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Doc. ID: REP-3365 **Version:** 8.0 **Publish date:** 2025/09/05

Summary of safety and clinical performance: RapidVit™ Cleave/RapidWarm™ Cleave

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	RapidVit Cleave/RapidWarm Cleave
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	RapidVit Cleave: 735002591AAWEN RapidWarm Cleave: 735002591AAXEQ
1.5	Global Medical Device Nomenclature (GMDN) code	42850
1.6	Class of device	Class III
1.7	Year when the first certificate (CE) was issued covering the device	2008
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

RapidVit Cleave/RapidWarm Cleave are medical devices intended for use in assisted reproductive technology (ART) for vitrification of cleavage-stage embryos and warming of vitrified cleavage-stage embryos, respectively.

2.2 Indication and target population

RapidVit Cleave: Media for vitrification of cleavage stage embryos.

RapidWarm Cleave: Media for warming of vitrified cleavage stage embryos.

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

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2.3 Contraindications and/or limitations

RapidVit Cleave/RapidWarm Cleave contain gentamicin. Do not use in patients with known hypersensitivity/allergy to the component. (However, according to the Indications for Use, RapidVit Cleave/RapidWarm Cleave do not have patient contact.)

3 Device description

3.1 Description of the device

RapidVit Cleave/RapidWarm Cleave are MOPS buffered media intended to support vitrification of cleavage-stage embryos and warming of vitrified cleavage-stage embryos, respectively.

The devices are sterile filtered using aseptic technique. RapidVit Cleave/RapidWarm Cleave are stable until the expiry date shown on the bottle labels and the LOT specific Certificate of Analysis. Media bottles should not be stored after opening. Discard excess media after completion of procedure. Based on regulatory guidelines, the medicinal components present in RapidVit Cleave/RapidWarm Cleave are gentamicin and human serum albumin (HSA). Gentamicin, an antibiotic, may cause sensitization or allergic reactions in the patient or user.



Figure 1. RapidVit Cleave/RapidWarm Cleave

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 RapidVit Cleave/RapidWarm Cleave on the market.

3.3 Description of any accessories which are intended to be used in combination with the device

Not applicable.

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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 heating stage, storage device and storage system.

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 Indications for Use, RapidVit Cleave/RapidWarm Cleave do 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 devices according to their IFUs. The benefit-risk analysis of these risks concluded that the benefits of including HSA in RapidVit Cleave/RapidWarm Cleave outweigh the risks associated with blood-borne contamination. No case reports of allergic/hypersensitivity reactions or infections associated with HSA during ART procedures have been reported. No adverse events have been reported for any of Vitrolife’s media devices that contain HSA. The source material is tested for blood-borne diseases by accredited laboratories. To mitigate risks, the raw materials for RapidVit Cleave/RapidWarm Cleave 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, contraindications, warnings and precautions by providing information on labels and the IFUs.

All the clinical risks that could occur during the use of RapidVit Cleave/RapidWarm Cleave are presented in below.

Effect	Hazardous situation
Patient	Patient exposed to contaminated human serum albumin (HSA)*
End user	Allergic user exposed to gentamicin
	User exposed to gentamicin
	User exposed to human serum albumin (HSA)
	User exposed to contaminated human serum albumin (HSA)*

*Unacceptable residual risks. All other clinical risks are acceptable after risk control measures.

4.2 Warnings and precautions

Precautions related to the use of RapidVit Cleave are listed.

- Discard product if bottle integrity is compromised. Do not use RapidVit Cleave if it appears cloudy.
- RapidVit Cleave 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.

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- The risk of reproductive toxicity and developmental toxicity for IVF media, including Vitrolife's IVF media, have not been determined and are uncertain.
- The long-term safety of vitrification on children born following this method of embryo cryopreservation is unknown.
- The safety and effectiveness of vitrification has not been fully evaluated in human embryos that have not yet reached the blastocyst stage of development.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer.
- Not for injection.
- Discard the product according to standard clinical practice for medical hazardous waste when the procedure is finished.

Precautions related to the use of RapidWarm Cleave are listed.

- Discard product if bottle integrity is compromised. Do not use RapidWarm Cleave if it appears cloudy.
- RapidWarm Cleave 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.
- The long-term safety of vitrification on children born following this method of embryo cryopreservation is unknown.
- The safety and effectiveness of vitrification has not been fully evaluated in human embryos that have not yet reached the blastocyst stage of development.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer.
- 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 RapidVit Cleave/RapidWarm Cleave during their lifecycles.

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.

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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 on the safety and performance of RapidVit Cleave/RapidWarm Cleave. Post-warming survival rates reported after use of RapidVit Cleave/RapidWarm Cleave [1-6] align with the Alpha competency value of ≥70% [7]. Clinical pregnancy rates (CPRs) reported after use of RapidVit Cleave/RapidWarm Cleave [3, 6, 8-11] generally align with the European results published by ESHRE [12]. Several studies reported data on live births after the use of RapidVit Cleave/RapidWarm Cleave [2, 3, 6, 9-11] which supports the safety of the devices. According to the results from the literature search, no deviation was found in the safety or performance of the devices. No post-market clinical follow-up (PMCF) studies have been conducted for RapidVit Cleave/RapidWarm Cleave. However, results from a PMCF end-user survey confirm the safety and performance of RapidVit Cleave/RapidWarm Cleave 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. RapidVit Cleave/RapidWarm Cleave have been on the market since 2008, and no non-serious incidents or undesirable side-effects have been identified after their use with a frequency or severity that negatively impact their benefit-risk profile.

5.4 An overall summary of the clinical performance and safety

According to the Indications for Use, the clinical benefit of RapidVit Cleave/RapidWarm Cleave is as media to support vitrification of cleavage-stage embryos and warming of vitrified cleavage-stage embryos, respectively.

Post-warming survival rates reported after use of RapidVit Cleave/RapidWarm Cleave [1-6] generally align with the Alpha competency value [7]. CPRs reported after use of RapidVit Cleave/RapidWarm Cleave [3, 6, 8-11] generally align with the yearly European results published by ESHRE [12]. Several studies reported data on live births after use of RapidVit Oocyte/RapidWarm Oocyte [2, 3, 6, 9-11] which supports the safety of the devices. Data from post-market surveillance, including a PMCF end-user survey, and risk management also support the safety and performance of RapidVit Cleave/RapidWarm Cleave. There are no indications of any negative effects from use of RapidVit Cleave/RapidWarm Cleave. 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 devices outweigh the risks associated with blood-borne contamination. All other risks 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 HSA, gentamicin or antibiotics when used for ART procedures is low. No new risks have been identified or are expected when the devices are used according to their 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 RapidVit Cleave/RapidWarm Cleave. However, general PMCF procedures, such as screening scientific literature, searching adverse event databases and performing a PMCF end-user survey will be performed.

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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. Currently, 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.

Cryopreservation methods include slow freezing and vitrification. Current evidence indicates that vitrification is superior to slow freezing in terms of cryosurvival rates and clinical outcomes for cleavage-stage embryos. Devices with similar intended uses as RapidVit Cleave/RapidWarm Cleave 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 use the devices according to their IFUs. As no special design feature or safety concerns were identified for RapidVit Cleave/RapidWarm Cleave, 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.

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9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
1	2021/03/24	Initial version of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.1.0)	
2	2021/07/14	Initial version of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.2.0)	
3	2022/05/01	Annual update of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.3.0)	
4	2022/10/04	Address DNV clinical NCs (REP-3365-v.4.0)	☑ Yes Validation language: English
5	2023/07/10	Annual update of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.5.0)	
6	2024/04/19	Annual update of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.6.0)	
7	2025/04/10	Edit Section 6 of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.7.0)	☑ Yes Validation language: English
8	See publish date	Annual update of SSCP for RapidVit Cleave/RapidWarm Cleave (REP-3365-v.8.0)	☑ Yes Validation language: English

10 References

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5. Omidi M, Khalili MA, Halvaei I, Montazeri F, Kalantar SM: Quality of Blastocysts Created by Embryo Splitting: A Time-Lapse Monitoring and Chromosomal Aneuploidy Study. *Cell J* 2020, 22(3):367-374.
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Document reviewed by Helena Wenåker, Kristina Schildauer
Document approved by Hans Lehmann on 2025/09/01
Document QA approved by Elaine Limé on 2025/09/05

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