Summary of safety and clinical performance SpermRinse™

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	SpermRinse
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	735002591ABEDM
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	2006
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	Det Norske Veritas (DNV) Product Assurance AS Veritasveien 3, 1363 Høvik Norway 2460

2 Intended use of the device

2.1 Intended purpose

SpermRinse is a medical device intended for use in assisted reproductive technology (ART) as a medium for sperm preparation.

2.2 Indication and target population

SpermRinse: Medium for sperm preparation.

The patient target group is an adult or reproductive-age population that undergoes *in vitro* fertilization (IVF) treatment or fertility preservation.

2.3 Contraindications and/or limitations

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

3 Device description

3.1 Description of the device

SpermRinse is a bicarbonate and HEPES buffered, physiological salt solution that contains human serum albumin (HSA) and gentamicin. Based on its Indication for Use, SpermRinse will have contact with sperm.

The device is sterile-filtered delivered in gamma-irradiated, presterilized 30 mL and 125 mL bottles (Figure 1). SpermRinse is ready to use after equilibration at +37˚C and 5% CO_2 or ambient atmosphere. SpermRinse is stable until the expiry date shown on the container labels and the LOT-specific Certificate of Analysis. Media bottles should not be stored after opening and excess media should be discarded after completion of the procedure.

Based on regulatory guidelines, the medicinal components present in SpermRinse are gentamicin and HSA. Gentamicin is an antibiotic that could result in sensitization or allergic reaction in the patient or user.

Figure 1. SpermRinse REF 10146 (125 mL) and REF 10101 (30 mL)

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

There have been no previous versions of SpermRinse 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, warm incubator, centrifuge and SpermGrad.

4 Risks and warnings

4.1 Residual risks and undesirable effects

After mitigation, there are two unacceptable residual risks due to the presence of HSA, with the hazardous situations, “Patient exposed to contaminated human serum albumin (HSA)” and “User exposed to contaminated human serum albumin (HSA)”. However, according to the Indication for Use, SpermFreeze Solution does not have contact with the patient. The end user (IVF professional) is expected to follow the ESHRE revised guidelines for good practice in IVF laboratories and use the device according to its IFU. The benefit-risk analysis of these risks concluded that the benefits of including HSA in SpermRinse outweigh the risks associated with blood-borne contamination. No case reports of allergic/hypersensitivity reactions or infections associated with the use of HSA during ART procedures have been reported. No adverse events (AEs) and undesirable side-effects have been reported for the device during its time on the market. To control risks, raw materials for SpermRinse are quality tested and each LOT of the final product is tested for pH, osmolality, sterility, embryo toxicity and bacterial endotoxins. Additionally, the user is informed about the device components, contraindication, and precautions by providing information on labels and the IFU.

All the potential clinical risks that could occur during the use of SpermRinse are listed below.

Effect	Hazardous situation
Patient	Patient exposed to non-biocompatible product.
	Patient exposed to contaminated human serum albumin (HSA).
End user	User exposed to gentamicin.
	Allergic user exposed to gentamicin.
	User exposed to human serum albumin (HSA) or recombinant human albumin (rHA).
	User exposed to contaminated human serum albumin (HSA).

4.2 Warnings and precautions

Precautions related to the use of SpermRinse are listed.

- Discard product if bottle (sterile packaging) integrity is compromised. Do not use SpermRinse if it appears cloudy.
- SpermRinse 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.
- Re-use may result in microbiological contamination and/or property changes in the product.
- To avoid contamination Vitrolife strongly recommends that media should be opened and used only with aseptic technique.
- The risks 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 FSCAs have been taken for SpermRinse 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

No pre-market clinical investigations were performed.

5.3 Summary of clinical data from other sources, if applicable

A systematic literature search was conducted to identify clinical data supporting the safety and performance of SpermRinse. In one study [1], where post-preparation sperm motility was assessed, the motility rate following the use of SpermRinse aligned with the ESHRE competency value [2]. Fertilization rates reported after use of SpermRinse [3-9] align with the ESHRE competency values [2]. Clinical pregnancy rates (CPRs) reported after use of SpermRinse [3-5, 7, 9] align with the annual European results published by ESHRE [10]. Several studies also provided data on live births following the use of SpermRinse [3, 4, 7, 9, 11].

The literature search did not identify any deviations or AEs related to the safety or performance of SpermRinse. No post-market clinical follow-up (PMCF) studies have been conducted for SpermRinse. However, results from a PMCF end user survey confirm its safety and performance, maintaining the acceptability of the benefit-risk ratio. No emerging risks or unknown side-effects were identified, and no known side-effects or contraindications were found.

SpermRinse has been on the market since the late 1990s, and no non-serious incidents or undesirable side-effects have been reported with a frequency or severity that would negatively impact its benefit-risk profile.

5.4 An overall summary of the clinical performance and safety

Data from literature, post-market surveillance, including a PMCF end user survey, and risk management activities support the safety and performance of SpermRinse. There are no indications of any negative effects from the use of SpermRinse. As identified in the risk management documents, two residual risks due to the presence of HSA are unacceptable. However, after benefit-risk evaluation, the benefits of using HSA in the device outweigh the risks associated with blood-borne contamination. All other risks are deemed acceptable after risk control measures. According to the results of the literature search, the risk of an allergic/hypersensitivity reaction (or infection) associated with HSA, gentamicin or antibiotics when used for ART procedures is low. The biological evaluation of SpermRinse confirmed that the device is biologically safe and biocompatible within the intended use. No new risks have been

identified or are expected when the device is used according to its Indications for Use. Therefore, the benefit-risk profile is considered acceptable according to current knowledge/state of the art.

5.5 Ongoing or planned post-market clinical follow-up

There are no ongoing or planned PMCF studies for SpermRinse. However, general PMCF procedures, including screening of scientific literature, searching AE databases and conducting a PMCF end user survey will be performed.

6 Possible diagnostic or therapeutic alternatives

ART is a treatment option for patients unable 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.

Sperm preparation is an important step in ART procedures, and it can significantly impact reproductive outcomes. Conventional preparation techniques, such as swim-up and DGC, are standard practices [12]. Devices with similar intended use 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 ART field to use the device according to its IFU. Since no special design or safety concerns were identified for SpermRinse, no specific training is 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/A11:2021. Medical Devices. Application of risk management to medical devices. 31 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 of the MDR.

9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
1	2021-09-16	Initial version of SSCP for SpermRinse (REP-4142-v.1.0)	

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
2	2022-09-16	Addition of NB address, conformity assessment, and update of section 6 (REP-4142-v.2.0)	☑ Yes Validation language: English
3	2022-10-10	Annual update in 2022	
4	2023-08-22	Annual update in 2023	
5	2024-11-07	Annual update in 2024	
6	See publish date	Remove table with detailed similar devices	☑ Yes Validation language: English

10 References

1. Kaleli, S., et al., *Evaluating the efficacy of ovulation stimulation with intrauterine insemination in women with diminished ovarian reserve compared to women with normal ovarian reserve.* Int J Gynaecol Obstet, 2023. 160(2): p. 620-627.
2. ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine, *The Vienna consensus: report of an expert meeting on the development of ART laboratory performance indicators.* Reprod Biomed Online, 2017. 35(5): p. 494-510.
3. Jiang, L., et al., *Effect of early rescue ICSI and split IVF-ICSI in preventing low fertilization rate during the first ART cycle: A real-world retrospective cohort study.* Reprod Med Biol, 2022. 21(1): p. e12420.
4. Mei, J., et al., *Magnetic-activated cell sorting of nonapoptotic spermatozoa with a high DNA fragmentation index improves the live birth rate and decreases transfer cycles of IVF/ICSI.* Asian Journal of Andrology, 2022. 24(4): p. 367.
5. Ten, J., et al., *Sperm DNA fragmentation on the day of fertilisation is not associated with assisted reproductive technique outcome independently of gamete quality.* Hum Fertil (Camb), 2022. 25(4): p. 706-715.
6. Le, M.T., et al., *Physiological intracytoplasmic sperm injection does not improve the quality of embryos: A cross-sectional investigation on sibling oocytes.* Clin Exp Reprod Med, 2023. 50(2): p. 123-131.
7. Zhang, X., et al., *Embryo development and live birth resulted from artificial oocyte activation after microdissection testicular sperm extraction with ICSI in patients with non-obstructive azoospermia.* Front Endocrinol (Lausanne), 2023. 14: p. 1123541.
8. Lo, W.C., et al., *The fertility outcome of assisted oocyte activation combined with spindle view-assisted intracytoplasmic sperm injection in patients with low fertilization rate.* Taiwan J Obstet Gynecol, 2024. 63(4): p. 513-517.
9. Zhang, K., et al., *Decreased AKAP4/PKA signaling pathway in high DFI sperm affects sperm capacitation.* Asian J Androl, 2024. 26(1): p. 25-33.
10. Smeenk, J., et al., *ART in Europe, 2019: results generated from European registries by ESHRE.* Hum Reprod, 2023. 38(12): p. 2321-2338.
11. Ling, L., et al., *Effect of interval time between hysterosalpingography and intrauterine insemination on the pregnancy outcome of infertile patients.* Front Endocrinol (Lausanne), 2023. 14: p. 1175278.
12. ESHRE Guideline Group on Good Practice in IVF Labs, et al., *Revised guidelines for good practice in IVF laboratories (2015).* Hum Reprod, 2016. 31(4): p. 685-6.

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