Summary of safety and clinical performance Ultra RapidWarm™ Blast

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	Ultra RapidWarm Blast
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	735002591ACJE2
1.5	Global Medical Device Nomenclature (GMDN) code	44046
1.6	Class of device	III
1.7	Year when the first certificate (CE) was issued covering the device	New device
1.8	Authorized representative if applicable; name and SRN	Not applicable
1.9	NB's name, address and single identification number	DNV Product Assurance AS, Veritasveien 1, 1363 Høvik, Norway 2460

2 Intended use of the device

2.1 Intended purpose

Ultra RapidWarm Blast is a medical device intended for use in assisted reproductive technology (ART) for warming of vitrified human blastocyst stage embryos.

2.2 Indication(s) and target population(s)

Ultra RapidWarm Blast: Medium for warming of vitrified human blastocyst stage embryos.

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

2.3 Contraindications and/or limitations

Ultra RapidWarm Blast contains gentamicin. The product is only in direct contact with embryos. Ensure appropriate precautions are taken to minimize the risk of contact with individuals with known hypersensitivity/allergy to gentamicin.

3 Device description

3.1 Description of the device

Ultra RapidWarm Blast is a MOPS buffered medium intended to support warming of vitrified human blastocyst stage embryos. Based on its Indication for Use, Ultra RapidWarm Blast has embryo contact.

The device is sterile filtered using aseptic technique. Ultra RapidWarm Blast is stable until the expiry date shown on the bottle label and the LOT specific Certificate of Analysis.

Media bottles can be used for up to two weeks after first opening, use aseptic technique and minimize the time outside the refrigerator. Record opening date on the bottle. Discard excess media no later than two weeks after first opening.

Based on regulatory guidelines, the medicinal components present in Ultra RapidWarm Blast are gentamicin and human serum albumin (HSA). Gentamicin is an antibiotic that could result in sensitization or allergic reaction in the patient or user.

Figure 1. Ultra RapidWarm Blast

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

There have been no previous versions of Ultra RapidWarm Blast 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 heating stage, storage device and storage system and sterile non-toxic disposables for the IVF lab.

4 Risks and warnings

4.1 Residual risks and undesirable effects

After mitigation, there are three 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, Ultra RapidWarm Blast is only in direct contact with embryos. 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 Instruction for Use. The benefit-risk analysis of these risks concluded that the benefits of including HSA in Ultra RapidWarm Blast 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 control risks, raw materials for Ultra RapidWarm Blast 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 IFU.

All the clinical risks that could occur during the use of Ultra RapidWarm Blast are presented 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 Ultra RapidWarm Blast are listed.

- Ultra RapidWarm Blast contains human serum albumin and gentamicin.
- 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.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.
- To avoid contamination Vitrolife strongly recommends that media should be opened and used only with aseptic technique.

- Discard product if bottle integrity is compromised. Do not use Ultra RapidWarm Blast if it appears cloudy.
- Do not resterilize after opening.
- Discard the product according to standard clinical practice for medical hazardous waste when the procedure is finished.
- Currently, research literature indicates the long-term effects of warming vitrified embryos remain unknown.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

Not applicable. Ultra RapidWarm Blast is a new device.

5 Summary of clinical evaluation and post-market clinical follow-up

5.1 Summary of clinical data related to equivalent device, if applicable

The conformity of Ultra RapidWarm Blast was assessed based on equivalence. Relevant data on RapidWarm Blast support the safety and performance of Ultra RapidWarm Blast. RapidWarm Blast (Basic UDI-DI: 735002591AAVEL), a class III medical device manufactured by Vitrolife Sweden AB, is indicated for warming of vitrified human blastocyst stage embryos. To establish the equivalence of the two devices, a comprehensive comparison was conducted, considering clinical, technical, and biological characteristics. The SSCP for RapidWarm Blast can be found at www.vitrolife.com.

Recent research indicates that a multi-step warming procedure is not necessary. Lammers et al. [1] conducted both a pilot study and a cohort study to assess the efficiency and safety of ultra-fast warming (2 minutes) using Warm 1 Blast compared to standard warming with RapidWarm Blast (15 minutes; including Warm 1 Blast, Warm 2 Blast, and Warm 3 Blast). Ultra Warm Blast is identical to Warm 1 Blast. Single-step ultra-fast warming was comparable to multi-step standard warming in terms of embryological and clinical outcomes, with the added benefit of time saving and reducing blastocyst exposure time to ambient atmosphere. The blastocyst survival rates after ultra-fast warming with Warm 1 Blast align with the European Society of Human Reproduction and Embryology (ESHRE) competency value of ≥90% [2]. The clinical pregnancy rate (CPR) after ultra-fast warming with Warm 1 Blast also aligns with the European results published by ESHRE [3]. The study also reported live births after ultra-fast warming with Warm 1 Blast. As Ultra RapidWarm Blast is identical to Warm 1 Blast in composition and duration of use, these data support the performance and safety of Ultra RapidWarm Blast.

A systematic literature search was conducted to identify clinical data on the safety and performance of RapidWarm Blast. The blastocyst survival rates reported after use of RapidWarm Blast [4, 5] align with the ESHRE competency value of ≥90% [2]. The CPRs reported after use of RapidWarm Blast [5-9] generally align with the European results published by ESHRE [3]. Several studies reported data on live births after the use of RapidWarm Blast [5, 7-9], which supports the safety of the device. According to the results from the literature search, no deviation was found in the safety or performance of the device. The literature data supporting the performance and safety of RapidWarm Blast also confirm the performance and safety of Ultra RapidWarm Blast, as they are considered equivalent devices.

No post-market clinical follow-up (PMCF) studies have been conducted for RapidWarm Blast.

RapidWarm Blast has been on the market since 2008, and no non-serious incidents or undesirable side-effects have been identified after its use, with a frequency or severity that negatively impact its benefit-risk profile.

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

Not applicable.

5.4 An overall summary of the clinical performance and safety

According to the Indication for Use, the clinical benefit of Ultra RapidWarm Blast is as a medium to support the warming of vitrified blastocysts, which is supported by data from a study on ultra-fast warming using Warm 1 Blast, and scientific literature and post-market surveillance (PMS) on the equivalent device—RapidWarm Blast. The blastocyst survival rates reported after use of RapidWarm Blast [4, 5] align with the ESHRE competency value of ≥90% [2]. The CPRs reported after use of RapidWarm Blast [5-9] generally align with the European results published by ESHRE [3]. Several studies reported data on live births after the use of RapidWarm Blast [5, 7-9]. According to the results from the literature search, no deviation was found in the safety or performance of the device. Data from PMS and risk management also support the safety and performance of RapidWarm Blast. As identified in the risk management documents, the 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 acceptable after risk control measures. According to the results of a 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 device is used according to their Indication 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 Ultra RapidWarm Blast. However, general PMCF procedures, such as screening of scientific literature, searching adverse event databases and performing a PMCF end-user survey will be performed after CE-marking and launch.

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. Hence, there are no therapeutic alternatives for patients at this stage.

Currently available similar devices include:

Thawing media	Manufacturer
Oocyte/Embryo Thawing Media (VT602)	Kitazato
Vit Kit-Thaw	FUJIFILM Irvine Scientific
Vit Kit-Thaw NX	FUJIFILM Irvine Scientific
Global Blastocyst Fast Freeze Thawing Kit	CooperSurgical Fertility Solutions
Global DMSO Blastocyst Vitrification Warming Kit	CooperSurgical Fertility Solutions
MediCult Vitrification Warming	CooperSurgical Fertility Solutions
SAGE Warming Kit	CooperSurgical Fertility Solutions
Warming Solution Set	Cryotech

Thawing media	Manufacturer
FertiVit Warming Kit	FertiPro
VitriThaw kit	FertiPro
VitriThaw ES kit	FertiPro
RapidWarm Omni	Vitrolife
RapidWarm Blast	Vitrolife

The blastocyst post-warming survival rates reported after the use of the similar devices [10-18] generally align with the ESHRE competency value [2]. To our knowledge, no randomized controlled comparative studies on Ultra RapidWarm Blast and the similar devices have been performed.

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 device according to its IFU. As no special design or safety concerns were identified for Ultra RapidWarm Blast, no specific training is required for end-users.

8 Reference to any harmonised 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 15223-1:2021. Medical devices — Symbols to be used with information to be supplied by the manufacturer. Part 1: General requirements. July 2021
- ISO/TR 20416:2020. Medical devices — Post-market surveillance for manufacturers
- EN ISO 20417:2021. Medical devices — Information to be supplied by the manufacturer
- EN 62366-1:2015. Medical devices — Part 1: Application of usability engineering to medical devices
- 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 2020-5. Clinical Evaluation – Equivalence. A guide for manufacturers and notified bodies. April 2020
- 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 Annex IX in the MDR (EU) 2017/745.

9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
REP-6458-v.1.0	2024/01/18	Initial version of SSCP for Ultra RapidWarm Blast	□ Yes Validation language: English
REP-6458-v.2.0	2024/03/28	Remove highlighting on text	□ Yes Validation language: English
REP-6458-v.3.0	2024/10/17	Revise reference citations	□ Yes Validation language: English
REP-6458-v.4.0	See publish date	SSCP validated by DNV	☑ Yes Validation language: English

10 References

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