Summary of safety and clinical performance ASP™

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	ASP™
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	735002591AAADA
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 (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

ASP is a medical device intended for use in assisted reproductive technology (ART) as a medium for oocyte retrieval and rinsing (follicle flushing).

2.2 Indication and target population

The Indication for Use of the ASP is "medium for oocyte retrieval and rinsing (follicle flushing)". The intended target group is an adult or reproductive-age population that undergoes oocyte retrieval.

2.3 Contraindications and/or limitations

ASP contains gentamicin and heparin. Do not use in patients with known hypersensitivity/allergy to these components.

3 Device description

3.1 Description of the device

ASP is bicarbonate and HEPES buffered medium intended to support oocyte retrieval and rinsing (follicle flushing). Based on its Indication for Use, ASP may have contact with the patient.

ASP 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. Excess media should be discarded after completion of the procedure. The device is sterile filtered using aseptic technique.

Based on regulatory guidelines, the medicinal components present in ASP are heparin and gentamicin. The medicinal components could result in sensitization or allergic reaction in the patient or user.

Figure 1. ASP in a 125 mL bottle with HDPE closure and a tamper-evident seal

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 ASP 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 including CO_2 incubator and thermostat-warming block and sterile non-toxic disposables for the *in vitro* fertilization (IVF) lab. For oocyte retrieval, oocyte aspiration needles and transvaginal ultrasound equipment are required.

4 Risks and warnings

4.1 Residual risks and undesirable effects

There are no unacceptable residual risks for ASP after risk control measures. No adverse events or undesirable side-effects have been reported for the device during its time on the market. To control

risks, raw materials for ASP are quality tested and each LOT of the final product is tested for pH, osmolality, sterility, bacterial endotoxins, embryo toxicity and heparin anti-IIa activity. Additionally, the user is informed about the device components, contraindication, and precautions by providing information on labels and the Instruction for Use.

All the clinical risks that could occur during the use of ASP are presented in below.

Effect	Hazardous situation
Patient	• Patient exposed to gentamicin • Patient exposed to heparin • Patient exposed to non-biocompatible product • Patient exposed to contaminated media or high level of endotoxins • Patient exposed to high level of endotoxins • Patient exposed to microbial contamination in media • Allergic patient exposed to gentamicin • Allergic patient exposed to heparin • Patient exposed to unintended product
End user	• User exposed to gentamicin • User exposed to heparin • User exposed to contaminated heparin • Allergic user exposed to gentamicin • Allergic user exposed to heparin

4.2 Warnings and precautions

Precautions related to the use of ASP are listed below.

- Discard product if bottle integrity is compromised. Do not use ASP if it appears cloudy.
- 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.
- Not to be used as an injectable product other than follicle flushing during oocytes retrieval.
- 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 ASP 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 systematic literature search was conducted to identify clinical data on the safety and performance of ASP. The fertilization rates reported after use of ASP [1-4] align with the ESHRE competency value [5]. The clinical pregnancy rates (CPRs) reported after use of ASP [1, 2, 6] align with the yearly European results published by ESHRE [7]. Three publications provide data on deliveries after use of ASP [1, 2, 6]. According to the results from the literature search, no deviation was found in the safety or performance of the device. No post-market clinical follow-up (PMCF) studies have been conducted for ASP. No non-serious incidents or undesirable side-effects were identified after use ASP with a frequency or severity that 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 ASP is to support oocyte retrieval and rinsing (follicle flushing), which is supported by data from published scientific literature. The fertilization rates reported after use of ASP [1-4] align with the ESHRE competency value [5]. The CPRs reported after use of ASP [1, 2, 6] align with the yearly European results published by ESHRE [7]. Data from post-market surveillance (PMS) and risk management also support the safety and performance of ASP. There are no indications of any negative effects from use of ASP. Risk management has been effective: there are no unacceptable risks after risk evaluation and no new risks have been identified or are expected. Therefore, the benefit-risk profile is considered to be 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 ASP. However, general PMCF procedures, such as screening of scientific literature and searching adverse event 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.

Oocyte retrieval is almost always achieved using transvaginal ultrasound-guided follicle aspiration. In general, follicle flushing has little impact on oocyte yield or live birth rate. However, more data are required to determine whether follicular flushing is beneficial in specific populations. Devices with similar intended uses as ASP 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 the ART field and to understand the Indication for Use of ASP. As no special design feature or safety concerns were identified for ASP, no specific training is required for end-users.

8 Reference to any harmonized standards and common specifications applied

- Medical Devices Regulation (EU) 2017/745 (MDR)
- EN ISO 13485:2016. Medical devices — Quality management systems — Requirements for regulatory purposes
- 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
- ISO/TR 20416:2020. Medical devices — Post-market surveillance for manufacturers
- EN ISO 20417:2021. Medical devices — Information to be supplied by the manufacturer
- MEDDEV 2.7/1 revision 4. Clinical evaluation – A guide for manufacturers and notified bodies under Directives 93/42/EEC and 90/385/EEC. June 2016
- 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	2021/03/08	Initial version of draft SSCP for ASP (PLN-2726-v.1.0)	
2	2021/03/24	Correction of draft SSCP for ASP (PLN-2726-v.2.0)	
3	2022/03/28	Update of SSCP for ASP (PLN-2726-v.3.0)	
4	2022/06/03	Revised SSCP according to DNV clinical NCs (REP-2726-v.4.0)	☑ Yes Validation language: English
5	2023/02/06	Annual update of SSCP for ASP (REP-2726-v.5.0)	
6	2023/09/19	Address comment from Swedish MPA (REP-2726-v.6.0)	
7	2024/02/13	Annual update of SSCP for ASP (REP-2726-v.7.0)	
8	See publish date	Edit Section 6 of SSCP for ASP (REP-2726-v.8.0)	☑ Yes Validation language: English

References

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2. Savasi V, Ferrazzi E, Lanzani C, Oneta M, Parrilla B, Persico T: Safety of sperm washing and ART outcome in 741 HIV-1-serodiscordant couples. *Hum Reprod* 2007, 22(3):772-777.
3. Zhu WJ, Li XM, Chen XM, Zhang L: Follicular aspiration during the selection phase prevents severe ovarian hyperstimulation in patients with polycystic ovary syndrome who are undergoing in vitro fertilization. *Eur J Obstet Gynecol Reprod Biol* 2005, 122(1):79-84.
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5. ESHRE Special Interest Group of Embryology, 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):494-510.
6. Katayama KP, Jambor V, Milosavljevic S, Vanschaick M, Katayama A: Uterine sperm-egg transfer: a cost-effective alternative to IVF? *Reprod Biomed Online* 2010, 20(6):764-767.
7. Smeenk J, Wyns C, De Geyter C, Kupka M, Bergh C, Cuevas Saiz I, De Neubourg D, Rezabek K, Tandler-Schneider A, Rugescu I *et al*: ART in Europe, 2019: results generated from European registries by ESHRE. *Hum Reprod* 2023, 38(12):2321-2338.

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