Summary of safety and clinical performance: G-RINSE™

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	G-RINSE™
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	735002591AAJDU
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	2004
1.8	Authorized representative if applicable; name and SRN	Not applicable
1.9	NB's name, address, (the NB that will validate the SSCP) and the NB's single identification number	Det Norske Veritas (DNV) Product Assurance AS Veritasveien 3, 1363 Høvik Norway 2460 Single Identification Number: 2460

2 Intended use of the device

2.1 Intended purpose

G-RINSE is a medical device intended for use in Assisted Reproductive Technology (ART) as a solution for rinsing of contact materials and for washing of the cervix.

2.2 Indication(s) and target population(s)

The Indication for use of G-RINSE is "solution for rinsing of contact materials and for washing of the cervix. Not for culture". 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-RINSE contains gentamicin. Do not use in patients with known hypersensitivity/allergy to the component.

3 Device description

3.1 Description of the device

G-RINSE is a bicarbonate buffered, physiological salt solution containing gentamicin, intended to support ART procedures by rinsing of contact materials and washing the cervix. It is ready to use after equilibration at +37˚C and 6% CO_2. The medium is sterile filtered using aseptic technique and supplied in a gamma-sterilized bottle with tamper evident seal (Figure 1). Media bottles can be used for up to two weeks after first opening. Based on its Indication for Use, G-RINSE will have patient contact.

Figure 1. G-RINSE

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

The previous version of G-RINSE was G-RINSE version 3 which was part of Vitrolife G III Series media containing penicillin G as an antibiotic. In 2007, Vitrolife shifted from penicillin G to gentamicin due to the greater longevity of gentamicin. The previous version of G-RINSE is not available on the market.

NOTE: Apart from multicenter evaluation which included the previous version of G-RINSE, all the data presented in this document apply to the current version of G-RINSE sold 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 in the IVF lab including CO_2 incubator.

4 Risks and warnings

4.1 Residual risks and undesirable effects

All the risks associated with the use of G-RINSE including biological risks are acceptable after risk control measures.

The clinical risks that could occur during the use of G-RINSE are:

- Patient exposed to gentamicin.
- Patient exposed to non-biocompatible product.
- Patient exposed to contaminated media or high level of endoxtoxins.
- Patient exposed to microbial contaminated/contamination in media.
- Patient exposed to unintended product.
- Allergic patient exposed to gentamicin.
- User exposed to gentamicin.
- Allergic user exposed to gentamicin.

No adverse events or undesirable side-effects have been reported for the device during its time on the market. To control the risks related to the use of G-RINSE, all 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. Biological evaluation concluded that all components are nutrients that are either naturally present in mammal tissues or have been used in the handling or treatment of human cells for an extended period. No materials or substances are listed as harmful. All chemicals, bottles and final products are tested to confirm non-toxicity. Stability studies confirm that the product is not toxic during its entire lifetime. Additionally, 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

The precautions related to the use of G-RINSE are:

- Discard product if bottle integrity is compromised. Do not use G-RINSE 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 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

No field safety corrective action has been taken for G-RINSE during its lifecycle.

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

Not applicable.

5.3 Summary of clinical data from other sources, if applicable

A multicenter evaluation of Vitrolife's GIII Series media including G-RINSE has been performed during the development phase of G-RINSE (Vitrolife's internal data). Clinical pregnancy and implantation rates following 800-day 3 or day 5 embryo transfers supported the safety and performance of G-RINSE. The reported clinical pregnancy rates (48% and 40%) aligned with the European results published by ESHRE (Wyns et al. 2022).

A systematic literature search was performed during the clinical evaluation of G-RINSE to identify clinical data supporting the safety and performance of the device. Several publications included the use of G-RINSE for rinsing of contact materials and washing of cervix prior to oocyte retrieval (Balaban and Urman 2005; Urman et al. 2008; Hallberg et al. 2021) or embryo transfer (Ata et al. 2007; Ergin et al. 2007; Vicdan et al. 2007; Cetin et al. 2010; Hatirnaz et al. 2016; Gursu et al. 2022; Gursu et al. 2023). Fertilization and implantation rates were in line with the competency values reported in 2017 by the ESHRE Special Interest Group of Embryology and Alpha Scientists (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine 2017). The clinical pregnancy rates reported after the use of G-RINSE aligned with the yearly European results published by ESHRE (Wyns et al. 2022). Four key references provided data on live birth after the use of G-RINSE (Hatirnaz et al. 2016; Hallberg et al. 2021; Gursu et al. 2022; Gursu et al. 2023). From a safety perspective, all key references reported successful reproductive outcomes including clinical pregnancy and/or live birth following a treatment that included G-RINSE (Balaban and Urman 2005; Ata et al. 2007; Ergin et al. 2007; Vicdan et al. 2007; Urman et al. 2008; Cetin et al. 2010; Hatirnaz et al. 2016; Hallberg et al. 2021; Gursu et al. 2022; Gursu et al. 2023). According to the literature search outcomes, no deviation was found in the safety or performance of the device.

No post-market clinical follow-up (PMCF) studies has been conducted for G-RINSE. However, results from a PMCF end-user survey confirm the safety and performance of of G-RINSE and ensure the continued acceptability of the benefit-risk ratio. No emerging risks or unknown side-effects were identified, and no known side-effects and/or contraindications were found. G-RINSE has been on the market since 2002, and no serious incidents, or trend reports on non-serious incidents/undesirable side effects were identified during the PMS of G-RINSE.

5.4 An overall summary of the clinical performance and safety

According to the Indication for Use, the clinical benefit of G-RINSE is intended to support ART procedures by rinsing of contact materials and washing the cervix which is supported by data from multicenter evaluation, national registry, and scientific literature. The fertilization and implantation rates reported after the use of G-RINSE were in line with the competency values reported in 2017 by the ESHRE Special Interest Group of Embryology and Alpha Scientists (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine 2017). Likewise, the clinical pregnancy rates following a treatment that included G-RINSE aligned with the yearly European results published by ESHRE (Wyns et al. 2022). Data from PMS including national registry data also support the safety and performance of

G-RINSE. There are no indications of any negative effects resulting from the use of G-RINSE. The risk management has been effective: there are no unacceptable residual risks and no new risks have been identified. Therefore, the benefit-risk profile is considered acceptable according to the current knowledge/state of the art.

5.5 Ongoing or planned post-market clinical follow-up

There are no ongoing or planned PMCFs. However, general PMCF procedures, such as end user survey, screening of scientific literature and searching AE databases will be performed.

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.

Fertility preservation can serve as a therapeutic alternative for patients undergoing ART, offering a proactive measure to safeguard reproductive potential, particularly in cases where medical conditions or treatments may impact fertility.

G-RINSE is a medium intended for use in ART as a solution for rinsing of contact materials and for washing of the cervix. To the best of our knowledge, there are currently no devices with similar intended uses as G-RINSE 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 ART field to understand the Indication for Use of G-RINSE. Since no special design or safety concerns were identified for G-RINSE, there is no specific training required for the end-users.

8 Reference to any harmonised 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 Annex IX in the MDR (EU) 2017/745.

9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
1	2021-04-30	Initial version of draft SSCP for G-RINSE (REP-3585-v.1.0)	
2	2022-09-07	Annual update of SSCP (REP-3585-v.2.0)	
3	2023-03-13	Edit address of the notified body in section 1 (REP-3585-v.3.0)	
4	2023-08-22	Annual update of SSCP for G-RINSE (REP-3585-v.4.0)	
5	2024-05-15	Annual update of SSCP for G-RINSE (REP-3585-v.5.0)	
6	See publish date	Edit Section 6 of SSCP for G-RINSE (REP-3585-v.6.0)	☑ Yes Validation language: English

10 References

Ata B, Isiklar A, Balaban B, Urman B. 2007. Prospective randomized comparison of Wallace and Labotect embryo transfer catheters. *Reprod Biomed Online* **14**: 471-476.

Balaban B, Urman B. 2005. Comparison of two sequential media for culturing cleavage-stage embryos and blastocysts: embryo characteristics and clinical outcome. *Reprod Biomed Online* **10**: 485-491.

Cetin MT, Kumtepe Y, Kiran H, Seydaoglu G. 2010. Factors affecting pregnancy in IVF: age and duration of embryo transfer. *Reprod Biomed Online* **20**: 380-386.

Ergin E, Oztel Z, Sohtorik T, Ozay A, Elter K, Ozornek H. 2007. Comparison of pregnancy and implantation rates for two different embryo transfer catheters. *Fertility and sterility* **88**: S333-S334, P-682.

ESHRE Special Interest Group of Embryology, Alpha Scientists in Reproductive Medicine. 2017. The Vienna consensus: report of an expert meeting on the development of ART laboratory performance indicators. *Reprod Biomed Online* **35**: 494-510.

Gursu T, Celik HG, Eraslan A, Angun B, Ozaltin S, Yeh J, Bastu E. 2022. Comparison of pregnancy outcomes of 7515 same donor oocyte cycle fresh and cryopreserved-thawed oocytes in 609 donor oocyte recipient cycles: A single institution analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology* **277**: 110-115.

Gursu T, Eraslan A, Angun B, Celik HG, Yeh J, Bastu E. 2023. Comparison of pregnancy outcomes of cervical mucus washing with physiologic saline solution or G-Rinse medium solution, in elective single-embryo transfers. *J Assist Reprod Genet* **40**: 865-871.

Hallberg I, Plassmann M, Olovsson M, Holte J, Damdimopoulou P, Sjunnesson YCB, Benskin JP, Persson S. 2021. Suspect and non-target screening of ovarian follicular fluid and serum - identification of anthropogenic chemicals and investigation of their association to fertility. *Environ Sci Process Impacts* **23**: 1578-1588.

Hatirnaz S, Hatirnaz E, Dahan MH, Tan SL, Ozer A, Kanat-Pektas M, Ata B. 2016. Is elective single-embryo transfer a viable treatment policy in in vitro maturation cycles? *Fertility and sterility* **106**: 1691-1695.

Urman B, Yakin K, Ata B, Isiklar A, Balaban B. 2008. Effect of hyaluronan-enriched transfer medium on implantation and pregnancy rates after day 3 and day 5 embryo transfers: a prospective randomized study. *Fertility and sterility* **90**: 604-612.

Vicdan K, Isik AZ, Akarsu C, Sozen E, Caglar G, Dingiloglu B, Tuncay G. 2007. The effect of retained embryos on pregnancy outcome in an in vitro fertilization and embryo transfer program. *European journal of obstetrics, gynecology, and reproductive biology* **134**: 79-82.

Wyns C, De Geyter C, Calhaz-Jorge C, Kupka MS, Motrenko T, Smeenk J, Bergh C, Tandler-Schneider A, Rugescu IA, Goossens V. 2022. ART in Europe, 2018: results generated from European registries by ESHRE. *Hum Reprod Open* **2022**: hoac022.

Vitrolife, internal data on file. A-H Jakobsson. GIII Series™ Multi Centre Evaluation. Results from 800 embryo transfers.