Doc. ID:	Version:	Publish date:
REP-4296	6.0	2025/04/10

Summary of Safety and Clinical Performance ICSI™

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

Table 1. Device identification

1.1	Device trade name	ICSI™
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	735002591AANE4
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	Det Norske Veritas (DNV) Product Assurance AS Veritasveien 1, NO-1363 Høvik, Norway Single Identification Number: 2460

2 Intended use of the device

2.1 Intended purpose

ICSI™ is a medical device intended for use in Assisted Reproductive Technology (ART) as a medium for immobilization and isolation of sperm prior to intracytoplasmic sperm injection (ICSI).

2.2 Indication and target population

ICSI™: Medium for immobilization and isolation of sperm prior to intracytoplasmic sperm injection, ICSI.

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

2.3 Contraindications and/or limitations

ICSI™ contains recombinant human albumin (rHA, produced in yeast). Do not use in patients with known hypersensitivity/allergy to the component. However, according to the Indication for Use, ICSI™ does not have patient contact. The contraindication and precautions are described in the package insert and are listed in section 4.2.

3 Device description

3.1 Description of the device

ICSI™ is a viscous sperm handling solution containing polyvinylpyrrolidone (PVP) and rHA for use after equilibration at +20 ± 5°C and ambient atmosphere. The composition of ICSI™ has been developed to support immobilization and isolation of sperm prior to ICSI. Based on its Indication for Use, ICSI™ does not have patient contact.

ICSI™ (REF 10111) is available as 5 × 0.1 mL vials (Figure 1). The media is sterile filtered using aseptic technique. Media bottles should not be stored after opening. Discard excess media after completion of the procedure.

Based on regulatory guidelines, the medicinal component present in ICSI™ is rHA.

Figure 1. ICSI™

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 ICSI™ 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 OVOIL.

4 Risks and warnings

4.1 Residual risks and undesirable effects

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

For ICSI™, all the clinical risks with the potential to affect the end user's health are presented in Table 2 below.

Effect	Hazardous situation
End user	User exposed to recombinant human albumin (rHA).
	Allergic user exposed to yeast.

All these risks were acceptable after risk control measures. To control risks related to the use of ICSI™, 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. Biological evaluation conclude that all components are nutrients that are either naturally present in mammal tissues, or they 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 MEA tested to confirm non-toxicity. Stability studies confirm the product is non-toxic for the 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

Warnings or precautions related to the use of ICSI™ are listed.

- Discard product if bottle integrity is compromised. Do not use ICSI™ 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 risk of reproductive toxicity and developmental toxicity for IVF media, including Vitrolife´s IVF media, have not been determined and are uncertain.
- Not for injection.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer.
- 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 actions (FSCAs) have been taken for ICSI™ during its lifetime.

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 ICSI™. Several studies confirm fertilization at normal rates after the use of ICSI™ (Abed et al. 2020; Calza 2021; Do and Dinh 2021; Tepla et al. 2021; Zhou et al. 2021; Kadoura et al. 2022; Lara-Cerrillo et al. 2023; Le et al. 2023; Yetkin Yıldırım et al. 2023; Zhang et al. 2023; Klami et al. 2024).

The clinical pregnancy rates reported after use of ICSI™ align (Calza 2021; Zhou et al. 2021; Kadoura et al. 2022; Lara-Cerrillo et al. 2023; Le et al. 2023; Tepla et al. 2023; Yetkin Yıldırım et al. 2023; Zhang et al. 2023; Klami et al. 2024) with the European results published by ESHRE (Wyns et al. 2022). Several references reported data on live births after use of ICSI™ (Carvalho et al. 2020; Hatirnaz et al. 2020; Zhou et al. 2021; Lara-Cerrillo et al. 2023; Zhang et al. 2023; Klami et al. 2024). 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 ICSI™. There were no non-serious incidents or undesirable side-effects identified after use ICSI™ 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 ICSI™ is to support immobilization and isolation of sperm prior to ICSI. The clinical pregnancy rate reported after use of ICSI™ aligns with the yearly European results published by (ESHRE) (Wyns et al. 2022). Data from PMS and risk management also support the safety and performance of ICSI™. There are no indications of any negative effects from use of ICSI™. All risks for ICSI™ that affect the patient, end user or gamete/embryo are acceptable after risk control measures. According to the results of the literature search, the risk of an allergic/hypersensitivity reaction (or infection) associated with rHA when used for ART procedures is low. 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 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 ICSI™. However, general PMCF procedures, such as screening of scientific literature, searching adverse event databases and performing 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.

ICSI™ is a medium intended for use in ART for immobilization and isolation of sperm prior to intracytoplasmic sperm injection, ICSI.

Devices with similar intended uses as ICSI™ 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 follow Good Laboratory Practice and use the devices according to their IFUs. As no special design feature or safety concerns were identified for ICSI™, 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 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	2021-10-08	Initial version of SSCP for ICSI™ (REP-4296-v.1.0)	
2	2022-09-16	Address DNV clinical NCs (REP-4296-v.2.0)	
3	2023-02-13	Updated version of REP-4296-v.3.0	
4	2024-01-09	Annual update of SSCP (REP-4296-v.4.0)	
5	2025-01-20	Annual update of SSCP (REP-4296-v.5.0)	
5	See publish date	Edit Section 6 of SSCP (REP-4296-v.6.0)	☑ Yes Validation language: English

References

Abed F, Fallah-Karkan M, Zolbin MM, Naghizadeh P, Aliakbari F, Yazdekhasti H. 2020. Effects of vascular endothelial growth factor supplementation and alginate embedding on human oocyte maturation in vitro. *Asian Pacific Journal of Reproduction* **9**: 129-134.

Calza N, Ciotti, P.M., Tranquillo, M.L., Notarangelo, L., Zuffa, S., Damiano, G., Cipriani, L., Dirodi, M., Franceschelli, A., Porcu, E. 2021. Use of dimethylxanthine theophylline in surgical retrieved sperms that do not recover motility after thawing. *Human reproduction* **36**.

Carvalho M, Leal F, Mota S, Aguiar A, Sousa S, Nunes J, Calhaz-Jorge C. 2020. The effect of denudation and injection timing in the reproductive outcomes of ICSI cycles: new insights into the risk of in vitro oocyte ageing. *Human reproduction* **35**: 2226-2236.

Do MT, Dinh LT. 2021. Improving IVF clinical results with centrifugation-free sperm preparation method. *Fertility and sterility* **116**: e280.

Hatirnaz S, Hatirnaz ES, Basbug A, Kanat Pektas M, Erol O, Dahan M, Tan S. 2020. In vitro maturation with letrozole priming: Can it be a solution for patients with cancerophobia? A pilot study. *Turk J Obstet Gynecol* **17**: 247-252.

Kadoura S, Alhalabi M, Nattouf AH. 2022. Follicular fluid PlGF and IVF/ICSI outcomes among PCOS and normo-ovulatory women using different controlled hyperstimulation protocols: A prospective case-control study. *Ann Med Surg (Lond)* **79**: 104096.

Klami R, Tomas C, Mankonen H, Perheentupa A. 2024. ICSI outcome after microdissection testicular sperm extraction, testicular sperm aspiration and ejaculated sperm. *Reprod Biol* **24**: 100825.

Lara-Cerrillo S, Urda Muñoz C, de la Casa Heras M, Camacho Fernández-Pacheco S, Gijón de la Santa J, Lacruz-Ruiz T, Rosado-Iglesias C, Gonçalves-Aponte V, Badajoz Liébana V, García-Peiró A. 2023. Microfluidic sperm sorting improves ICSI outcomes in patients with increased values of Double-Strand Breaks in sperm DNA. *Rev Int Androl* **21**: 100338.

Le MT, Nguyen HTT, Van Nguyen T, Nguyen TTT, Dang HNT, Dang TC, Nguyen QHV. 2023. Physiological intracytoplasmic sperm injection does not improve the quality of embryos: A cross-sectional investigation on sibling oocytes. *Clinical and experimental reproductive medicine* **50**: 123-131.

Tepla O, Topurko Z, Jirsova S, Moosova M, Fajmonova E, Cabela R, Komrskova K, Kratochvilova I, Masata J. 2023. Timing of ICSI with Respect to Meiotic Spindle Status. *International journal of molecular sciences* **24**: 105.

Tepla O, Topurko Z, Masata J, Jirsova S, Frolikova M, Komrskova K, Minks A, Turanek J, Lynnyk A, Kratochvilova I. 2021. Important parameters affecting quality of vitrified donor oocytes. *Cryobiology* **100**: 110-116.

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.

Yetkin Yıldırım G, Ay N, Çiçek G, Akyol D, Köroğlu N, Polat I, Salihoğlu Z. 2023. The effect of anesthetic agents used in oocyte collection on intracytoplasmic sperm injection results in patients treated for infertility due to male factor. *Annals of Clinical and Analytical Medicine*.

Zhang X, Li L, Zhang W, Luo Y, Mao Y, Du H, Li L. 2023. 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)* **14**: 1123541.

Zhou W-J, Huang C, Jiang S-H, Ji X-R, Gong F, Fan L-Q, Zhu W-B. 2021. Influence of sperm morphology on pregnancy outcome and offspring in in vitro fertilization and intracytoplasmic sperm injection: a matched case-control study. *Asian journal of andrology* **23**: 421.