to DNV comments (REP-2379)	
v.5.0	2023-03-16	Edits address of DNV in section 1 (REP-2379)	☒ Yes Validation language: English
v.6.0	2023-10-12	Annual update	
v.7.0	2024-09-30	Annual update	
v.8.0	See publish date	Edit section 6 and adjust the citation format	☒ Yes Validation language: English
v.9.0	See publish date	Annual update in 2025	☒ Yes Validation language: English

10 References

1. Smeenk, J., et al., *ART in Europe, 2019: results generated from European registries by ESHRE*. Hum Reprod, 2023. **38**(12): p. 2321-2338.
2. Horiuchi, Y., et al., *Efficacy of Hyaluronan-Enriched Transfer Medium for Low-Grade Frozen Embryo Transfer*. Cureus, 2023. **15**(5).
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5. Ferrandiz, A.G., et al., *Comparison of biochemical and clinical pregnancy rate and first outcomes with or without non-invasive preimplantation genetic testing for aneuploidies: a retrospective cohort study*. Journal of IVF-Worldwide, 2023. **1**(4).
6. Koch, J., et al., *Sonographer-guided frozen embryo transfer vs ultrasound-assisted frozen embryo transfer—A randomised controlled study*. Australian and New Zealand Journal of Obstetrics and Gynaecology, 2023.
7. Yan, Q., et al., *Effect of hyaluronic acid-enriched transfer medium on frozen-thawed embryo transfer outcomes in RIF patients: a single-centre retrospective study*. Frontiers in Endocrinology, 2023. **14**: p. 1170727.
8. Lee, J., et al., *P-139 Comparison of clinical outcomes between two hyaluronan-rich transfer medium*. Human Reproduction, 2023. **38**(Supplement_1): p. dead093. 503.
9. Bhoi, N.R., et al., *Effect of Hyaluronic Acid-Containing Transfer Media (EmbryoGlue®) on the Live Birth Rate in Frozen Thawed Embryo Transfer Cycles*. Cureus, 2024. **16**(1): p. e52713.
10. Mizobe, Y., et al., *Formation of the first plane of division relative to the pronuclear axis predicts embryonic ploidy*. Reproductive BioMedicine Online, 2024: p. 104110.
11. Sorak, M.P., et al., *Activity of enzymes in the follicular fluid and outcome of in vitro fertilization*. Medicine, 2024. **103**(4): p. e36851.
12. Illingworth, P.J., et al., *Deep learning versus manual morphology-based embryo selection in IVF: a randomized, double-blind noninferiority trial*. Nat Med, 2024. **30**(11): p. 3114-3120.
13. Kozinszky, Z., et al., *Pre- and Procedural Factors Influencing the Success of In Vitro Fertilization: Evaluating Embryo Quality and Clinical Pregnancy in Cases of Tubal Factor Infertility*. Journal of Clinical Medicine, 2024. **13**(19): p. 5754.
14. Shi, S., et al., *The impact of blastocyst grade on singleton birth weight in fresh IVF-ET cycles in ART: a retrospective study*. BMC Pregnancy Childbirth, 2024. **24**(1): p. 588.
15. Georgiou, E.X., et al., *The Effect of Assisted Reproductive Technologies on Human Sex Ratios*. Aust N Z J Obstet Gynaecol, 2025.
16. Bontekoe, S., et al., *Adherence compounds in embryo transfer media for assisted reproductive technologies*. Cochrane Database Syst Rev, 2014. **2**: p. CD007421.

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REP-2379	9.0	2025/08/14

17. Heymann, D., et al., *Hyaluronic acid in embryo transfer media for assisted reproductive technologies*. Cochrane Database Syst Rev, 2020. **9**: p. CD007421.
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