

Safety of incubation in the EmbryoScope™ time-lapse system

Establishing a safe environment for embryo development is a key consideration for ensuring consistent clinical outcome success in the IVF laboratory.

The EmbryoScope™ time-lapse system was developed and is manufactured taking into account current knowledge about best practices in embryo culture and handling. Based on more than twelve years of experience in optimal design and a specialized knowledge of all processes involved when incubating and monitoring embryos, Vitrolife and the EmbryoScope time-lapse system continues to offer safe embryo management through a platform of products and services.

Design of the EmbryoScope™ time-lapse incubator

The integrated design of the EmbryoScope time-lapse incubator has been developed to provide optimal conditions during embryo incubation and monitoring:

- ✓ Incubation in a small, bench top-like design ensures improved recovery times of incubation environment and culture conditions as compared with standard incubators (CO₂ recovery in 2 minutes and O₂ in 4.5 minutes) after addition of a patient slide).
- ✓ Direct heat transfer design and tri-gas system ensure minimum temperature changes (<0.2°C) and fast recovery of temperature and gas concentrations after load door openings.
- ✓ Constant re-circulation of gases through a HEPA filter and a carbon filter removes volatile organic compounds and particles above 0.3 µm (99,97%)
- ✓ Exposure to light during image acquisition is greatly reduced compared with standard monitoring by conventional microscopy. This is owing to the usage of only low-energy red light and the minimized exposure times. Please refer to the TECHNOTE entitled "Illumination during image acquisition in the EmbryoScope™ time-lapse system" for further information on this subject.
- ✓ Electric components are contained within a separate compartment, thereby shielding the embryos from all electric fields during incubation.



Production and testing

All materials used for the system components are subjected to extensive tests (including toxicity tests) before they are incorporated into the parts of our product line which come into contact with the embryos.

All components of both the EmbryoScope time-lapse incubator and gas system as well as the EmbryoSlide® culture dishes (including the packaging material) have passed such toxicity tests.

The toxicity tests are further described in the TECHNOTE "Mouse embryo assays for development and production of the EmbryoScope™ time-lapse system". During our internal toxicity test of the EmbryoSlide culture dishes, a number of mouse embryos are incubated and the acceptance criterion of the test is >80% of expanded blastocysts after 96 hours of culture.

Finally, all produced EmbryoScope time-lapse incubators must pass an additional mouse embryo assay test before they are released for clinical use.

Continual support

During the installation of the EmbryoScope time-lapse system, we provide a thorough, interactive demonstration of the system.

Half-yearly service visits ensure the continuous, optimal performance of all instrument components. Also, 24-hour technical support is at your disposal via our customer hotline which responds to all issues relating to the EmbryoScope time-lapse system. Both the half-yearly service visits and access to the 24-hour technical support requires a maintenance agreement.

In most regions you have an option to upload anonymous data from your clinic to Vitrolife. This facilitates support as our dedicated service and support team prior to service and maintenance of your instrument will inspect the uploaded data to assess the running conditions of the instrument.

Validation of safety for clinical use

More than 550 EmbryoScope time-lapse systems run clinically throughout the world and have been used for more than 370.000 clinical cycles.

The safety of the system was validated in two independent peer-reviewed publications^{1,2}. In each study, a group of embryos were incubated in the EmbryoScope time-lapse incubator and compared with a group of embryos incubated in a conventional incubator used in traditional IVF procedures. All of the embryos were monitored by

traditional microscopy. The two groups of embryos displayed no significant difference in their development at any of the investigated end points (including number of cells at specific points in time, blastocyst developmental rate and viability, clinical pregnancy rate, implantation rate and ongoing pregnancy rate).

More recently, two independent groups of clinical IVF users reported on obstetric and perinatal outcomes after transfers of embryos cultured in the EmbryoScope vs traditional systems^{3,4}. Analysis included pregnancy and neonatal outcomes. Both groups reported at least equivalent performance of cycles with transfers of embryos cultured in EmbryoScope compared to embryos cultured using traditional methods, validating the long term safety of IVF cycles benefitting from using the EmbryoScope time-lapse system.

Please note that these studies validate the safety of the EmbryoScope time-lapse system only, not of time-lapse monitoring systems in general. The design of such systems may vary with respect to incubation conditions, illumination, stability and other quality measures.

1. Cruz M, Gadea B, Garrido N et al. (2011): *J Assist Reprod Genet* 28(7): 569-573
2. Kirkegaard K, Hindkjaer JJ, Grondahl ML et al. (2012): *J Assist Reprod Genet* 29(6): 565-572
3. Insua MF, Cobo A, Larreategui Z et al. (2015): *Fertil Steril* 104(3): suppl: e212-e213
4. Zaninovic N, Zhan Q, Clarke R et al. (2015): *Fertil Steril* 104(3): suppl: e227-e228

