Summary of safety and clinical performance HSA-solution™

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	HSA-solution™
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	735002591AALDY
1.5	Medical device nomenclature description/text	Not available
1.6	Global Medical Device Nomenclature (GMDN) code	44046
1.7	Class of device	Class III
1.8	Year when the first certificate (CE) was issued covering the device	2006
1.9	Authorized representative if applicable; name and SRN	Not applicable
2.0	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

HSA-solution is a medical device intended for use in Assisted Reproductive Technology (ART) as a supplement for culture medium.

2.2 Indication(s) and target population(s)

The Indication for use of HSA-solution is “HSA-solution contains Human serum albumin solution (100 mg/mL) and is intended for use in assisted reproductive procedures which include gamete and embryo manipulation. These procedures include the use of HSA-solution™ as a supplement for culture medium. Not for use as an injectable product”. The intended target group is an adult or reproductive-age population that undergoes IVF treatment or fertility preservation.

2.3 Contraindications and/or limitations

There are no contraindications for HSA-solution when used according to its Indication for Use.

3 Device description

3.1 Description of the device

HSA-solution is an aseptically filtered antibiotic-free solution that is delivered in a gamma sterilized 10 mL bottle with tamper evident seal (primary packaging) and a cardboard capsule (secondary packaging) (Figure 1). HSA-solution 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. HSA-solution contains HSA which is regarded as a medicinal component based on regulatory guidelines. According to the Indication for Use, HSA-solution is not intended to have patient contact.

Figure 1. Picture of HSA-solution

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

Not applicable

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 G-MOPS and G-PGD.

4 Risks and warnings

4.1 Residual risks and undesirable effects

All known and foreseeable risks and undesirable side-effects associated with the use of HSA-solution were assessed and mitigated as far as possible during risk management. For HSA-solution, there are two residual risks that remain unacceptable after risk mitigation. These risks are related to the presence of HSA in the device and have the hazardous situations 'Patient exposed to contaminated human serum albumin (HSA)' or 'User exposed to contaminated human serum albumin (HSA)'. However, according to the Indication for Use, HSA-solution is not intended to have patient contact, but in other media products from Vitrolife it has patient contact such as those used in IUI and embryo transfer. 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. HSA is derived from human blood and could theoretically be a vector for various diseases such as hepatitis B (HBsAg), hepatitis C (Anti-HCV) and HIV 1/2 (Anti-HIV 1/2). However, the probability of the patient or user being virally infected during IVF treatment is extremely small. No case reports of allergic/hypersensitivity reactions or infections associated with HSA during ART procedures have been identified. No adverse effect of or undesirable side-effect has been reported for any of Vitrolife's media containing HSA. The benefit-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 is tested for blood-borne diseases by accredited laboratories. Additionally, the end user is informed about the device components, precautions, and risk of using blood derived products by providing information on labels and Instruction for Use.

All the potential clinical risks that could occur during the use of HSA-solution are presented in the table below:

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

Biological evaluation confirmed that HSA-solution is biologically safe. HSA-solution contains HSA which originates from human blood and is not listed as a harmful substance. The bottles and final products are quality tested to confirm non-toxicity. Stability studies confirm the product is non-toxic for the entire lifetime.

4.2 Warnings and precautions

Precautions related to the use of HSA-solution are:

- Discard product if bottle integrity is compromised. Do not use HSA-solution if it appears cloudy.
- HSA-solution 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 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.

Additional information related to the use of the device can be found in the package insert.

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

Not applicable.

5.3 Summary of clinical data from other sources, if applicable

A systematic literature search was performed during the clinical evaluation of HSA-solution to identify clinical data supporting the safety and performance of HSA-solution. The literature search identified several key references reporting results on relevant endpoints for determination of benefit-risk profile including fertilization and/ or embryo development after the use of HSA-solution (Hu et al. 2019; Parrella et al. 2019; Cheung et al. 2020; Mackens et al. 2020; Segers et al. 2020;

Abdala et al. 2022; De Munck et al. 2022; Hao et al. 2022; Abdala et al. 2023; Ali et al. 2023; Cheung et al. 2023; Kocur et al. 2023; Cheung et al. 2024). Fertilization and blastocyst formation 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).

Successful clinical outcomes including clinical pregnancy, implantation and live birth were also reported after a treatment that included the use of HSA-solution (Cheung et al. 2019; Hernandez-Nieto et al. 2019; Kim et al. 2019a; Kim et al. 2019b; Mostinckx et al. 2019; Parrella et al. 2019; Sciorio et al. 2019; Cheung et al. 2020; Segers et al. 2020; Abdala et al. 2022; De Munck et al. 2022; Hao et al. 2022; Cheung et al. 2023; Kocur et al. 2023; Yan et al. 2023; Cheung et al. 2024). The clinical pregnancy rates aligned with the yearly European results published by ESHRE (Wyns et al. 2022). Two references described live birth parameters including gestational age and birthweight after supplementation of IVM medium with HSA-solution (Mostinckx et al. 2019; Segers et al. 2020).

According to the outcomes of the literature search, no deviation was found in the safety or performance of the device. The scientific validity of the identified data is acceptable. It should be noted that the same HSA raw material is included in several Vitrolife pre-supplemented media. Several publications including the use of these media and reporting clinical outcomes are archived in Vitrolife's internal literature database. There have been 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

According to the Indication for Use, the clinical benefit of HSA-solution is to supplement culture medium used in ART procedures which is supported by data from published scientific literature. Fertilization and blastocyst formation 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). Likewise, the clinical pregnancy rates following a treatment that included HSA-solution align with the yearly European results published by ESHRE (Wyns et al. 2022). There are no indications of any negative effects resulting from the use of HSA-solution. As identified in the risk management documents, the residual risks due to the presence of HSA are unacceptable. However, benefit-risk analysis concluded that the benefits of using HSA in the devices outweigh the risks associated with blood-borne contamination. All other risks including biological risks are acceptable after risk control measures. No new risks or hazards with a frequency or severity that negatively impacts the benefit-risk of HSA-solution were identified during the post-market surveillance or the clinical evaluation and the acceptability of the benefit-risk profile persists.

5.5 Ongoing or planned post-market clinical follow-up

There are no ongoing or planned PMCF studies for HSA-solution. 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 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.

Devices with similar intended uses as HSA-solution 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 understand the Indication for Use of HSA-solution. Since no special design or safety concerns were identified for HSA-solution, there is no specific training required for the end-users.

8 Reference to any harmonised standards and common specifications applied

- Medical Devices Regulation (MDR) (EU) 2017/745
- 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
- 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	2021-05-25	Initial version of SSCP for HSA-solution (REP-3711-v.1.0)	

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
2	2022-06-17	Annual update of SSCP for HSA-solution (REP-3711-v.2.0)	
3	2023-02-13	Address DNV clinical NCs (REP-3711-v.3.0)	
4	2023.11-03	Annual update of SSCP for HSA-solution (REP-3711-v.4.0)	
5	2025-01-20	Annual update of SSCP for HSA-solution (REP-3711-v.5.0)	
6	See publish date	Edit Section 6 of SSCP for HSA-solution (REP-3711-v.6.0)	☑ Yes Validation language: English

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