Appendix: KIDScore™ D5

Appendix: KIDScore D5, version 3.0

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1 Introduction

This appendix provides information on the KIDScore D5 model. The appendix should be used in conjunction with the user manual for the KIDScore decision support tool.

KIDScore D5 is defined by Vitrolife based on the knowledge and experience extracted from our available KID data (see the user manual for the EmbryoViewer software for a definition of KID data).

The model is based on morphology and morphokinetic traits associated with the implantation potential of embryos transferred on day 5. It is designed to help clinics differentiate between embryos with a high or low chance of implanting. This reduces the number of embryos that the clinic personnel need to consider for transfer or freezing.

1.1 Important restrictions and warnings

All users of the tool must agree to read and understand this user manual, observe the restrictions on use and read the following warnings.

Users should contact Vitrolife immediately to report any incident and/or injury to a patient, operator or maintenance employee that occurred as a direct or indirect result of operating the tool and associated hardware. Any serious incident that has occurred in relation to the tool should be reported to the competent authority of the Member State in which the user is established.

RESTRICTIONS ON USE
• All rights in the KIDScore models belong to Vitrolife. Your installation and use of a model are subject to the terms of the end-user licence agreement. • You may not copy, modify, decompile, reverse engineer, disassemble or convert a KIDScore model or assign, transfer, sell, rent or lease a model to any third party.

WARNING
• KIDScore models may only be used by clinic personnel who have been properly trained in their function and applicability by Vitrolife. Users must be qualified to operate the tool and qualified to perform procedures associated with tool use in accordance with local qualification standards.

WARNING
• The KIDScore model assigns a score to each embryo. The embryos with the lowest scores have the statistically poorest chance of implanting, and the embryos with the highest scores have the statistically best chance of implanting. However, there may be parameters not included in the model that are also indicative of implantation potential. The decision about which embryo(s) to transfer must therefore always be made by the user after an assessment of the quality of all relevant embryos.

WARNING
• KIDScore models may not be used for any other purpose than intended and specified by Vitrolife as such usage may result in incorrect decisions being made by the embryologist.

1.2 General cyber security recommendations

Users are advised and expected to take the following measures to reduce cyber security risk in order to ensure that the device will work as designed in the intended user environment:

- Ensure that personnel are properly trained in cyber security awareness
- Prevent physical access to the equipment by unauthorised users
- Use strong passwords (at least eight characters including both uppercase and lowercase letters, numbers and at least one special character).

Users must inform Vitrolife A/S without any undue delay upon becoming aware of a cyber security vulnerability incident or any suspected security events.

For details about how to reduce cyber security risk, please refer to the separate guide on this subject provided by Vitrolife.

1.3 Intended users

Embryologists, other laboratory personnel and clinic staff at IVF clinics trained by Vitrolife A/S-certified instructors.

1.4 Clinical benefit

As an accessory to a medical device, KIDScore D5 provides the indirect clinical benefit of improving the decision-making process by providing support for selection of embryos incubated in the incubator(s) connected to the system.

2 What KIDScore D5 is suitable for

KIDScore D5 is defined for use in standard incubation conditions and is suitable only for:

- Treatments with day 5 transfer
- ICSI and IVF treatments
- Incubation conditions:
    - 4% – 6% oxygen (reduced oxygen only)
    - Temperature level between 36.5°C and 37.5°C (97.7° F to 99.5°F).

2.1 What KIDScore D5 is NOT suitable for

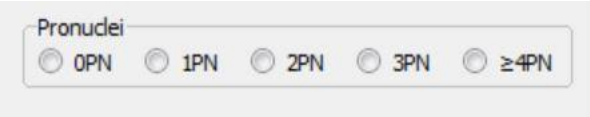
KIDScore D5 is NOT suitable for:

- Treatments in which a biopsy or any other disruptive procedure is performed during the culture period
- Ambient oxygen culture.

3 Mandatory annotation variables

As a minimum, the following variables that are used by KIDScore D5 must always be annotated when the model is used:

- **PN** (number of pronuclei):



- **t2** (time from insemination to complete division to two cells)
- **t3** (time from insemination to complete division to three cells)
- **t5** (time from insemination to complete division to five cells)
- **tB** (time from insemination to formation of blastocyst)
- **ICM** (inner cell mass evaluation) (see section 3.1)
- **TE** (trophectoderm evaluation) (see section 3.1).

If one of these mandatory variables has not been annotated for a specific embryo, the model may be unable to assign a score to that embryo. In such cases, the software will display the score **NA** for the embryo.

If tB, ICM and TE do not occur in the embryo and have therefore not been annotated, the model will assign a score to the embryo after 95 hours.

Other variables that are not included in the model may be indicative of implantation as well and should be part of your evaluation of the embryo before transfer.

3.1 The variables ICM and TE

You should annotate the variables Inner Cell Mass (ICM) and Trophectoderm (TE) between 115 and 120 hours after insemination. Both variables need to have a separate and independent grade from A to C where A signifies the highest quality and C signifies the lowest quality.

NOTE
• When evaluating the variables TE and ICM, it is important to consider the time-lapse sequence leading up to the grading stage in order to take into account e.g. cells that are excluded during the blastocyst formation process and parts of the ICM and TE layers that are not visible in all focal planes.

The grades A-C must be assigned as follows for the variables ICM and TE:

ICM grade	**ICM evaluation**
A	Many tightly packed cells. Cell boundaries are not distinct, and the layer is homogenous without vacuoles and debris.
B	Several cells, and the layer may be less tightly packed. The layer may be less homogenous, and few vacuoles or minor degenerations may be observed.
C	Very few cells that are loosely packed. Cells may be large and show distinct boundaries. The size of the ICM may differ in this group as a few big cells lead to an overall larger size. The larger size is, however, the result of poor compaction. The layer may show vacuoles, degenerated cells or independent cells. This grading group also covers cases where the ICM is not distinguishable.
NA	The variable could not be assessed by the embryologist.

TE grade	Trophectoderm evaluation
A	Many flattened cells (often > 40) forming a cohesive layer that lines the blastocoel cavity. The cells often contain clearly visible nuclei, and the cytoplasm is homogenous.
B	Several (often > 20) cells. The layer is not completely cohesive, and the shape of the cells varies within the layer. Cell cytoplasm may appear non-homogenous, and it may be difficult to distinguish nuclei.
C	Very few cells that are often large and stretched over a large area. Cytoplasm often appears non-homogenous, and vacuoles may be present.
NA	The variable could not be assessed by the embryologist.

4 Scores assigned to the embryos

When the model is applied, it assigns a score to each embryo that has been annotated as 2PN. The scores range from 1 to 9.9. The difference between two scores may thus be down to one decimal point.

Embryos that are not correctly fertilised (not 2PN) are given the score 0.

Three factors in combination determine the score assigned to each embryo:

- Cleavage regularity
- Developmental speed
- Blastocyst quality.

If one of the mandatory variables has not been annotated for a specific embryo (see section 3), the model may be unable to assign a score to this embryo. In such cases, the software will display the score **NA** for the embryo.

If the variables ICM, TE and tB have not been annotated at the time when the model calculates a score (95 hours after insemination), these variables are given the values C and 144h, respectively, until they are annotated differently according to their observed development.

CAUTION
• Embryos that have been assigned the same score by the model are not necessarily equivalent since additional parameters may also be indicative of embryo quality. Similarly, scores that differ only by a few decimal points may not indicate different implantation potentials.

5 Symbols and labels

Label	Description	Note
	Declaration by the manufacturer that the device meets all of the applicable requirements in the Medical Device Regulation (EU) 2017/745	-
	Medical device	-
	Unique device identifier	-
	Manufacturer name and address	See section 7.

6 Disposal of waste

In order to minimise the waste of electrical and electronic equipment, waste must be disposed in accordance with the Directive 2012/19/EU on waste electrical and electronic equipment (WEEE) as amended by Directive (EU) 2018/849. This includes: PCBs (lead-free HASL), switches, PC batteries, printed circuit boards and external electrical cables. All components are in accordance with the RoHS 2 Directive 2011/65/EU, which states that new electrical and electronic components do not contain lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls (PBB) or polybrominated diphenyl ethers.

7 Contact information

Urgently need help? Call our service hotline for support:

+45 7023 0500

(available 24 hours a day, 7 days a week)

E-mail support: support.embryoscope@vitrolife.com

(response within two working days)

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