SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

FERTICULT ASPIRATION MEDIUM

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 the intended users.

1 Device identification and general information

1.1 Device trade name(s)

FertiCult Aspiration medium

1.2 Manufacturer's name and address

FertiPro NV
Industriepark Noord 32
8730 Beernem
Belgium

1.3 Manufacturer's single registration number (SRN)

BE-MF-000000313

1.4 Basic UDI-DI

5411967ASPI1V4

1.5 Medical device nomenclature description/text

Applicable EMDN code: U08020502 - Materials/solutions for preparation/handling for assisted reproduction

1.6 Class of device

Class III according to Annex VIII of Regulation (EU) 2017/745

1.7 Year when the first certificate (CE) was issued covering the device

- CE-marking according to the Council Directive 93/42/EEC: 2015
- CE-marking according to Regulation (EU) 2017/745: 07/09/2023

1.8 Authorised representative if applicable; name and the SRN

Not applicable

1.9 NB's name and single identification number

BSI Group The Netherlands BV
NB identification number: 2797

2 Intended use of the device

2.1 Intended purpose

FertiCult Aspiration medium is used for oocyte aspiration and flushing of ovarian follicles during oocyte pick-up as part of Assisted Reproductive Technologies (ART) procedures.

2.2 Indication(s) and intended patient groups

- **Indications for use:** A heparin supplemented medium, like FertiCult Aspiration medium, is used to avoid blood clot formation in the tubing during oocyte aspiration and flushing of the ovarian follicles.

- **Intended users:** FertiCult Aspiration medium is used in specialized laboratories performing assisted reproductive techniques. The intended users are ART professionals (lab technicians, embryologists and medical doctors).

- **Intended patient populations:** FertiCult Aspiration medium is used during ART procedures of patients and couples undergoing infertility treatments.

2.3 Contraindications and/or limitations

There are no known contraindications and/or limitations for FertiCult Aspiration medium.

3 Device description

3.1 Description of the device

- For the principle of operation, reference is made to the IFU: FP09 I19 R01.
- FertiCult Aspiration medium is not intended for single use. Multiple single-procedures can be performed. The media can be used up to 7 days after bottle opening (when sterile conditions are maintained and the products are stored at 2-8°C).
- FertiCult Aspiration medium is sterilized using aseptic processing techniques (filtration).
- FertiCult Aspiration medium contains sodium heparin that complies with the European Pharmacopoeia monograph 0333 and that is certified by the European Directorate for the Quality of Medicines & HealthCare (EDQM). The inclusion of sodium heparin (which is a medicinal substance) in FertiCult Aspiration medium is approved by the Danish Medicines Agency.

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

No previous generation has been brought on the market.

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

No accessories identified.

3.4 Description of any other devices and products which are intended to be used in combination with the device

FertiCult Aspiration medium is to be used with general ART labware and/or media.

4 Risks and warnings

4.1 Residual risks and undesirable effects

The output from the clinical evaluation report is taken into account in the risk management file of FertiCult Aspiration medium in order to determine the benefits/risk ratio.

As evaluated in the risk assessment file, there are no risks that could not be reduced to an acceptable level.
Note that FertiCult Aspiration contains sodium heparin, which is a medicinal product that is animal-derived (i.e. porcine intestinal mucosa. No non-animal source is available). In order to disclose the overall risk regarding the incorporation of sodium heparin, the following relevant information is provided to the customer:

- The concentration of heparin is clearly indicated on the labels and instruction for use
- Instructions for use contains the following warnings: “FertiCult Aspiration medium contains heparin which is derived from porcine intestinal mucosa”.

No other known undesirable side-effects are identified.

4.2 Warnings and precautions

Besides the above, attention should be paid to the following warnings and precautions (as described in the instructions for use):

- Do not use the product if:
  - it becomes cloudy or shows any evidence of microbial contamination
  - seal of the container is opened or defect when the product is delivered
  - expiry date has been exceeded
- Do not freeze before use
- Keep away from sunlight
- Do not re-sterilize after opening

- Depending on the number of procedures that will be performed on one day, remove the required volume of medium under aseptic conditions in an appropriate sterile recipient. This is in order to avoid multiple opening/warming cycles of the medium. Discard excess (unused) media.
- FertiCult Aspiration medium contains heparin which is derived from porcine intestinal mucosa. The heparin is certified with a Certificate of Suitability (CEP). The animals from which the heparin is derived, are determined “fit for human consumption”.
- Aseptic technique should be used to avoid possible contamination.
- All human, organic material should be considered potentially infectious. Handle all specimens as if capable of transmitting HIV or hepatitis.
- Always wear protective clothing when handling specimens.
- Any serious incident (as defined in European Medical Device Regulation 2017/745) that has occurred should be reported to FertiPro and the competent authority of the Member State in which the user and/or patient is established.

4.3 Summary of any field safety corrective action (FSCA including FSN) if applicable

No field safety corrective actions with regard to FertiCult Aspiration medium were needed so far.

5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1 Real-world evidence analyses

A literature search is performed on a yearly basis, to investigate whether clinical embryology and ART outcomes obtained during the search are consistent with the clinical outcomes described in the following benchmark papers from the European Society of Human Reproduction and Embryology (ESHRE):

- Embryological outcomes:

ESHRE Special Interest Group of Embryology, 'The Vienna consensus: report of an expert meeting on the development of art laboratory performance indicators', Hum Reprod Open, 2017: hox011.	IVF normal fertilization rate: ≥60%. Accepted outcome: 50% ICSI normal fertilization rate: ≥65%. Accepted outcome: 55% Blastocyst development rate: ≥40%. Accepted outcome: 30%

- Clinical ART outcomes:

	In vitro fertilization (IVF):	**Intra cytoplasmic sperm injection (ICSI):**	**Frozen embryo transfer (FET):**
Smeenk, J., C. Wyns, C. De Geyter, M. Kupka, C. Bergh, I. Cuevas Saiz, D. De Neubourg, K. Rezabek, A. Tandler-Schneider, I. Rugescu, and V. Goossens. 2023. 'ART in Europe, 2019: results generated from European registries by ESHRE', Hum Reprod, 38(12): 2321–2338.	Clinical pregnancy rate per aspiration: 18.4 – 53.1% Clinical pregnancy rate per transfer: 27.4 – 63.0% Delivery rate per aspiration: 23.3 – 29.4% Delivery rate per transfer: 17.9 – 45.9%	Clinical pregnancy rate per aspiration: 16.0 – 46.1% Clinical pregnancy rate per transfer: 26.9 – 52.1% Delivery rate per aspiration: 10.6 – 28.6% Delivery rate per transfer: 12.1 – 39.4%	*Pregnancy rate per thawing: 22.5 – 50.1%* *Pregnancy rate per transfer: 22.5 – 56.0%* *Delivery rate per thawing: 7.2 - 41.4%* *Delivery rate per transfer: 8.4 – 42.4%*

There were 4 articles retrieved in literature studying the performance of FertiCult Aspiration medium, which are listed below.
Overall, it can be concluded from these papers that embryological and/or clinical ART outcomes when FertiCult Aspiration medium is used are consistent with the outcomes described in the benchmark papers.

- Sandi-Monroy, N. L., S. Musanovic, D. Zhu, Z. Szabo, A. Vogl, N. Reeka, K. Eibner, K. Bundschu, and F. Gagsteiger. 2019. 'Use of dimethylxanthine theophylline (SpermMobil((R))) does not affect clinical, obstetric or perinatal outcomes', Arch Gynecol Obstet, 300: 1435-43.
- Aghaways, I. H. A., K. M. Falah, and A. A. Ali. 2016. 'The difference in the outcomes between surgically retrieved and ejaculated spermatozoa for Intracytoplasmic Sperm Injection Cycles in Sulaimanyah province', Acta Medica International, 3: 30-38.
- Falah, KM., H. Banna, I. Aghaways, AR. Zangana, and Mohammad FL. 2014. 'Using in-vitro maturation of immature oocytes retrieved from poor responder patients to improve pregnancy outcomes in Sulaimani government region, Iraq', European Scientific Journal, 10: 195-211.
- Barbara, S., Oumeziane, A., Nanouche, F., Djerroudib, K., Boucekine, N., Chabane, N., ... & Devroey, P. (2023). Oocytes collected from small follicles after a dual trigger with gonadotropin-releasing hormone agonist (Gn-RHa) and human chorionic gonadotropin (hCG) for final oocyte maturation, in poor responder patient do not impact negatively ICSI cycles outcomes. Global Reproductive Health, 8(2), e67.

5.2 Device registries

Clinical data of more than 8000 ART procedures is obtained from IVF centers in Europe and Africa that use FertiCult Aspiration medium. Embryological and ART outcomes of these clinics are consistent with the published outcomes of the abovementioned benchmark papers.

5.3 Analysis complaints, customer/ market feedback, vigilance

No additional actions were initiated, based on the cumulative nature and/or occurrence of all complaints, customer/market feedback and vigilance (if any) during the PMCF analysis.

5.4 An overall summary of the clinical performance and safety

FertiCult Aspiration medium functions as stated by the manufacturer. This is established by clinical data obtained during literature screening and from IVF centers which show that embryological and ART-outcomes of procedures in which FertiCult Aspiration medium is used are consistent with published outcomes as reported by the Vienna consensus group and the ESHRE.

Furthermore, there is no evidence from the clinical data, as well as from the registered complains, market/customer feedback and/or vigilance that FertiCult Aspiration medium is toxic for gametes and embryos, nor that the medium has a risk for mutagenity, oncogenicity, teratogenity, carcinogenity, cytotoxicity, material-mediated pyrogenicity, allergenicity and irritancy for patients and users. No infrequent complications or problems were detected.

5.5 Ongoing or planned PMS/PMCF

PMS/PMCF for FertiCult Aspiration medium will be performed at least yearly and will include analyses of real-world evidence by performing a literature search, screening of device registers for clinical data, as well as analysis of all complaints, customer/market feedback, vigilance.

This SSCP will be updated with information from the PMS/PMCF, if this is needed to ensure that any clinical and/or safety information described in this document remains correct and complete.

6 Possible diagnostic or therapeutic alternatives

Other heparin-supplemented devices with similar intended use are available on the European Union or international markets. In addition, also non-heparin supplemented media with similar intended use are available. The choice to use a heparin-supplemented medium to avoid blood clotting in the tubing is the choice of the IVF clinic and professional that is performing the procedure.
Besides these media, there are no other alternative treatments that can be used.

7 Suggested profile and training for users

FertiCult Aspiration medium is used in specialized laboratories performing assisted reproductive techniques. The intended users are ART professionals (lab technicians, embryologists and medical doctors).

8 Reference to any applicable common specification(s), harmonized standard(s) or applicable guidance document(s)

The following technical standards apply to FertiCult Aspiration medium:

MDR 2017/745	European Medical Device Regulation 2017/745 of 5 April 2017.
(EN) ISO 13485:2016 (Amd 11:2021)	Medical devices — Quality management systems — Requirements for regulatory purposes.
(EN) ISO 20417:2021	Medical devices: information supplied by the manufacturer.
ISO 10993-1:2018/EN ISO 10993-1:2020	Biological evaluation of medical devices -- Part 1: Evaluation and testing.
(EN) ISO 10993-3:2014	Biological evaluation of medical devices -- Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity.
(EN) ISO 10993-5:2009	Biological evaluation of medical devices -- Part 5: Tests for in vitro cytotoxicity.
(EN) ISO 10993-9:2021	Biological evaluation of medical devices -- Part 9: Framework for identification and quantification of potential degradation products.
(EN) ISO 10993-10:2023	Biological evaluation of medical devices -- Part 10: Tests for irritation and skin sensitization.
ISO 10993-11:2017/EN ISO 10993-11:2018	Biological evaluation of medical devices – Part 11: Tests for systemic toxicity
ISO 10993-18:2020/Amd 1/2022 / EN ISO 10993-18:2020/A1:2023	Biological evaluation of medical devices – Part 18: Chemical characterization of medical device materials within a risk management process.
(EN) ISO 10993-23:2021	Biological evaluation of medical devices – Part 23: Tests for irritation
ISO 13408-1:2008 (Amd 1:2013)/EN ISO 13408-1:2015	Aseptic processing of health care products – Part 1: general requirements.
(EN) ISO 13408-2:2018	Aseptic processing of health care products – Part 2: Filtration.
(EN) ISO 14644-1:2015	Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration.
(EN) ISO 14644-3:2019	Cleanrooms and associated controlled environments - Part 3: Test methods
(EN) ISO 14971:2019 (Amd 11:2021)	Medical devices – Application of risk management to medical devices.
(EN) ISO 15223-1: 2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements.
(EN) ISO 17665-1:2006	Sterilization of health care products – Moist heat – Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices.
ISO 23640:2011/EN ISO 23640:2015	In vitro diagnostic medical devices: Evaluation of stability of in vitro diagnostic reagents (Applicable with exclusion of the following sections: No standard is available for the evaluation of stability of Medical Devices, therefore this standard is used as guideline for the set-up of the stability testing)
(EN) ISO 11737-1:2018, A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products
(EN) ISO 13408-6:2021	Aseptic processing of health care products – Part 6: Isolator systems.
(EN) ISO 22442-1: 2020	Medical devices utilizing animal tissues and their derivatives: Part 1: Application of risk management

EN 556-2:2015	Sterilization of medical devices – Requirements for medical devices to be designated 'STERILE' –Requirements for aseptically processed medical devices.
IEC 62366-1:2015 (Amd 1:2020)	Medical devices - Part 1: Application of usability engineering to medical devices.
NBOG BPG 2014-3	Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System
Ph. Eur. 0333	European Pharmacopoeia monograph 0333 - Heparin sodium

9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
A.3	01/06/2022	CE- conformity assessment according to Regulation (EU) 2017/745	Version A.3 is validated by the Notified Body Validation language: English
A.4	11/10/2022	Update 2022	Not submitted for validation, as there were no significant changes that required validation.
A.5	18/09/2023	Update 2023	Not submitted for validation, as there were no significant changes that required validation.
A.6	27/08/2024	Update 2024	Not submitted for validation, as there were no significant changes that required validation.

10 Summary of the safety and clinical performance of the device intended for patients

A summary of the safety and clinical performance of the device intended for patients, is not applicable as the device is for professional use only.