Summary of safety and clinical performance G-GAMETE™

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 (IFU) 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	G-GAMETE™
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	735002591AAEDJ
1.5	Global Medical device nomenclature (GMDN) code	44046
1.6	Class of device	Class III
1.7	Year when the first certificate (CE) was issued covering the device	2008
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 Single Identification Number: 2460

2 Intended use of the device

2.1 Intended purpose

G-GAMETE is a medical device intended for use in Assisted Reproductive Technology (ART) as a medium for handling and manipulating oocytes and embryos in ambient atmosphere.

2.2 Indication(s) and target population(s)

The Indication for use of the G-GAMETE is "medium for handling and manipulating oocytes and embryos in ambient atmosphere". The intended target group is an adult or reproductive-age population that undergoes IVF treatment or fertility preservation, respectively.

2.3 Contraindications and/or limitations

G-GAMETE™ contains gentamicin. Do not use in patients with known hypersensitivity/allergy to the component.

3 Device description

3.1 Description of the device

G-GAMETE is a MOPS and bicarbonate buffered, physiological salt solution intended to support handling of oocytes and embryos in ambient atmosphere. The device is to be used after equilibration at +37°C and 6% CO_2 atmosphere. Based on its Indication for Use, G-GAMETE is not intended to have patient contact.

G-GAMETE has a shelf life of 21 weeks from the date of manufacture and is stable until the expiry date shown on the container labels and the LOT-specific Certificate of Analysis. The device is sterile filtered using aseptic technique and is sold in 30 ml volumes in PETG bottle (pre-sterilized using gamma irradiation) with tamper evident seal (Figure 1). Based on regulatory guidelines, the medicinal components present in G-GAMETE include gentamicin and human serum albumin (HSA).

Figure 1. G-GAMETE

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

There have been no previous versions of G-GAMETE on the market.

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 including CO_2 incubator, microscope, OVOIL, G-IVF PLUS, G-1 PLUS, HYASE-10X and ICSI.

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 G-GAMETE are the following:

Risks related to G-GAMETE with an effect on patient or end user

Effect	Hazardous situation
Patient	Patient exposed to contaminated HSA
End user	User exposed to gentamicin
	User exposed to HSA
	User exposed to contaminated HSA
	Allergic user exposed to gentamicin

All the risks related to G-GAMETE are acceptable after risk control measures except for risks due to HSA with an effect on safety of the patient (patient exposed to contaminated HSA) or the end user (user exposed to contaminated HSA). These risks have the harm ‘permanent effect on patient: viral infection of patient’ or ‘permanent effect on user: viral infection of user’. HSA is derived from human blood and could theoretically be a vector for various diseases such as hepatitis B, hepatitis C and HIV 1/2. The probability of patient or user being virally infected during IVF treatment is extremely small, yet the risk is considered unacceptable. Systematic literature search conducted during clinical evaluation has not identified any negative effects or infection associated with the use of HSA in IVF media. No undesirable effect of adverse event has been reported for any of Vitrolife’s media containing HSA. The benefit-risk evaluation performed during risk analysis concluded that the benefits of using HSA in IVF media are greater than the risks associated with blood-borne contamination as Vitrolife applies relevant safety measures. The raw material source of HSA used in Vitrolife’s media has been tested for blood-borne diseases by accredited laboratories.

To control risks related to the use of G-GAMETE, all the raw materials are quality tested and each LOT of the final product is also tested for sterility, endotoxin, and embryo toxicity prior to its release. The end user is informed about the device components, contraindication, precautions, and risk of using blood derived products by providing information on labels and Instruction for Use.

4.2 Warnings and precautions

Contraindications

G-GAMETE contains gentamicin. Do not use in patients with known hypersensitivity/allergy to the component.

Precautions

- Discard product if bottle integrity is compromised. Do not use G-GAMETE if it appears cloudy.
- G-GAMETE contains human serum albumin.
- Caution: All blood products should be treated as potentially infectious. Source material from which this product was derived was found negative when tested for antibodies to HIV, HBc, HCV, and HTLV I/II and non-reactive for HbsAg, HCV RNA and HIV-1 RNA and syphilis. No known test methods can offer assurance that products derived from human blood will not transmit infectious agents.
- 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 the product according to standard clinical practice for medical hazardous waste when the procedure is finished.

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

Not applicable.

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 was no clinical investigation conducted for G-GAMETE before its CE-marking.

5.3 Summary of clinical data from other sources, if applicable

A systematic literature search has identified several publications reporting fertilization rates from treatment cycles including the use of G-GAMETE for washing of oocyte handling and manipulation in ambient atmosphere (Park et al. 2015b; Aydinuraz et al. 2016; Karabulut et al. 2018; Rehman et al. 2019; Kadoura et al. 2022). Fertilization rates following the use of G-GAMETE were in line with the competency values reported by the Vienna Consensus report on the ART laboratory performance indicators (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine 2017) (Smeenk et al. 2023). Successful clinical outcomes including clinical pregnancy, ongoing clinical pregnancy or delivery rates or live birth were also reported from treatment cycles that included the use of G-GAMETE (Park et al. 2015a; Park et al. 2015b; Aydinuraz et al. 2016; Karabulut et al. 2018; Rehman et al. 2019; Kadoura et al. 2022; Ahlström et al. 2023). The clinical pregnancy rates from studies by Park *et al.*, 2015a; Park *et al.*, 2015b; Aydinuraz *et al.*, 2016; Kadoura *et al.*, 2022 aligned with the yearly European results published by ESHRE (Wyns et al. 2022). There is no recommended competency value for clinical pregnancy and the yearly European results published by ESHRE is used as a reference (Wyns et al. 2022).

No undesirable side-effect, trends or vigilance reports have been identified for G-GAMETE during its post-market surveillance (PMS). Data from biological evaluation concluded biological safety and biocompatibility of G-GAMETE.

5.4 An overall summary of the clinical performance and safety

According to the Indication for Use, G-GAMETE is intended to provide clinical benefit by supporting handling and manipulation of oocytes and embryos in ambient atmosphere. Based on its use for oocyte or embryo handling/manipulation, the first measurable endpoint can be fertilization or embryo development rate. As described above, data from publication including the use G-GAMETE for handling and

manipulation of oocytes confirm the safety and performance of the device. According to the Indication for Use, G-GAMETE can be used for handling and manipulating embryos in ambient atmosphere. However, oocytes are more vulnerable to stress compared to embryos, and transient variation in temperature can cause irreversible disruption of the meiotic spindle in human oocytes (Pickering et al. 1990). Given that the oocyte is a single cell that is more vulnerable to stress than embryos, the data obtained on the use of G-GAMETE for oocyte handling and manipulation support its use for embryos handling and manipulation in ambient atmosphere. There are no indications of any negative effects resulting from the use of G-GAMETE. The clinical pregnancy rate after the use of G-GAMETE align with the yearly European results published by the European Society of Human Reproduction and Embryology (ESHRE) (Wyns et al. 2022). Data from PMS and risk management also add support to the safety and performance of G-GAMETE. No undesirable side-effects have been identified for G-GAMETE during its lifecycle and the benefit-risk profile is acceptable. Therefore, the benefit-risk profile is considered to be acceptable according to current knowledge/state of the art.

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

5.5 Ongoing or planned post-market clinical follow-up

There is sufficient clinical evidence confirming the conformity of G-GAMETE with applicable regulatory requirements. There are no unanswered questions regarding the performance and safety of the device. Risk management has been effective, no further risks have been identified during the clinical evaluation and the benefit-risk profile is acceptable. However, post-market surveillance will continuously monitor the device during its time on the market and general PMCF procedures such as end user survey, screening of scientific literature and adverse event databases will be conducted to identify any emerging risks, complications, and safety 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. Hence, there are no therapeutic alternatives for patients at this stage. Fertility preservation can be considered as a therapeutic alternative for patients undergoing ART. It serves as a proactive approach to safeguard reproductive potential, especially when medical conditions or treatments may impact fertility.

G-GAMETE is a medium intended for use in ART as medium for handling and manipulating oocytes and embryos in ambient atmosphere. Devices with similar intended uses as G-GAMETE are available in the European Union or other international markets.

7 Suggested profile and training for users

The end user (IVF professional) is expected to be trained and qualified within IVF field to understand the Indication for Use of G-GAMETE. Since no special design or safety concerns were identified for G-GAMETE, there is no specific training required for the end-users.

8 Reference to any harmonized standards and common specifications applied

- Medical Devices Regulation (EU) 2017/745 (MDR)
- EN ISO 14971:2019. Medical devices — Application of risk management to medical devices

- EN ISO 15223-1:2016. Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements
- EN ISO 20417:2021. Medical devices — Information to be supplied by the manufacturer MEDDEV 2.7/4
- EN ISO/TR 20416:2020. Medical devices — Post-market surveillance for manufacturers
- 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 will be performed according to the procedure outlined in Annex IX of the MDR (EU) 2017/745.

9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
1	2021-03-26	Initial version of draft SSCP for G-GAMETE (REP-3453-v.1.0)	
2	2022-03-28	Periodic update of SSCP for G-GAMETE (REP-3453-v.2.0)	
3	2022-09-16	Addition of DNV full address and conformity assessment procedure (REP-3453-v.3.0)	
4	2023-03-13	Edit the address of the notified body in section 1 (REP-3453-v.4.0)	
5	2023-05-31	Annual update of SSCP for G-GAMETE (REP-3453-v.5.0)	
6	2024-03-11	Annual update of SSCP for G-GAMETE (REP-3453-v.6.0)	
7	See publish date	Edit Section 6 of SSCP for G-GAMETE (REP-3453-v.7.0)	☑ Yes Validation language: English

10 References

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