

EmbryoViewer[®] software

User manual



Caution: Federal law restricts this device to sale by or on the order of a physician or a practitioner trained in its use.

EmbryoViewer software, version 7.9

User manual, first issue 2022.10.03, revised 2024.09.25/North America/American English



1 Introduction

The EmbryoViewer software is a class I medical device that conforms to the requirements of the Medical Device Regulation (EU) 2017/745.

In this user manual, all references to “EmbryoScope” cover both EmbryoScope D, EmbryoScope+, EmbryoScope Flex and EmbryoScope 8.

All image functionality in the EmbryoViewer software will be unavailable to users of the CulturePro incubator.

The manual contains images of annotation functionality. The number of wells in the culture dishes used in your clinic may differ from the images in this manual depending on the incubator used.

The manual covers annotation without the Guided Annotation tool. If the Guided Annotation tool is installed in your clinic, please refer to the separate Guided Annotation user manuals (detailed guidelines and quick guide) for information about this type of annotation.

1.1 Important restrictions and warnings

The following restrictions and warnings will ensure the safe and correct use of the EmbryoViewer software by qualified clinic personnel. Users must be qualified to operate the software and qualified to perform procedures associated with software use in accordance with local qualification standards. The EmbryoViewer software is used together with the EmbryoScope incubator by the user(s) to select viable embryos for transfer in fertility treatment.

Proper assessment and selection of embryos for transfer is essential to provide successful treatment to patients. All personnel using the EmbryoViewer software must therefore agree to read and understand this user manual, observe the restrictions regarding use and read the following warnings to be qualified to operate the EmbryoViewer software.

RESTRICTIONS ON USE
<ul style="list-style-type: none">• The EmbryoViewer software may only be used by qualified personnel trained by Vitrolife employees.• 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 EmbryoViewer software and associated hardware. Any serious incident that has occurred in relation to the software should be reported to the competent authority of the Member State in which the user is established.• Access to the EmbryoViewer software must be controlled so that only qualified and trained personnel are permitted access. Untrained personnel could inadvertently change the annotation or selection of embryos so it is essential that the EmbryoViewer software is installed in a secure place not accessible by patients or the public.

RESTRICTIONS ON USE

- While the EmbryoScope or CulturePro incubator facilitates safe handling and access to information about the embryos in a particular treatment, it can only supplement and NEVER replace proper security measures to ensure that the embryos selected and transferred belong to the proper patients. All standard procedures for labeling and validation of the identity for EVERY transfer of gametes and embryos between vessels MUST be maintained.
- The data received by the EmbryoViewer software about the performance of the EmbryoScope or CulturePro incubator cannot replace actual monitoring of the EmbryoScope or CulturePro incubator. The performance of the EmbryoScope or CulturePro incubator must therefore be checked on a regular basis through control of the EmbryoScope or CulturePro incubator itself.
- Upload of data may only be initiated IF THIS IS PERMISSIBLE BY LAW AND THE REGULATIONS in the country in which the EmbryoViewer software has been installed.
- The clinic is solely responsible for ensuring that all local rules and regulations are observed in connection with the upload of data to Vitrolife and that patients are informed about such upload of data.
- Only anonymous data may be uploaded to Vitrolife.

WARNING

- The EmbryoScope or CulturePro incubator may only be operated by trained personnel. Only trained personnel may annotate and select embryos as personnel that are not properly trained could inadvertently or deliberately change the embryos that are selected for transfer.
- It is essential that the identity of embryos selected for transfer is verified before transfer from the culture dish to the transfer catheter. The appearance of the embryo in the microscope used for loading the embryo in the catheter must match the appearance of the embryo on the last acquired image as printed out on the laboratory data report. The patient ID and patient name on the laboratory data report must match the label on the culture dish AND the label on the catheter.
- Backups of image and patient data must be performed at regular intervals. The clinic is solely responsible for setting up backups of data to a safe external hard disk. The EmbryoViewer software is NOT delivered with any integrated backup facilities.
- The user MUST ensure that antivirus software is installed on the computer.

WARNING

- When a score for embryos is calculated by applying a model on the **Compare & Select** page, the embryos given the highest score will be the ones that best meet the requirements specified in the model. This does not necessarily imply that these embryos are the ones most suitable for transfer. The decision about which embryos to transfer must always be made by the user after assessing the quality of all relevant embryos.
- Before clinical use, a model should always be validated by the clinic in which it will be used.

INSTALLATION AND MAINTENANCE

- Installation, inspection and adjustment of the EmbryoViewer software can only be carried out by a person certified by Vitrolife.
- The hardware on which the EmbryoViewer software is installed must remain at the location where it was set up by a person certified by Vitrolife and may only be moved by such certified person or upon express written authorization.

CONFIDENTIALITY

- All names and treatment data presented in this manual are purely fictional.

1.2 Intended use

The EmbryoViewer is a software package intended to be used together with an incubator as part of fertility treatment.

1.3 Indications for use

The EmbryoViewer software is intended for displaying and comparing images generated by the EmbryoScope+ incubator. This software includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software does not control any hardware components in the EmbryoScope+ incubator.

The KIDScore D3 and KIDScore D5 tools are optional tools that can be used in conjunction with the EmbryoViewer software. KIDScore D5 is not available in the US.

The KIDScore D3 tool provides decision support for prediction of the likelihood of embryos developing to the blastocyst stage by scoring them according to their statistical viability. Adjunctive information provided by KIDScore D3 aids in the selection of embryo(s) for either transfer on day 3, freezing or continued embryo development when, following morphological assessment on day 3, there are multiple embryos deemed suitable for transfer or freezing. The KIDScore D3 tool is only to be used with the EmbryoScope time-lapse incubator systems.

1.4 Intended users

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

1.5 Clinical benefit

As an accessory to a medical device, the EmbryoViewer software provides the indirect clinical benefit of efficient evaluation and improved selection of embryos incubated in the incubator(s) connected to the system, thereby supporting:

- Improved implantation/pregnancy rate
- Reduced pregnancy loss rate.

1.6 Proposed workarounds

For details about any known anomalies and limitations in the software as well as proposed workarounds, please refer to the separate handout on this subject provided by Vitrolife.

1.7 Minimum hardware requirements

The EmbryoViewer software must be installed on a computer with the following minimum requirements:

- Microsoft Windows
- Intel Core i5 quad-core processor
- 3 GB RAM
- 100 GB hard disk
- Graphic card capable of running a resolution of 1920 x 1200 pixels
- Gigabit LAN connection
- Mouse
- Jog wheel
- Keyboard
- 24" LED display capable of running a resolution of 1920 x 1200 pixels
- Compliance with the requirements of the IEC 61010-1 and IEC 61326 (or equivalent) standards.

A person certified by Vitrolife will perform the device set-up, software installation and training of personnel involved in the routine workflow of using the device. Training and instruction of

personnel will be performed by a person certified by Vitrolife in connection with the installation of the EmbryoScope or CulturePro incubator and the EmbryoViewer software.

1.8 Backup

WARNING
<ul style="list-style-type: none">It is the sole responsibility of the clinic to set up backups of image and patient data to a safe external hard disk. The clinic may decide to use either a backup program integrated in the Windows operating system, a script or an external backup tool.

It is the sole responsibility of the clinic to ensure that all data are stored safely and to choose a program that will perform scheduled backups of clinic data. Therefore, you should install a suitable backup program. You are advised to perform daily backups.

1.9 General cybersecurity recommendations

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

- Ensure that personnel are properly trained in cybersecurity awareness
- Prevent physical access to the equipment by unauthorized 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 cybersecurity vulnerability incident or any suspected security events.

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

Table of contents

1	Introduction	2
1.1	Important restrictions and warnings.....	2
1.2	Intended use	4
1.3	Indications for use	4
1.4	Intended users	5
1.5	Clinical benefit	5
1.6	Proposed workarounds	5
1.7	Minimum hardware requirements	5
1.8	Backup.....	6
1.9	General cybersecurity recommendations	6
2	General description of the EmbryoViewer software.....	12
2.1	Overview of menus and functions in the navigation panel	13
2.2	Association between various IDs	14
2.2.1	Patient name and ID	14
2.2.2	Treatment ID.....	14
2.2.3	Culture dish ID.....	15
2.2.4	Well ID.....	15
2.2.5	Embryo ID	15
2.3	Color guide	15
2.4	User logon	16
2.5	Concurrent users	18
2.6	Logging of data changes.....	19
2.7	Licenses	20
3	Running menu	21
3.1	View Running page.....	21
3.1.1	Running culture dishes	23
3.1.2	Warning alarm status.....	23
4	Patients menu	24
4.1	View All Patients page	24
4.1.1	Creating or deleting a patient.....	24
4.2	Patient Details page.....	25
4.2.1	Treatment tab	26

4.2.1.1	Medication group box.....	27
4.2.1.2	Oocyte group box.....	27
4.2.1.3	Culture group box	27
4.2.1.4	Culture dish and embryo information.....	27
4.2.1.5	Insemination group box.....	28
4.2.2	Transfer tab	29
4.2.2.1	Transfer Details group box	29
4.2.2.2	FET Stimulation group box.....	29
4.2.2.3	Transfer Media group box	29
4.2.2.4	Outcome group box.....	29
4.2.3	Saving patient details.....	30
5	Slides menu	30
5.1	View Slide page	30
5.1.1	Viewing time-lapse images of embryo development	30
5.1.1.1	Using the jog wheel.....	31
5.1.1.2	Using the navigation buttons	31
5.1.1.3	Using the mouse	31
5.1.1.4	Using the keyboard	31
5.1.2	Viewing different focal planes	32
5.1.3	Embryo selection buttons.....	33
5.1.4	Entering information about culture dishes	34
5.1.5	Saving your changes	34
5.1.6	Selecting embryos for annotation.....	34
5.2	Timeline page	35
5.2.1	Selecting embryos on the Timeline page	35
5.2.2	Viewing various focal planes on the Timeline page.....	36
5.2.3	Morphological grade	36
5.3	Annotate page	36
5.3.1	Blastomere activity.....	38
5.3.2	Using the annotation table	38
5.3.3	Annotating cell divisions	39
5.3.4	Annotating the number of visible nuclei.....	39
5.3.5	Annotating dynamic score, Z score and morphological grade	39
5.3.6	Annotating appearance and disappearance of pronuclei and extrusion of polar bodies.....	40

5.3.7	Annotating the number of pronuclei	40
5.3.8	Annotating the degree of fragmentation	40
5.3.9	Annotating multinucleation.....	40
5.3.10	Annotating inner cell mass and trophectoderm evaluation	41
5.3.11	Annotating division regularity and blastomere symmetry	41
5.3.12	User-defined annotation variables	41
5.3.13	Selecting embryos on the Annotate page	42
5.3.14	Viewing time-lapse embryo development on the Annotate page	42
5.3.15	Measuring blastomere size	43
5.3.16	Indicating important visible characteristics of the embryo	44
5.3.17	Adding text to an embryo image	45
5.3.18	Saving your changes	46
5.4	Compare & Select page.....	46
5.4.1	User rights on the Compare & Select page.....	47
5.4.2	Compare & Select table.....	47
5.4.2.1	Fixed columns in the Compare & Select table	48
5.4.2.2	Variable columns in the Compare & Select table.....	48
5.4.2.3	Missing or coinciding timing variables	50
5.4.2.4	Logical variables	50
5.4.2.5	Embryos with the highest score in the model	51
5.4.2.6	Applying a model to a culture dish.....	51
5.4.2.7	Viewing embryos side by side	52
5.4.3	Selecting fresh embryos and registering the outcome of embryos transferred on a specific date.....	54
5.4.4	Transferring a thawed embryo from an existing treatment without culturing the embryo further	55
5.4.5	Continuing culturing thawed embryos and selecting one or more embryos for transfer	57
5.5	Report page	58
5.5.1	Generating a patient treatment report	59
5.5.2	Generating an annotation and evaluation report	59
5.5.3	Printing a report	60
5.6	Video page.....	60
5.6.1	Generating a video of the embryos	61
5.6.2	Generating images of the embryos	63

5.7	Incubation page	64
5.7.1	Summary tab	66
5.7.2	Alarms tab	67
5.7.3	Warnings tab	67
5.7.4	Log tab	67
5.7.5	Other tab	68
5.7.6	Saving QC status and comments.....	69
6	Database menu	69
6.1	View All Slides page.....	69
6.1.1	List of culture dishes	70
6.2	Instrument page.....	71
6.2.1	Average incubation conditions for all culture dishes.....	71
7	Settings menu.....	71
7.1	General tab.....	71
7.2	User tab	72
7.2.1	Creating, editing and deleting users.....	73
7.2.2	User roles	74
7.2.3	Automatic logout and screen saver settings.....	74
7.3	Annotations tab.....	75
7.3.1	User rights and user-defined variables.....	76
7.3.2	Adding a new user-defined variable	76
7.3.3	Deleting a user-defined variable	77
7.3.4	Redefining a user-defined variable	77
7.4	Models tab	77
7.4.1	User rights on the Models tab	79
7.4.2	Variables in models	79
7.4.3	List of available pre-defined variables	80
7.4.4	Defining custom expressions	81
7.4.5	Editing custom expressions	83
7.4.6	Deleting custom expressions	83
7.4.7	Designing a new model	83
7.4.8	Hierarchical models	86
7.4.9	Additive models	87
7.4.10	Multiplicative models.....	89

7.5	Validating models.....	91
7.5.1	Morphokinetic variables used in models	91
7.5.2	Selecting a data sample	92
7.5.3	Known implantation data (KID)	92
7.5.4	Statistical evaluation.....	93
7.5.5	How to validate models.....	93
7.6	Embryo Details tab.....	94
7.6.1	Adding embryo details parameters	94
7.6.2	Editing embryo details parameters.....	95
7.6.3	Deleting embryo details parameters	95
7.7	Brands tab	96
7.8	Export tab	98
7.9	About tab	103
8	Failure of the EmbryoViewer software	104
9	Symbols and labels	104
10	Disposal of waste	105
11	Index.....	105
12	Contact information	106

CohortView, CulturePro, EmbryoScope, EmbryoSlide, EmbryoViewer, Guided Annotation, iDAScore and KIDScore are trademarks or registered trademarks belonging to the Vitrolife Group.

©2024 Vitrolife A/S. All rights reserved.

2 General description of the EmbryoViewer software

The EmbryoViewer software provides:

- High-resolution time-lapse images of single embryos
- Embryo annotation tools that assist the user in selecting embryos
- Inspection of incubation details, e.g. temperature and gas conditions
- Export of data for statistical analysis
- Support for integration with the ES server.

The EmbryoViewer software must be used with the ES server in order to access any databases. The ES server is a separate Vitrolife product that acts as a central data storage unit. This central unit allows all users who are connected to the same database to view and update the same data. Please contact Vitrolife to learn more about the ES server.

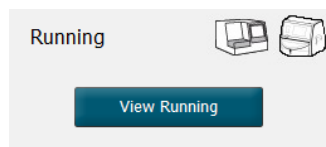
The EmbryoViewer software does not perform any diagnostics, but only shows data from the connected EmbryoScope and CulturePro incubators and data entered by the user. Data from the EmbryoScope and CulturePro incubators include embryo images, incubation details, alarms, log files and other instrument parameters.

The EmbryoScope and CulturePro incubators provide an environment with controlled temperature and CO₂ (and other gases) for the development of embryos. EmbryoScope incubators have an integrated inverted microscope and imaging system for embryo viewing. Device use is limited to five days (120 hours) covering the time from post-fertilization to day 5 of development.

NOTE
<ul style="list-style-type: none">• The EmbryoViewer software does not control any hardware components in the EmbryoScope and CulturePro incubators and thus does not affect the incubation of embryos. If the EmbryoViewer software fails or is shut down, e.g. due to a power failure, the EmbryoScope or CulturePro incubator continues to run and data are saved.

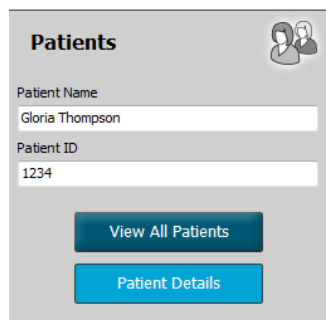
2.1 Overview of menus and functions in the navigation panel

The main navigation tool in the EmbryoViewer software is the navigation panel (left part of the screen). The navigation panel is organized in a number of main menus, each menu containing one or more functions (command buttons).



Overview of treatments in the incubator.

See section 3.



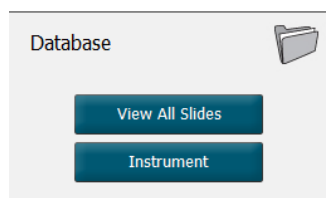
Overview of all patients, patient details and treatments.

See section 4.



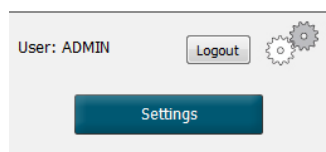
Details about culture dishes and reporting.

See section 5.



Data on culture dishes, patient and QC databases.

See section 6.

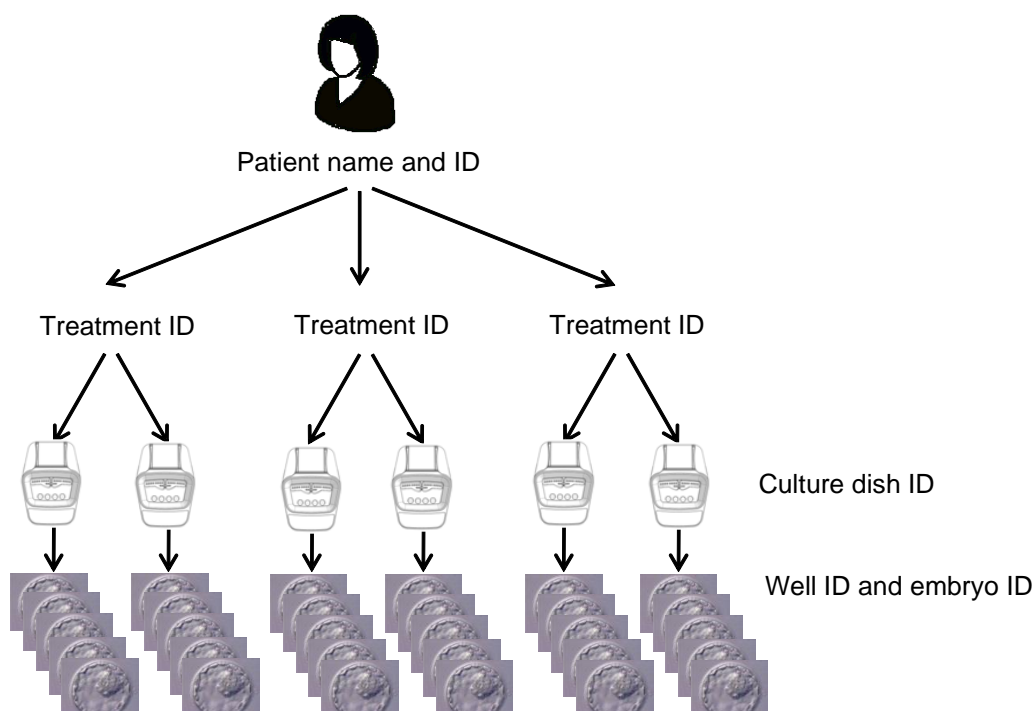


Settings for data export, user roles, **Compare & Select** model design, etc.

See section 7.

2.2 Association between various IDs

The data available in the EmbryoScope and CulturePro incubators and the EmbryoViewer software contain various IDs. This section describes these IDs, and the following illustration provides an overview of the association between patient ID, treatment ID, culture dish ID, well ID and embryo ID:



For information on how to link a culture dish ID to a treatment ID, see section 4.2.1.4.

2.2.1 Patient name and ID

You can add the patient name and ID number to the patient file either via the EmbryoScope or CulturePro incubator or via the EmbryoViewer software.

If you add a new culture dish to the EmbryoScope or CulturePro incubator, a new patient will be registered with the patient information from the EmbryoScope or CulturePro incubator. You can also register a new patient in the EmbryoViewer software when a culture dish is added to the EmbryoScope or CulturePro incubator. The patient and treatment information will then automatically be linked.

2.2.2 Treatment ID

Each patient has one or more associated treatments, and each treatment can be associated with data from one or more culture dishes. All new treatments are named when registered on the EmbryoScope or CulturePro incubator. You can rename the treatment both from the EmbryoScope or CulturePro incubator and from the EmbryoViewer software. It is recommended to ensure that each treatment carries a unique name. This will enable you to distinguish more easily between successive treatments.

Treatments can be created and handled both from the EmbryoViewer software and from the EmbryoScope or CulturePro incubator. See section 4.2.1.

2.2.3 Culture dish ID

Each culture dish carries a unique number consisting of two letters (AA, AB, AC, etc.), the date when the culture dish was entered into the EmbryoScope or CulturePro incubator, a sequential number and an instrument number.

2.2.4 Well ID

Each well in a culture dish is identified by two letters (AA, AB, AC, etc.) that indicate which culture dish the well belongs to and the number of the well in this culture dish. For example, AA-1 is the first well in the first culture dish, and AB-3 is the third well in the second culture dish.

2.2.5 Embryo ID

Each embryo has an ID number that is automatically generated when a culture dish is added to the EmbryoScope or CulturePro incubator. The embryo ID is displayed on the **Patient Details** page, on the **Report** page and in the blue title bar of the image shown at the bottom of the **Compare & Select** page when you click on a well ID.

2.3 Color guide

The EmbryoViewer software marks buttons or frames on the pages in different colors to indicate whether these elements are available, activated or disabled.



Dark blue: Button or frame is available, but not activated.



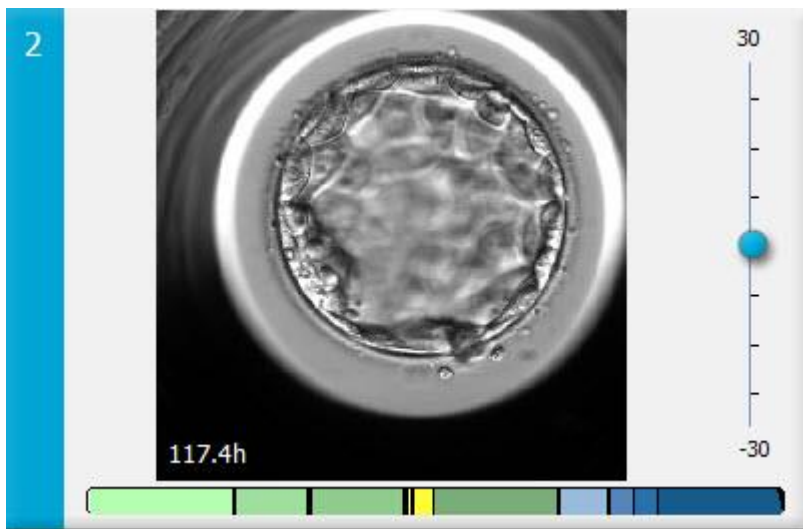
Light blue: Button or frame is activated.



Gray: Button is disabled, appears dark blue when the function can be used.

The following illustration is an example of an activated frame (frames are boxes on the page that hold other page elements such as embryo images).

When you have chosen an embryo image, e.g. because you want to annotate that particular embryo, the image frame will be colored light blue:



2.4 User logon

All users of the EmbryoViewer software will need a user name and password to be able to log in, which is required both at start-up and if an automated logout occurs after an idle time period.

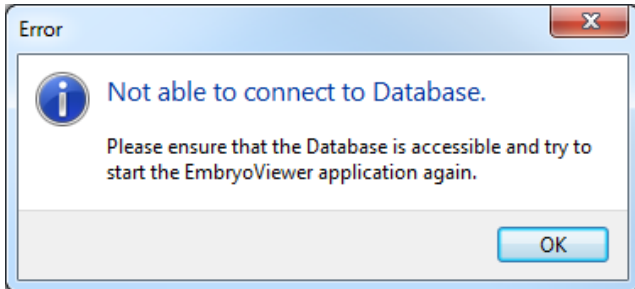
Users log in from the following screen:



If you enter the wrong user information four times in a row, the screen will be locked for 60 seconds. After this period, the screen is unlocked, and you can attempt to log in again.

In addition to entering a password, all users need to specify which database they want to connect to. There may be more than one available database in your clinic.

If there is no connection to the selected database when you attempt to log in, you will see the following message:



Check whether you have indeed selected the correct database during login. If so, you should contact your system administrator to report the problem. The database may need to be restarted.

The connection to the database may also be lost while you are editing data. You will then be returned to the login screen, which will inform you that the connection has been lost:



When the database is accessible again, another message will communicate this to you. You will now be able to log in:



2.5 Concurrent users

Because of the integration between the EmbryoViewer software and the ES server, data can be shared between users. However, when sharing data, several users may potentially edit the same data at the same time or one of the users may not see the latest updates.

To handle this situation, the EmbryoViewer software will display a warning when several users are viewing the same patient data. When this situation occurs:

- The updates made by one or more users may be overwritten by another user.
- One or more users may be viewing outdated information.

The following scenarios are possible:

- **Scenario 1:**

User 1 has reader rights and user 2 has reader rights OR

User 1 has reader rights and user 2 has editor/administrator rights:

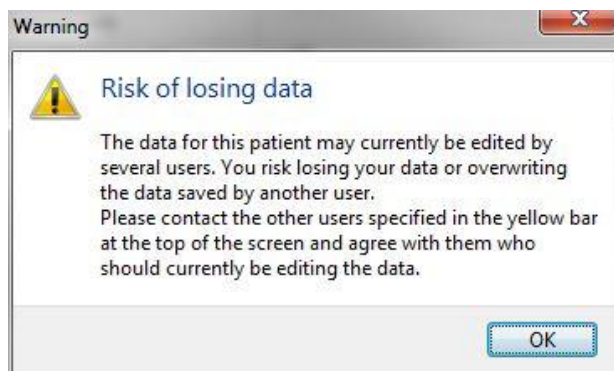
There is no risk that this combination will compromise the data or that one of the users may be viewing outdated information. In this situation, no warning will be displayed.

- **Scenario 2:**

User 1 has editor/administrator rights and user 2 has editor/administrator rights:

There is a risk that both users are simultaneously updating the same data. This means that the user who last clicks the **Save** button will overwrite the updates just made by the other user.

The following warning will only be displayed in scenario 2 where one or more users have rights that allow them to update the data (even if one of the users only intends to view the data):



When the user clicks **OK**, another warning at the top of the current page will let the user know which other users are also currently using the same patient data. The warning will remain on the page until one of the users is no longer viewing the data:

WARNING: Risk of losing data because of multiple concurrent users. Patient data currently accessed by: ADMIN.							
Patient ID	Patient Name	Age	Birth Year	Birth Month	BMI	Diagnosis	Patient Comments
1234	qqq						

These are the users who should be contacted to decide who will currently be editing the data. This is a manual process. No users will be automatically logged off to handle the situation.

If all logged-in users have only reader rights, no warnings or messages are displayed as this will not have any unwanted side effects.

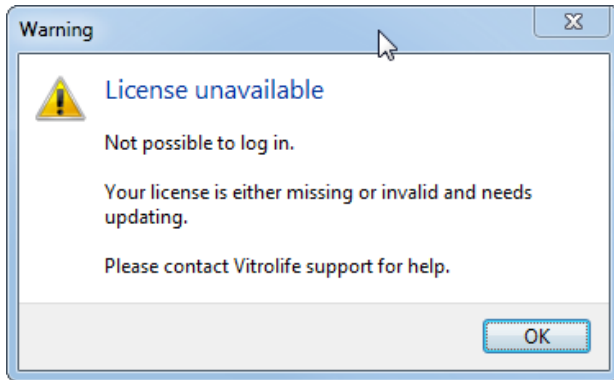
2.6 Logging of data changes

The EmbryoViewer software does not keep a log of changes made to the data. However, if the user makes any changes to the QC status or on the **View Slide**, **Annotate** or **Incubation** pages and saves these changes, the user name and, for the **View Slide** and **Incubation** pages, the date of the last change will be stamped on the page.

2.7 Licenses

A license needs to be installed for all computers that run the EmbryoViewer software. The license determines which functions are available in the software.

In case the license is either missing or invalid, you will be unable to log into the software. A message will inform you that there is a problem with the license:

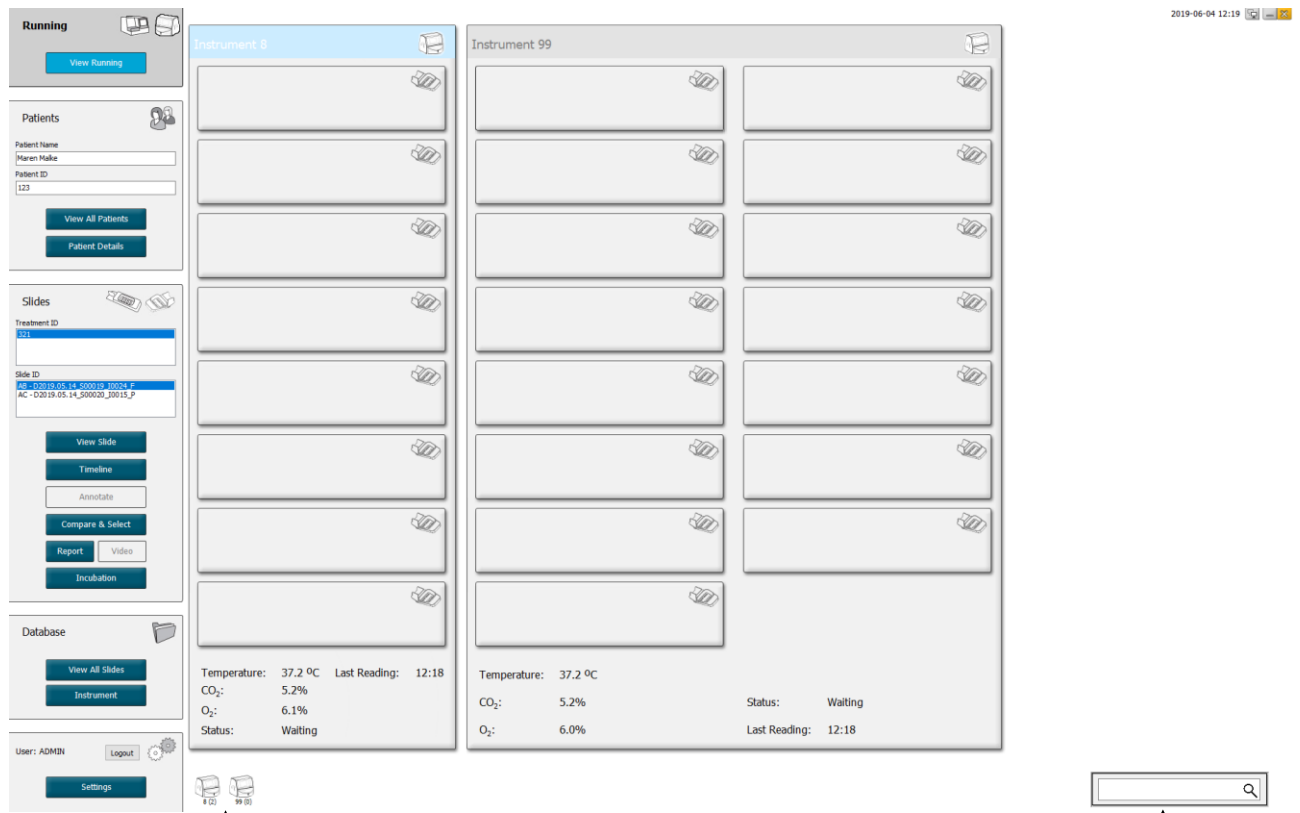


If you see this message, please contact either your system administrator or the Vitrolife support team.

3 Running menu

From the **Running** menu, you can open the **View Running** page. On this page, you can inspect the treatments currently running in an EmbryoScope or CulturePro incubator connected to the EmbryoViewer software. You can also search for a specific patient or treatment.

3.1 View Running page



The screenshot shows the 'View Running' page in the EmbryoViewer software. The interface is divided into a sidebar on the left and a main content area. The sidebar contains navigation links for 'Running', 'Patients', 'Slides', 'Database', and 'User'. The main content area displays two incubator panels, 'Instrument 8' and 'Instrument 99'. Each panel shows a grid of culture dish thumbnails and a summary of environmental parameters: Temperature (37.2 °C), CO₂ (5.2%), O₂ (6.1%), and Status (Waiting). A search bar is located at the bottom right of the interface.

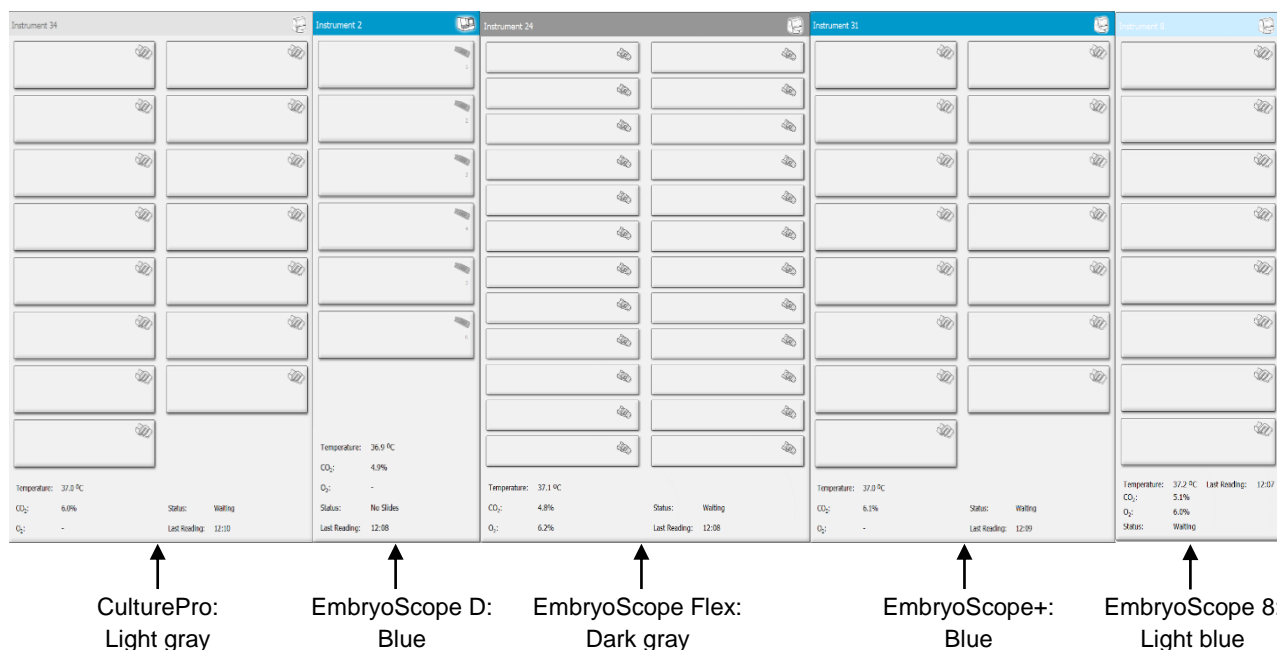
↑

All incubators connected to the EmbryoViewer software (instrument number followed by the number of active culture dishes in the incubator)

↑

Search field to search for a specific patient or treatment

The **View Running** page displays all currently running culture dishes from all EmbryoScope and CulturePro incubators connected to the EmbryoViewer software. Each type of incubator is indicated by the icon and color of the heading:



The following information is displayed:

- Data from all running culture dishes in each of the connected EmbryoScope and CulturePro incubators.
- Patient name, patient ID and days since insemination for each patient treatment. **D0** is the day of insemination.
- Current incubation conditions (incubation temperature and gas concentrations) for each connected EmbryoScope or CulturePro incubator.
- Status of the EmbryoScope or CulturePro incubator.
- Time of the last data read-out from the EmbryoScope or CulturePro incubator.

A warning will be displayed above the incubator information if the ES server hard disk is running out of space (see section 7.9). Contact Vitrolife for support if you see this warning.

You can use the search field in the lower right corner of the **View Running** page to search for a specific patient or treatment.



Click the **View Running** button in the **Running** menu to close the search result and return to the overview screen.

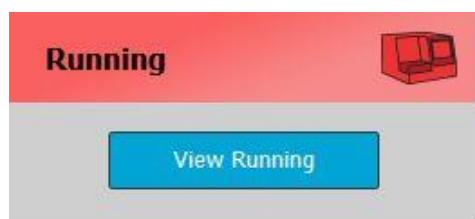
3.1.1 Running culture dishes

To display the information related to a specific running culture dish, click on the desired culture dish. The application now displays an overview of this culture dish.

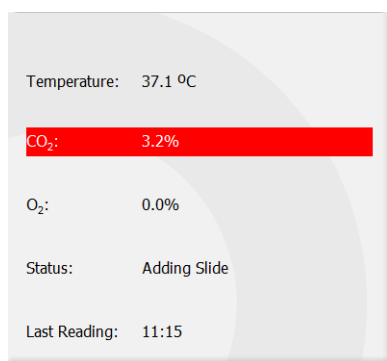
Note that running culture dishes are not displayed on the **View All Slides** and **Instrument** pages. On these pages, only completed culture dishes will be displayed.

3.1.2 Warning alarm status

If a warning alarm is issued by the EmbryoScope or CulturePro incubator, the title bar will be colored red.

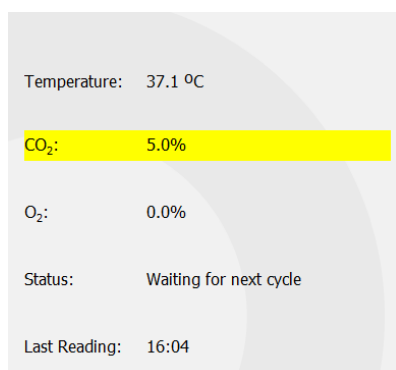
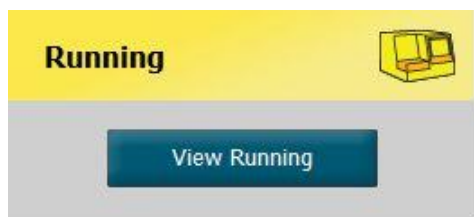


To check which parameter caused the warning alarm, click the **View Running** button. A red bar indicates whether the warning alarm is related to temperature, CO₂ or O₂ or whether the warning alarm indicates that the connection between the EmbryoScope or CulturePro incubator and the EmbryoViewer software has been lost. In this case, the application will display the time of the last reading.



For detailed information on how to handle warning alarms on the EmbryoScope or CulturePro incubator, please consult the user manual delivered with the EmbryoScope or CulturePro incubator.

When the warning alarm in the EmbryoScope or CulturePro incubator stops because the parameter that caused the warning alarm is back within the accepted range, the color of the alarm bar will change to yellow, both on the title bar and on the specific parameter. This color indicates that a warning alarm has occurred.



When the warning alarm has been reset on the EmbryoScope or CulturePro incubator, the color of the title bar and the specific parameter will change from yellow to gray, which is the default color.

4 Patients menu

From the **Patients** menu, you can open the **View All Patients** and **Patient Details** pages. These pages allow you to navigate through all available patient and treatment details. When you have highlighted a patient on the **View All Patients** page, the **Patients** menu of the navigation panel displays the name and ID of this patient.

4.1 View All Patients page

The **View All Patients** page lists all patients in the database.

The data can be sorted by clicking on the header row of each column. Double-clicking on a patient row opens the **Patient Details** page.

4.1.1 Creating or deleting a patient

If you click the **Delete** button, all data related to the highlighted patient will be deleted, provided that this patient does not have any associated time-lapse data. If you click the **New** button, you create a new patient who can be linked to a specific time-lapse data file or a treatment ID.

It is possible to create a new patient on this page before loading any culture dishes into the EmbryoScope or CulturePro incubator. You can associate the created treatment data with the patient on the EmbryoScope or CulturePro incubator.

WARNING

- It is important to select the correct patient ID on the EmbryoScope or CulturePro incubator if you add a new treatment to an existing patient.

4.2 Patient Details page

The **Patient Details** page provides you with detailed information on patients, treatments, culture dishes and the outcome of transferred embryos.

Patient Details

Patient ID: 001
 Patient Name: Heidi Schmith
 Date of Birth: 1991-07-01
 BMI: 25 Basal Serum FSH (IU/l): 3.2
 Diagnosis: Tubal factor

Patient Comments

Treatment **Transfer**

All Treatments: X1X6_2020, X1X1_2020
 New Treatment, Rename Treatment, Print Barcode Label, Reprint Barcode Label

Treatment Comments

PGT-A / PGT-M

Medication: Medication Protocol (Long Agonist), Medication Brand, Triggering (HCG), Total FSH Dose (IU) (1000), LH Supplement, Medication Comment

Oocyte: Oocyte Source (Autologous), Oocyte History (Fresh), Oocytes Aspirated (4), Sibling Embryos in Standard Incubator (No), Oocyte Comment

Culture: Media Type (Single Step), First Medium Brand (Vitrolife), Second Medium Brand, Media Change (None), Culture Comment

Slide(s) in Treatment: AB-D2000.01.01-510001.10001.P
 Slide Treatment ID: X1X1_2020
 Slide Description
 Slide Type: Human Clinical

Insemination: Insemination Date (2016-09-28), Insemination Time (hh:mm) (11:40), Insemination Method (Normal IVF), Insemination Comment

Well	Embryo ID	Decision	Embryo Description
1	AB1		
2	AB2		
3	AB3		
4	AB4		
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			

The upper part of the page provides general patient information that applies to all treatments, e.g. the patient's date of birth and BMI. If you have previously worked with an older version of the EmbryoViewer software in which only the patient's year and month of birth were registered, the existing data will automatically be converted. As the software does not know the exact date, a notification to confirm the date will be shown next to the **Date of Birth** field until you have selected the correct date and saved the data. You can make other changes without confirming the date of birth, but the notification will remain until you have done so.

The **Patient Comments** field is a free-text field in which you can enter comments related to the patient. If relevant, you can select a diagnosis from the **Diagnosis** drop-down list.

Below the general patient information, the page contains two tabs: **Treatment** and **Transfer**. The information on these tabs is specific to a particular culture dish or treatment.

4.2.1 Treatment tab

On the **Treatment** tab, you can enter information about a particular treatment.

The upper part of the tab contains information related to the treatment, e.g. medication, whereas the lower part of the tab contains information about the culture dish(es) associated with the treatment and the insemination time and method.

The screenshot displays the 'Treatment' tab in the EmbryoViewer software. The interface is organized into several sections:

- All Treatments:** A list box showing 'Unknown' and 'Algorithm'. Below it are buttons for 'New Treatment', 'Rename Treatment', 'Print Barcode Label', and 'Reprint Barcode Label'.
- Treatment Comments:** A large text area for entering comments. Below it is a checkbox for 'PGT-A / PGT-M'.
- Medication:** Fields for 'Medication Protocol', 'Medication Brand', 'Triggering', 'Total FSH Dose (IU)', 'LH Supplement', and 'Medication Comment'.
- Oocyte:** Fields for 'Oocyte Source', 'Oocyte History', 'Oocytes Aspirated', 'Sibling Embryos in Standard Incubator', and 'Oocyte Comment'.
- Culture:** Fields for 'Media Type', 'First Medium Brand', 'Second Medium Brand', 'Media Change', and 'Culture Comment'.
- Slide(s) in Treatment:** A list box showing '8-D2020.01.01-50001-0000'. Below it are fields for 'Slide Treatment ID' (Unknown), 'Slide Description', and 'Slide Type' (Unknown).
- Insemination:** Fields for 'Insemination Date' (2017-08-21), 'Insemination Time (hh:mm)' (13:09), 'Insemination Method', and 'Insemination Comment'.
- Table:** A table with columns 'Well', 'Embryo ID', 'Decision', and 'Embryo Description'. The 'Well' column lists numbers 1 through 16, and the 'Embryo ID' column lists numbers 1 through 4.

The **All Treatments** box shows a list of the patient's treatments. If you want to add a comment to the selected treatment, you can do so in the **Treatment Comments** field. Select the **PGT-A / PGT-M** check box if pre-implantation genetic testing for aneuploidy (PGT-A) or pre-implantation genetic testing for monogenic disease (PGT-M) has been carried out.

Click the **New Treatment** button to create a new treatment in the EmbryoViewer software. Enter a treatment ID in the dialog box displayed, and click **OK**. All new treatments are named when registered on the EmbryoScope or CulturePro incubator. You can rename a treatment by clicking the **Rename Treatment** button. Treatments can be added or renamed on the EmbryoScope or CulturePro incubator, but only the EmbryoViewer software allows you to add or change treatment details.

Click the **Print Barcode Label** button to print barcodes for one or more culture dishes. If you want to reprint a barcode label for a culture dish that has already been running, click the **Reprint Barcode Label** button. This may be relevant if you have changed the name or ID of a patient, changed the name of a treatment or moved an existing culture dish to another treatment. In this case, barcode labels already printed will be invalidated and can no longer be used in the incubators.

The gray drop-down lists contain pre-defined values that cannot be edited. Only the drop-down lists and fields displayed in white color allow you to enter new information. Previously entered user-defined values will be saved and subsequently made available from the editable fields for easy and quick reuse in later sessions. You may e.g. create medication brands and media brands as user-defined values from the **Brands** tab of the **Settings** page. However, even if there are pre-defined values, you can still freely enter any brand in these fields.

4.2.1.1 Medication group box

In the **Medication** group box, you can enter information about which medication has been prescribed for the patient in this treatment. You may e.g. want to enter information about medication protocol, medication brand, type of triggering and total FSH dose. The group box also contains a check box that lets you indicate whether an LH supplement has been prescribed and a free-text field where you can enter any comments related to the medication.

4.2.1.2 Oocyte group box

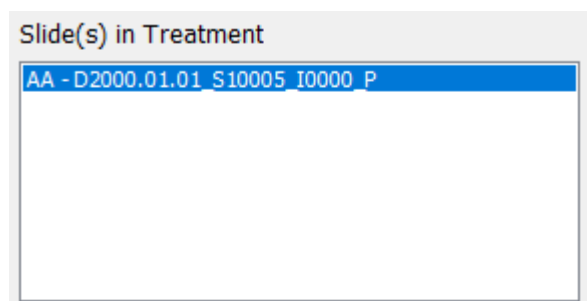
In the **Oocyte** group box, you can enter information about oocytes, i.e. oocyte source (autologous, donor, other), oocyte history (fresh, thawed, other) and the number of oocytes aspirated. If any embryos from the same treatment are incubated in a standard incubator, this should be indicated in the **Sibling Embryos in Standard Incubator** field. You can enter any comments related to the oocytes in the **Oocyte Comment** field.

4.2.1.3 Culture group box

In the **Culture** group box, you can enter information about the embryo culture conditions, i.e. media type, first medium brand and second medium brand. You may also specify whether a medium change has been performed and enter any relevant comments on the culture conditions in the **Culture Comment** field.

4.2.1.4 Culture dish and embryo information

All culture dishes associated with a particular treatment are listed in the **Slide(s) in Treatment** list box in the left side of the lower part of the **Treatment** tab.




The culture dish ID highlighted in blue color is the one for which information is displayed in the lower part of the **Treatment** tab. When you choose a different culture dish ID in the **Slide(s) in Treatment** list box, the information in the lower part of the **Treatment** tab will be updated to display information on the chosen culture dish.

WARNING

- It is important to choose the correct patient ID on the EmbryoScope or CulturePro incubator if you add a new culture dish.

From the **Slide Treatment ID** drop-down list, you can link a culture dish to an existing treatment.



Slide Treatment ID
134253-132 Treatment_1

The **Slide Description** box is a free-text field in which you can enter a description of a culture dish. You can select the type of culture dish from the **Slide Type** drop-down list.

The right side of the lower part of the **Treatment** tab lists information about a specific embryo: **Well**, **Embryo ID** and **Decision**. If needed, you can freely enter a description of each embryo under **Embryo Description**.

4.2.1.5 Insemination group box

The **Insemination** group box in the middle of the lower part of the **Treatment** tab displays information about the insemination date, insemination time and insemination method.

The insemination date and insemination time are received from the EmbryoScope or CulturePro incubator. When you start a new culture dish on the EmbryoScope or CulturePro incubator, you need to specify the time of insemination. If the time is incorrect, you can manually change it after ending the culture dish on the EmbryoScope or CulturePro incubator.

You can also specify which insemination method has been applied and freely enter any relevant comments.

NOTE

- It is important to enter the exact date and time of insemination as the timing of e.g. cell divisions will be specifically related to this information.

NOTE

- If you change the insemination date and time and click the **Save** button, you will overwrite the original date and time from the EmbryoScope or CulturePro incubator. The original data can only be restored by re-importing the raw data from the EmbryoScope or CulturePro incubator.
- Please note that raw data files will be deleted from the EmbryoScope or CulturePro incubator at regular intervals.

4.2.2 Transfer tab

On the **Transfer** tab, you can verify and enter the details of the patient's transfers. When opened, the tab contains data about the transfers decided on the **Compare & Select** page. The **All Transfers** box in the left side of the screen lists all transfers carried out for the patient. Click the **Delete Transfer** button if you want to delete the selected transfer.

Treatment ID	Slide ID	Well	Embryo ID	Decision
Unknown	D2000.01.01_S1002_1000	9	AA9	FET

4.2.2.1 Transfer Details group box

In the **Transfer Details** group box and the table to the right of the group box, you can verify which embryos were transferred on which date and whether this was a fresh or a frozen embryo transfer.

The **Transfer Type** field is read-only as the information in the field is inherited from the **Compare & Select** page where you decide whether to transfer a fresh or a thawed embryo (see sections 5.4.3, 5.4.4 and 5.4.5).

If relevant, you can select a number of embryos in the **Embryos from Other Sources** field and freely write a comment in the **Transfer Comment** field.

4.2.2.2 FET Stimulation group box

In the **FET Stimulation** group box, you can specify the medication protocol used and enter any relevant comments.

4.2.2.3 Transfer Media group box

In the **Transfer Media** group box, you can select the transfer medium used (**EmbryoGlue** or **Other**) from the drop-down list and enter any relevant comments in the **Transfer Media Comment** field, e.g. a specification of the medium used if you select **Other**.

4.2.2.4 Outcome group box

In the **Outcome** group box, you can enter information about the outcome of the treatment, i.e. the result of the hCG test, whether a miscarriage occurred, the number of gestational sacs, the number

of fetal heart beats observed and the number of live-born babies. You can freely write an outcome comment if relevant.

4.2.3 Saving patient details

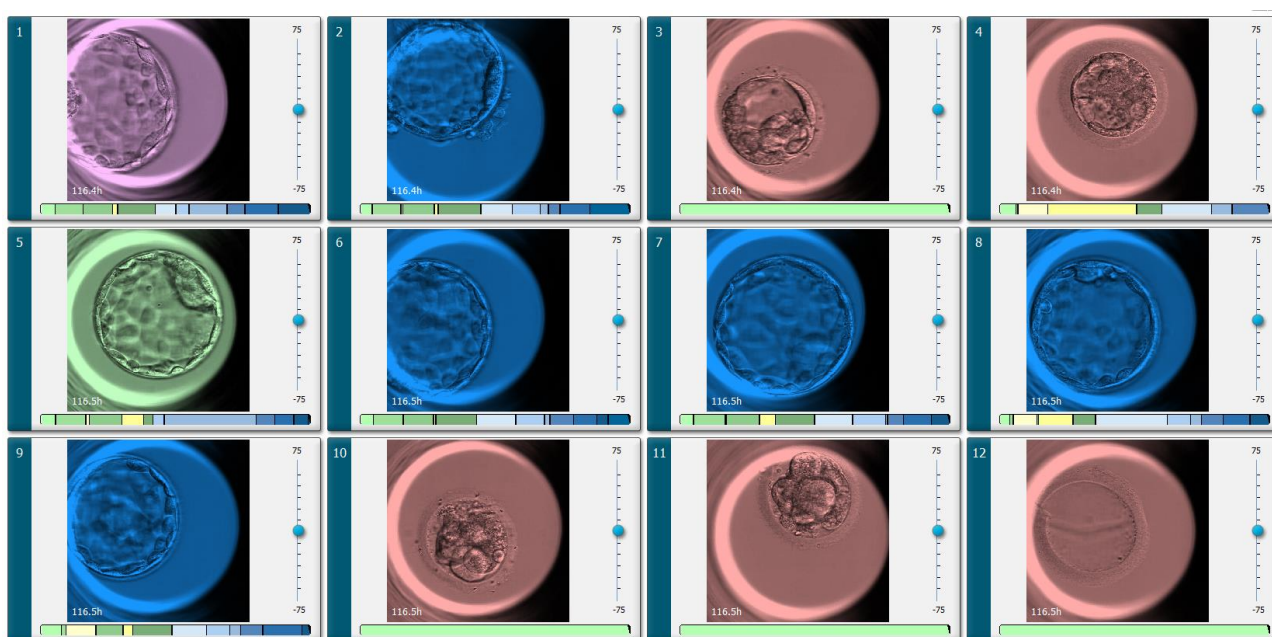
Click the **Save** button to save all updated patient information from all parts of the page.

5 Slides menu

From the **Slides** menu of the navigation panel, you can open the **View Slide** page. This page provides an overview of the available embryo time-lapse information.

5.1 View Slide page

Click the **View Slide** button to display images of all embryos in this specific culture dish.



5.1.1 Viewing time-lapse images of embryo development

On the **View Slide** page, you can view time-lapse images of all embryos in a culture dish simultaneously. If you want to see time-lapse images of one specific embryo only, you can do this

on the **Annotate** page. The playback options described in the following sections can be used on both pages.

5.1.1.1 Using the jog wheel

You can follow the chronological development of an embryo by using the jog wheel. Turn the wheel clockwise to play the video of the embryos forward or counter-clockwise to play the video backward. Remember to change the batteries in the jog wheel as required.

The black arrow on the division chart indicates the position of the current image relative to the complete video.

5.1.1.2 Using the navigation buttons

Instead of using the jog wheel to see a time-lapse video of how an embryo has developed, you can use the navigation buttons at the bottom of the page:



- Click to display the previous images in the time-lapse series.
- Click to play the time-lapse video for all embryos present in the culture dish. When you click the same button again, the new button appears and the video pauses.
- Click to display the next images in the time-lapse series.
- Use the **Film Speed** drop-down list to indicate your preferred video speed.

5.1.1.3 Using the mouse

If you prefer to use the mouse to indicate which image to display, place the pointer on a new position of your choice in the division chart and click.

5.1.1.4 Using the keyboard

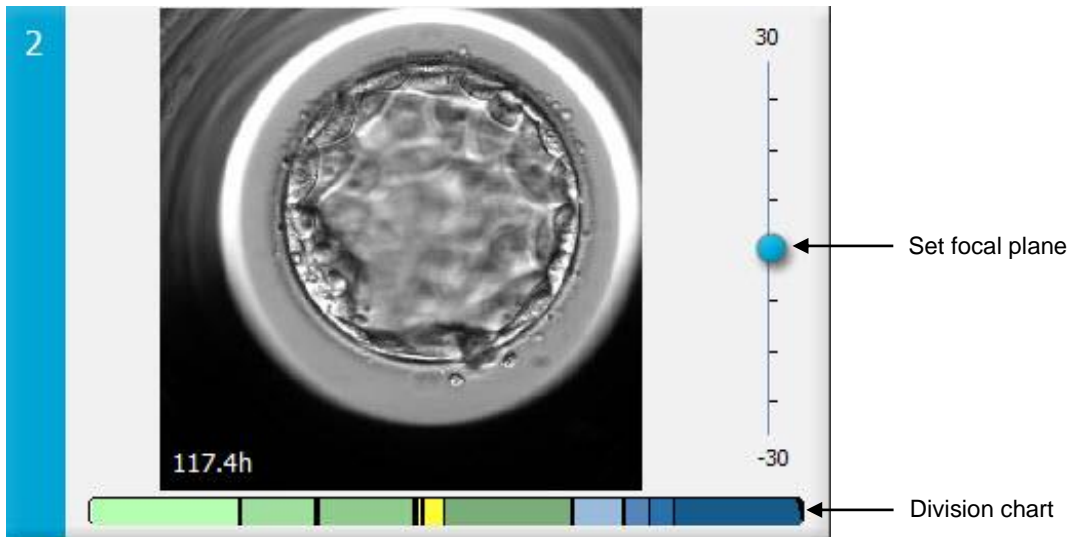
Press the right arrow or left arrow on your keyboard to move the time-lapse series one image forward or backward, respectively. This is useful if you want to check specific details.



Press and hold the Page Up or Page Down keys to play the video forward or backward at high speed, and press the space bar to start or stop the video anytime.

5.1.2 Viewing different focal planes

The EmbryoScope incubator provides images of the embryos in several focal planes. To the right of each image, you see a bar with tick marks. This bar represents the currently displayed image stack (a collection of images that are grouped together). The blue slider on the bar indicates the focal plane of the displayed image.



If you want to display an image of the embryo in a different focal plane, move the blue slider up or down. If you click just above (or below) the slider, the EmbryoViewer software displays the focal plane just above (or below) the image that is currently displayed.

You may also place the cursor over the image and press the arrow up or down keyboard buttons to move the focal plane up or down, respectively. Finally, it is possible to use the scroll wheel on your mouse to scroll up or down through the images to see various focal planes.



The color code on the division chart is:

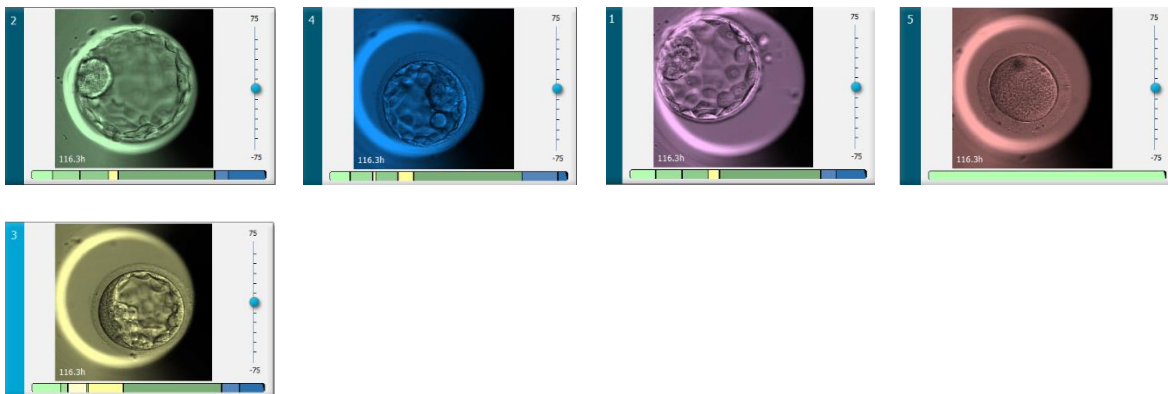
- Green: 1, 2, 4 and 8 cells
- Yellow: 3, 5, 6 and 7 cells
- Blue: M (morula), B (blastocyst), EB (expanded blastocyst) and HB (hatching blastocyst)
- Red: Atretic.

As an example, a division pattern could look like this:








The black vertical lines in the division chart indicate the time when a cell division occurred.



5.1.3 Embryo selection buttons



The buttons used for marking selected embryos are listed in the panel below the images:



- The  button marks fresh embryos selected for transfer. Images of fresh embryos selected for transfer will have a green color overlay or frame.
- The  button marks embryos selected for freezing. Images of embryos selected for freezing will have a blue color overlay or frame.
- The  button marks frozen embryos selected for transfer. Images of frozen embryos selected for transfer will have a purple color overlay or frame.
- The  button marks embryos to be avoided. Images of embryos selected to be avoided will have a red color overlay or frame.
- The  button marks embryos that are inconclusive at the time of marking. Images of embryos for which no decision can currently be made will have a yellow color overlay or frame.

As an example, when you click the  button, the () icon will follow the cursor. This indicates that the fresh transfer selection tool is active. You can now mark one or more embryos for fresh transfer by clicking on the images. Selected images will be displayed with a green color overlay or frame. To return the cursor to its normal use, click the fresh transfer tool button again. The four remaining buttons function in a similar way.

You can also view or change your selections from the **Compare & Select** page (see section 5.4).

5.1.4 Entering information about culture dishes

Annotation Status	Annotation Comment
Annotated ▾	KIDScore D5 ES+ MN2 (W: 1,2,4,7,9) MN4 (W: 3,4,7,9)

At the bottom of the **View Slide** page, you can enter the annotation status of the culture dish in the **Annotation Status** field (**Not Checked**, **In Progress** or **Annotated**) and an annotation comment in the **Annotation Comment** field.

5.1.5 Saving your changes

To save the information you have updated on the **View Slide** page, click the **Save** button. If you attempt to update or leave the page before saving your data, a dialog box will prompt you to decide whether you want to save your changes before proceeding.

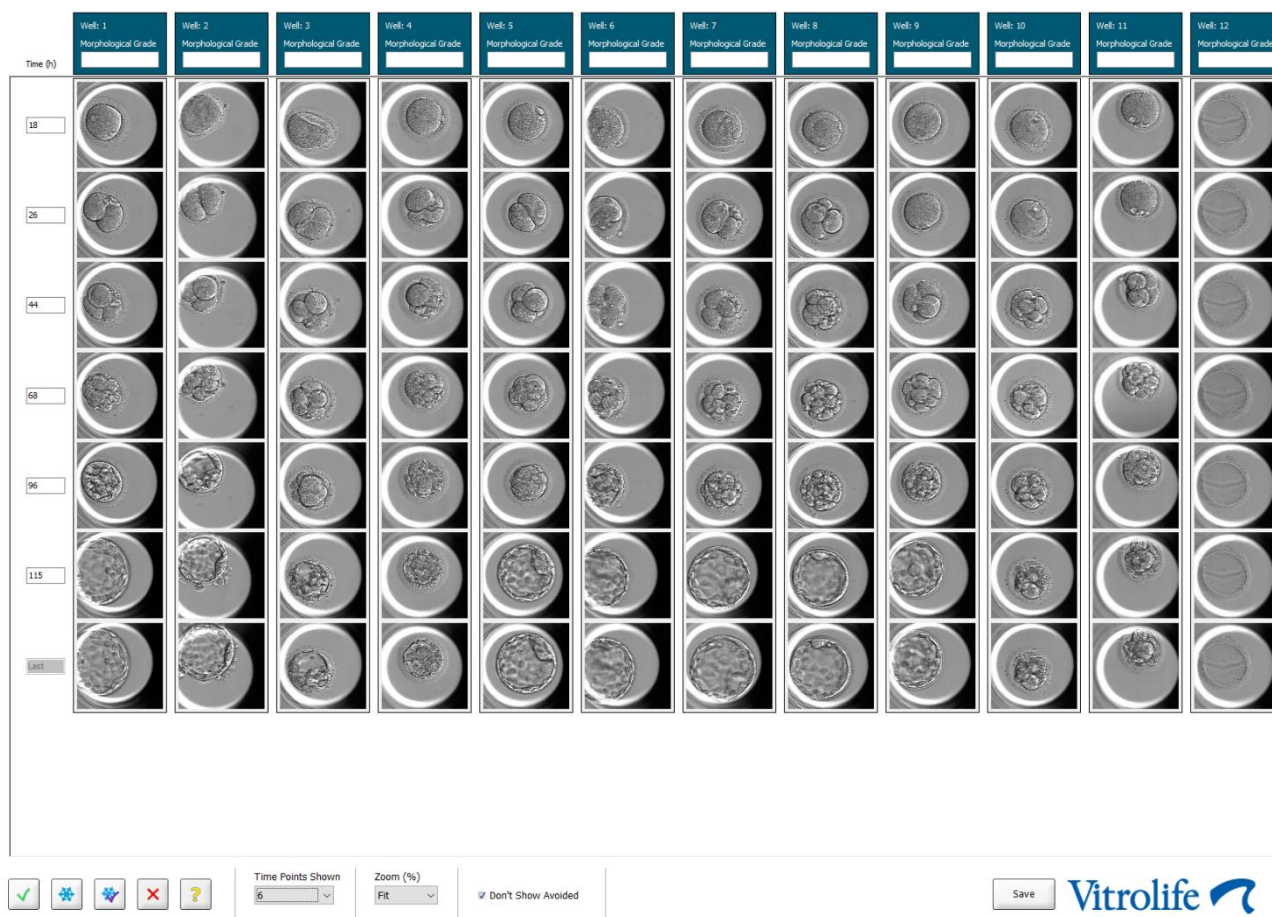
5.1.6 Selecting embryos for annotation

On the **View Slide** page, you can select an embryo by clicking once on its image. The dark blue bar to the left of the image will now be highlighted in a light blue color. You can select a maximum of three images for subsequent display on the **Annotate** page (this feature is not available if you use the Guided Annotation tool).

5.2 Timeline page

If you click the **Timeline** button, the embryos in a specific culture dish will be shown at pre-defined points in time.


The **Timeline** page provides you with a quick overview of all embryos in a culture dish. You can magnify one of the small images by double-clicking the desired image.



5.2.1 Selecting embryos on the Timeline page

The five embryo selection buttons used to indicate whether the embryo should be transferred (frozen or fresh embryo), frozen, avoided or further observed are also available from the **Annotate** and **Compare & Select** pages (see sections 5.3 and 5.4).



Mark embryos that should be avoided using the  button. This will display the marked embryos with a red color overlay or frame. Select the **Don't Show Avoided** check box if you want to hide these embryos and display the remaining embryos only.

Save your embryo selections by clicking the **Save** button. If you attempt to update or leave the page before saving your changes, a dialog box will appear and prompt you to decide whether you want to save your changes before proceeding.

You can also view and change your selections from the **Compare & Select** page of the EmbryoViewer software.

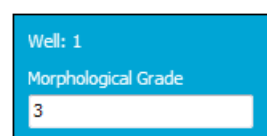
5.2.2 Viewing various focal planes on the Timeline page

If you want to view various focal planes of an image, place the cursor over an image (without clicking the image) and use the scroll wheel on the mouse to change the focal plane. If you have double-clicked on an image to enlarge it, you can also use the up and down arrows on your keyboard for this purpose.



5.2.3 Morphological grade

In the header box above each row of images, you can assign a morphological grade to each embryo based on the information currently available about the embryo. The grade will also be displayed on the **Annotate** and **Compare & Select** pages. If you use the Guided Annotation tool, the grade will only be displayed on the **Annotate** and **Compare & Select** pages if it is part of your annotation strategy.

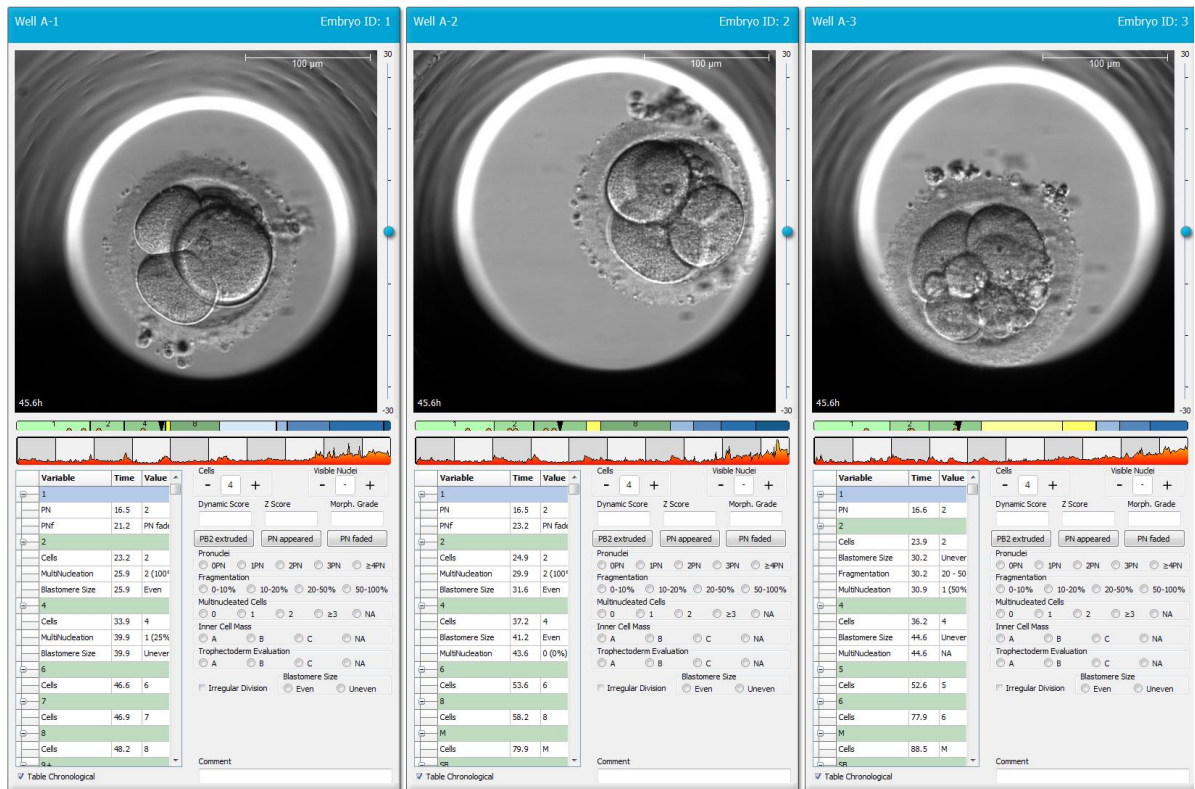
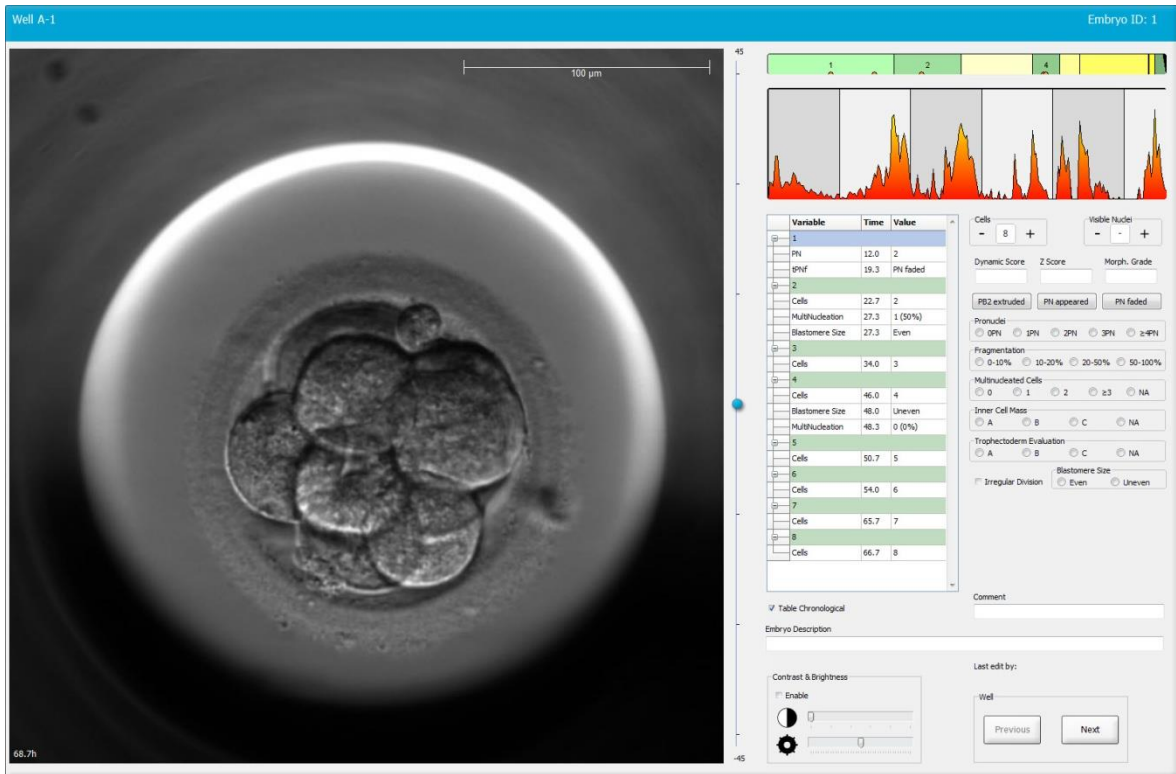


5.3 Annotate page

This section covers annotation without the Guided Annotation tool. If the Guided Annotation tool is installed in your clinic, please refer to the description of the **Annotate** page provided in the separate Guided Annotation user manuals (detailed guidelines and quick guide).

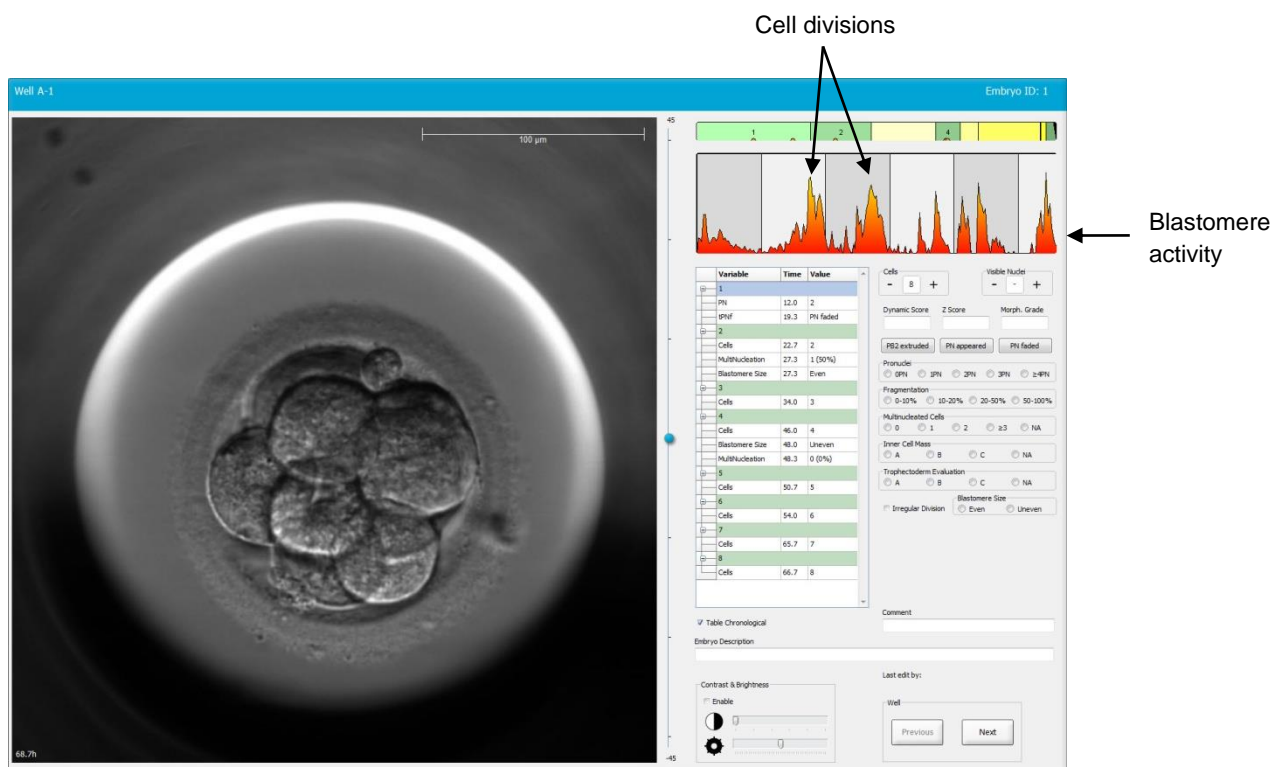
The **Annotate** button becomes active when you have selected 1-3 embryos on the **View Slide** page or the **Timeline** page.

You can also double-click on one of the headers of the embryo timeline to open the **Annotate** page with the chosen embryo. The **Annotate** page lets you perform detailed embryo annotations.



5.3.1 Blastomere activity

The blastomere activity is a numerical value that reflects the difference between two consecutive images in the time-lapse image series. The blastomere activity has NO DIAGNOSTIC USE, but can be used to assist the user in identifying periods in the time series where events of interest may be occurring. Peaks in the blastomere activity often occur when cell divisions take place as the cell divisions lead to movement and thus differences between two consecutive images. An example is given in the following illustration.



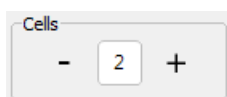
Note that peaks in the blastomere activity may be the result of events other than cell divisions, such as the removal of culture dishes for medium change or embryo biopsy.

5.3.2 Using the annotation table

When you perform an annotation, a value is inserted in the list of annotation variables. The software will automatically insert a time (hours since insemination).

The annotations that can be made in the EmbryoViewer software are described in the following sections.

5.3.3 Annotating cell divisions

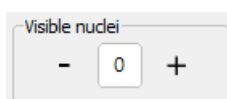


When a cell division has been completed, you can annotate the event by clicking the plus or minus sign in the **Cells** group box. Click until the relevant number of cells is displayed. A black vertical line now appears in the division chart to indicate the time when the cell division occurred.

Alternatively, you can perform the annotation by clicking inside the field that shows the number of cells. This action opens a drop-down list from which you can select one of the following options:

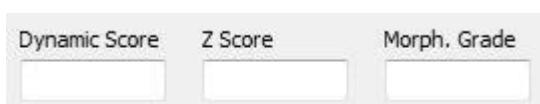
- 1, 2, 3, 4, 5, 6, 7, 8 or 9+ for the number of cells
- SC (start of compaction), M (morula), SB (start of blastulation), B (blastocyst), EB (expanded blastocyst) or HB (hatching blastocyst) for further development or AT for atretic embryos.

5.3.4 Annotating the number of visible nuclei



In the **Visible nuclei** group box, you can annotate the number of nuclei visible in the image. Click the plus or minus sign until the number in the box matches the total number of nuclei visible on the embryo image. In the annotation table, the number of visible nuclei will be listed together with the number of hours post insemination (**Time**) to specify at which embryo development stage the annotation was performed. This lets you register whether or not all of the visible nuclei appeared and disappeared at the same time.

5.3.5 Annotating dynamic score, Z score and morphological grade



In these fields, you can assign a dynamic score, a Z score and a morphological grade to the embryos based on the grading system adopted in your clinic. Note that the clinic alone determines which grading system to use as a basis for annotating grades and scores. The EmbryoViewer software is not delivered with any pre-defined grading system.

- In the **Dynamic Score** field, you can assign an overall score to the embryos. The score is determined on the basis of the available time-lapse information.
- In the **Z Score** field, you can enter a grade for the pattern of the pronuclei and the pattern of the nuclear precursor bodies in the pronuclei.
- In the **Morph. Grade** field, you can enter a grade based on the timeline images.

5.3.6 Annotating appearance and disappearance of pronuclei and extrusion of polar bodies

Three buttons are available to annotate the following dynamic embryo development events:

- **PB2 extruded:** The time when the second polar body was extruded (hours after insemination).
- **PN appeared:** The time when the second pronucleus appeared (hours after insemination).
- **PN faded:** The time when all pronuclei have disappeared (hours after insemination).

When you have annotated one of these events, it will appear in the list of annotations, and the time of the event will automatically be recorded:

	Variable	Time	Value
1	PB2	17.9	PB2 extruded
	PNa	46.9	PN appeared
	PNf	50.3	PN faded

5.3.7 Annotating the number of pronuclei

Pronuclei

☐ 0PN
 ☐ 1PN
 ☒ 2PN
 ☐ 3PN
 ☐ ≥4PN

In the **Pronuclei** group box, you can specify the number of pronuclei present prior to the first cell division, from 0 pronuclei (**0PN**) to four or more pronuclei (**≥4PN**).

5.3.8 Annotating the degree of fragmentation

Fragmentation

☒ 0-10%
 ☐ 10-20%
 ☐ 20-50%
 ☐ 50-100%

In the **Fragmentation** group box, you can specify the relative degree of fragmentation in the embryo.

5.3.9 Annotating multinucleation

Multinucleated Cells

☐ 0
 ☐ 1
 ☐ 2
 ☐ ≥3
 ☐ NA

In the **Multinucleated Cells** group box, you can specify the number of blastomeres in which multinucleation has been observed. Each annotation of multinucleation is associated with the number of hours that has passed since insemination. Multinucleation can be annotated up to ten times for each embryo.

NA (not assessable) means that your observations were inconclusive, i.e. you were unable to clearly identify whether or not multinucleation had formed in some of the blastomeres. However, if you later apply a model in which multinucleation is taken into account, the model will handle the value **NA** as if you were able to conclude that multinucleation does not exist in the blastomeres. In effect, models will thus handle **NA** the same way as 0.

5.3.10 Annotating inner cell mass and trophectoderm evaluation

The variables **Inner Cell Mass** and **Trophectoderm Evaluation** can be annotated as **A**, **B**, **C** or **NA**. For further information on how to annotate the variables, please see the appendix for the KIDScore D5 model (not available in the US). If the KIDScore D5 model is applied, it is very important that these variables are correctly annotated.



The screenshot shows two separate groups of radio buttons. The first group, titled "Inner Cell Mass", contains four radio buttons labeled A, B, C, and NA. The second group, titled "Trophectoderm Evaluation", also contains four radio buttons labeled A, B, C, and NA. In both groups, the "NA" radio button is selected.

5.3.11 Annotating division regularity and blastomere symmetry



The screenshot shows two controls. On the left is a checkbox labeled "Irregular Division". To its right is a group box titled "Blastomere Size" containing two radio buttons: "Even" and "Uneven". The "Uneven" radio button is selected.

Select the **Irregular Division** check box to indicate that the embryo exhibits irregular cell division.

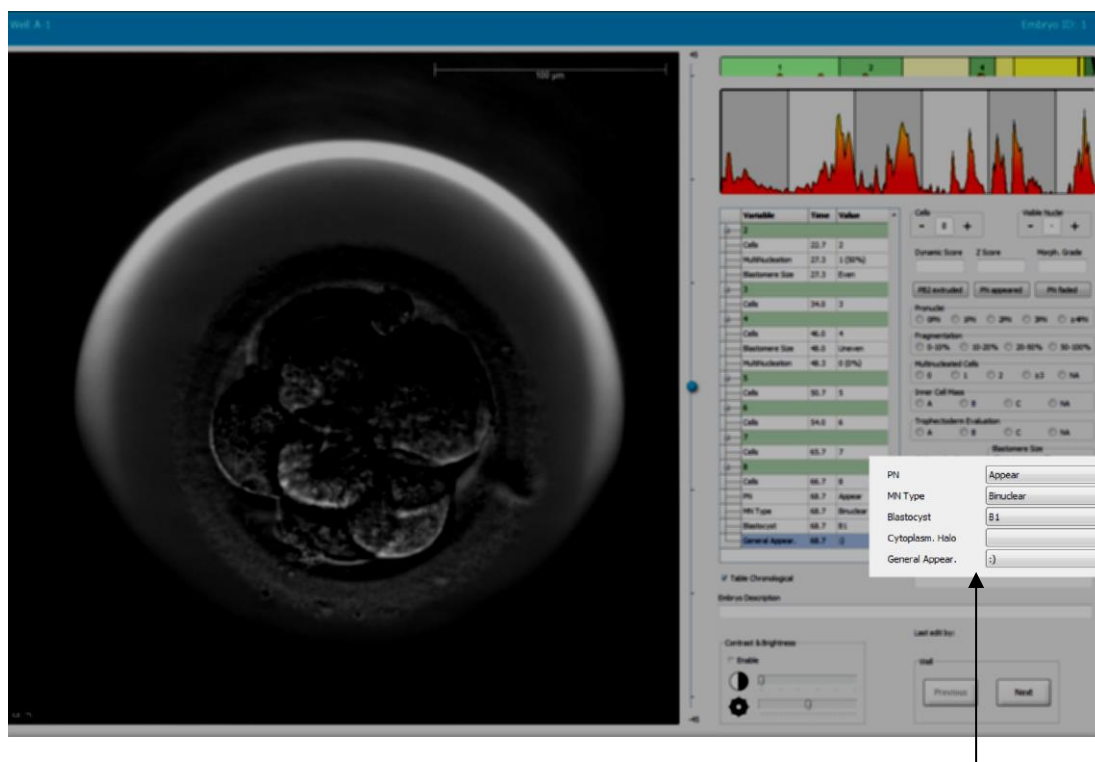
In the **Blastomere Size** group box, you can indicate the spatial symmetry/asymmetry of the blastomeres, e.g. at the 2nd, 4th and 8th blastomere stage. Even or uneven blastomere size can be annotated up to ten times.

5.3.12 User-defined annotation variables

On the **Annotate** page, the user-defined variables specified by the clinic on the **Settings** page are accessible and can be used to annotate embryo observations or patterns. It is possible to create and specify up to five user-defined annotation variables with a maximum of ten different values each. The values that have been defined for a specific variable are listed in the annotation table together with the number of hours since the embryo was inseminated.

The user-defined variables cannot be included in a model on the **Models** tab. It is therefore not possible to use them on the **Compare & Select** page.

The user-defined variables annotated for a specific embryo are saved and can be exported as any other annotation listed in the annotation table. See section 7.3.2 for additional information on how to create user-defined annotation variables.



Values for user-defined annotation variables can be selected from the scroll fields

NOTE

- User-defined annotation variables cannot be included in **Compare & Select** models.

5.3.13 Selecting embryos on the Annotate page



The five embryo selection buttons used to mark embryos to be transferred fresh, frozen, transferred after freezing, avoided or pending decision are also available from the **Annotate** page. See sections 5.1.3 and 5.4 for further information on how to use the embryo selection buttons.

5.3.14 Viewing time-lapse embryo development on the Annotate page




On the **Annotate** page, you can view the embryo time-lapse videos by clicking the play, forward and backward buttons. You can also indicate how fast you want to play the video (**Film speed** drop-down list).

This option is also available from the **Compare & Select** page.

5.3.15 Measuring blastomere size

Follow these steps to estimate e.g. the area of a blastomere or a fragment:

1. Click the ellipse tool button .
2. Click on the image where you want the measurement to start (e.g. on the edge of a blastomere).
3. Press the left mouse button while dragging the ellipse. The estimated area is shown in the list of annotations (see the following illustration).


You may now need to adjust the size and/or position of the ellipse. In this case, click on the ellipse to re-activate it.

4. If necessary, adjust the size of the ellipse to match the blastomere or fragment by clicking the small red squares that encircle the activated ellipse. Then resize by dragging the ellipse.
5. If necessary, rotate the ellipse by clicking one of the red dots that appear on the activated ellipse. Then rotate by dragging the ellipse.

Note that it may be difficult to adjust the ellipse to accurately match e.g. an ovoid blastomere or a blastomere visible from multiple focal planes. An inaccurate match may affect the estimate.

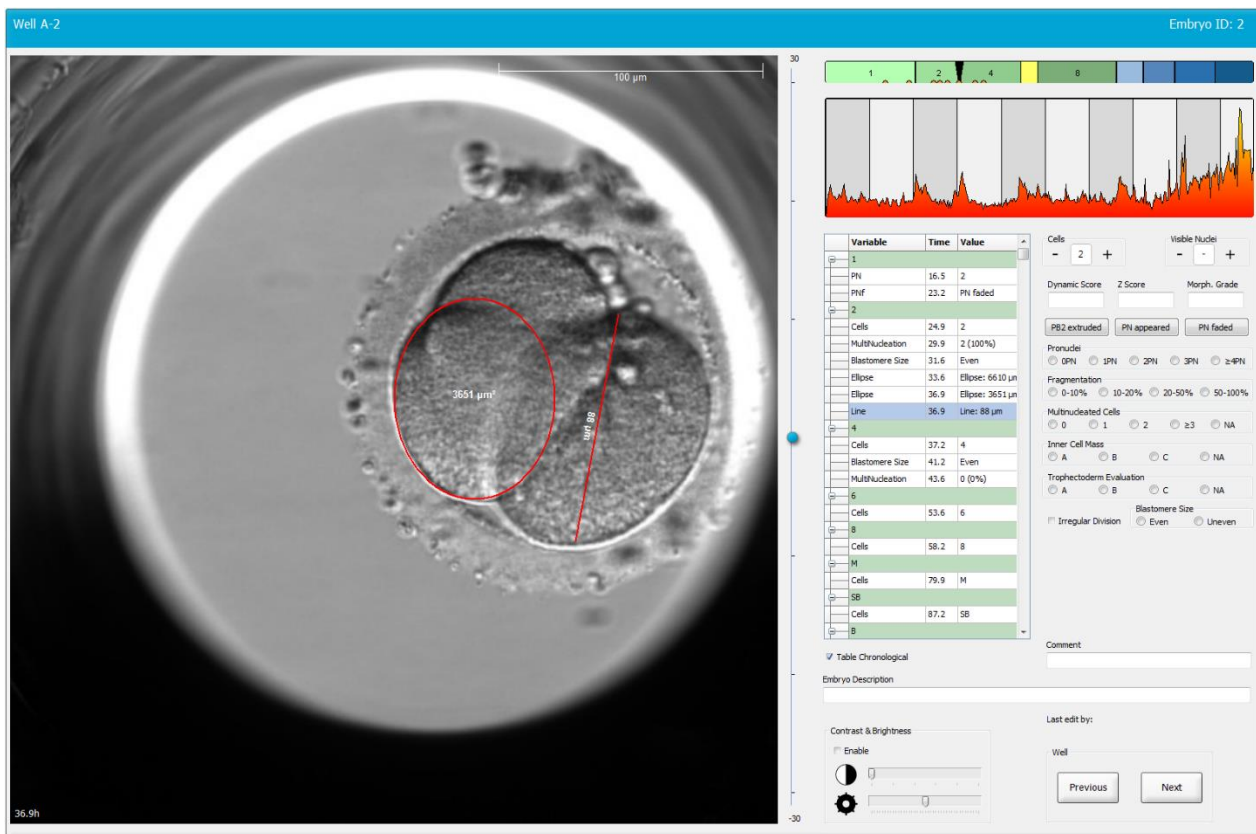
6. Click the **Save** button to save your changes.

Follow these steps to measure the diameter of a blastomere or fragment or the thickness of the zona pellucida:

1. Click the distance tool button .
2. Click on the image where you want the measurement to start.
3. Press the left mouse button while dragging the line. The estimated distance is shown in the list of annotations (see the following illustration).

You may now need to adjust the length and/or position of the line. In this case, re-activate the line by clicking it.


4. If necessary, adjust the length of the line by dragging the small red squares at the end of the activated line.
5. If necessary, move the line by clicking the line itself and dragging it to the desired position.

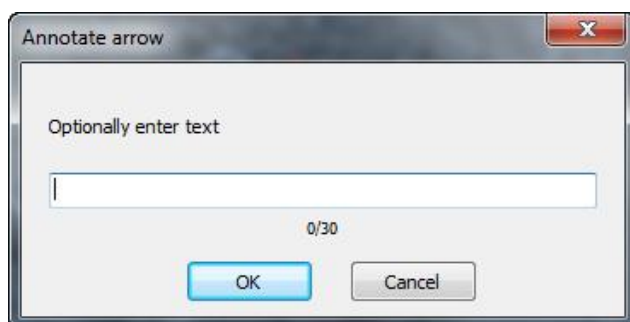


- Click the **Save** button to save your changes.

5.3.16 Indicating important visible characteristics of the embryo

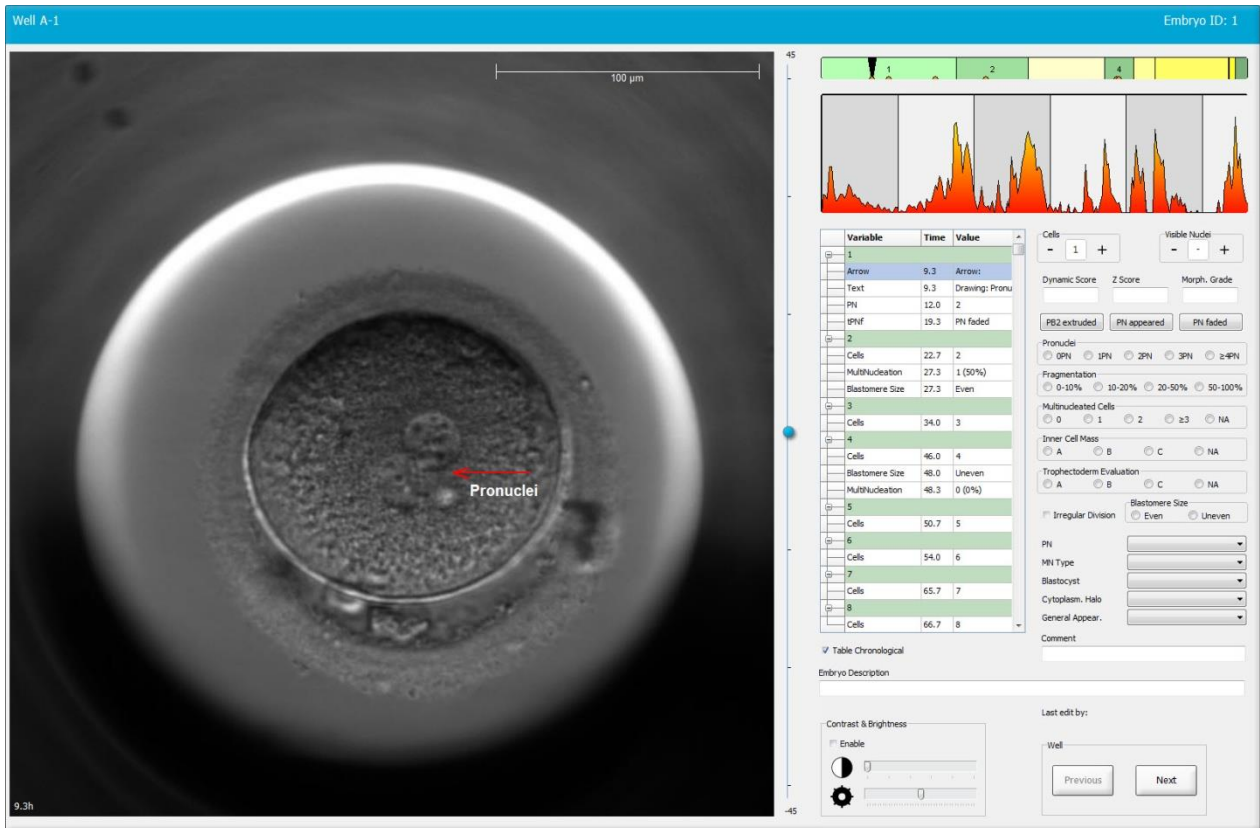
You can draw an arrow on the embryo image to indicate the presence of important embryo characteristics. To do this:

- Click the arrow tool button .
- Click on the image where you want the arrow to start, and drag while holding the left mouse button to indicate the size of your arrow.
- In the **Annotate arrow** dialog box, optionally enter a text to be displayed with your arrow and click **OK**:



You may now need to adjust the size and/or position of the line. In this case, re-activate the line by clicking it.


- If necessary, adjust the arrow to the desired size by dragging the small red squares that encircle the arrow.
- If necessary, have the arrow point to the correct part of the image by clicking on the arrow itself and dragging it to the desired location.

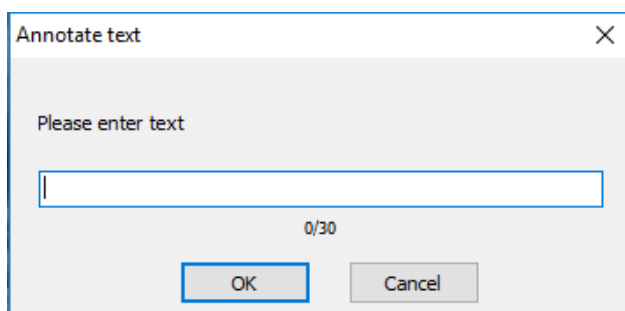


- Click the **Save** button to save your changes.

5.3.17 Adding text to an embryo image

Follow these steps to add a text box to an embryo image:

- Click the text tool button .
- Click on the image where you want to insert your text box, and drag the text box to the desired size while holding the left mouse button.
- Enter your text (up to 30 characters) in the **Annotate text** dialogue box, and click **OK**:



4. You may now need to adjust the size and/or position of the text box:

- Adjust the size of the text box by dragging the small red squares at the corners.
- Rotate the text box by clicking the red dot on the edge of it and turning it while holding the left mouse button.
- Move the text box by clicking inside of it and dragging it the desired position while holding the left mouse button.

5.3.18 Saving your changes

Before leaving the **Annotate** page, click the **Save** button to save all annotations. If you attempt to update or leave the **Annotate** page before saving your changes, a dialog box will prompt you to save before proceeding.

5.4 Compare & Select page

When you have completed the annotation of a patient's embryos on the **Annotate** page, you can click the **Compare & Select** button in the navigation panel to go directly to the **Compare & Select** page. On this page, you can evaluate the embryos before you decide which embryos to transfer, freeze or avoid. The **Compare & Select** button will also become active when you have selected a patient with a treatment and a culture dish either from the **View Running** page, from the **View All Patients** page or from the **View All Slides** page.

On the **Compare & Select** page, you can apply a user-defined model to the embryos in a culture dish. The models applied to the embryos on the **Compare & Select** page are defined or imported on the **Models** tab available from the **Settings** menu (see section 7.4).

When you create a model, you can include several variables. These are the variables you want the model to take into account when calculating a score for the embryo. For the purpose of comparing the embryos, the variables thus represent the requirements that you want the embryos to fulfill.

The model will calculate a score for each embryo indicating how well the development pattern of each embryo satisfies these requirements. The embryos given the highest score will be the ones that best meet the requirements of the applied model. The score will be calculated based on your annotations (see section 5.3) as well as the weight given to each variable in the model.

For further information on how to design models, see section 7.4.7.

NOTE
<ul style="list-style-type: none">• Even though the embryos given the highest score are the ones that best meet the requirements defined in the model, this does not necessarily imply that these are the embryos best suitable for transfer. This decision must always be made by the user after an assessment of the quality of all relevant embryos.

5.4.1 User rights on the Compare & Select page

Only users with the **Administrator** or **Editor** role will be allowed to save the scores calculated by applying a model on the **Compare & Select** page.

See section 7.2.2 for further information on user roles and rights.

5.4.2 Compare & Select table

The **Compare & Select** page opens with a table, which will be empty until you have chosen a model. You can choose an active model from the drop-down list in the upper right corner of the page. When you have chosen a model, the variables included in this model will automatically be filled into the **Compare & Select** table.






The screenshot shows the 'Compare & Select' interface. A large table on the left contains columns for 'Well', 'Dec.', 'Current score', and several data columns. The first column of the table lists wells from AA-1 to AA-12. Annotations with arrows point to specific elements:

- Last annotated cell stage**: Points to the 'Last stage' column header.
- Morphological grade**: Points to the 'Morph. grade' column header.
- Last acquired time-lapse image**: Points to the 'Last image' column header.
- Last saved score**: Points to the 'Saved score' column header.
- Model selection drop-down list**: Points to the 'Current Model' dropdown menu on the right.
- View all of this patient's embryos from all treatments**: Points to the 'View All Patient Embryos' checkbox.
- Information about the transfer date of the selected embryo**: Points to the 'Transfer Date' field showing '2018-06-07'.

The right-hand panel includes sections for 'Current Model' (with a dropdown), 'Saved Model' (with a 'Save Score' button and 'No saved model' text), and 'Transfer Info' (with a 'Save Info' button and a date field).

5.4.2.1 Fixed columns in the Compare & Select table

The **Compare & Select** table contains both fixed and flexible content columns. You will find these seven fixed columns in the table:

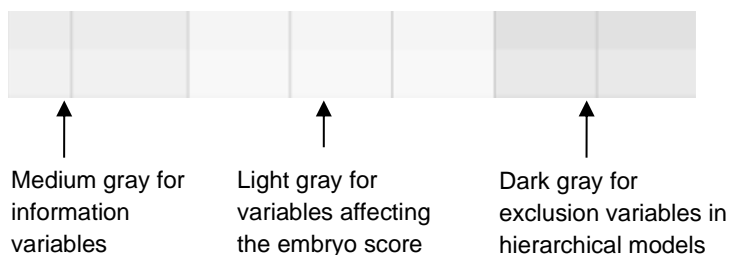
- **Well:** Displays the well ID. The number will be displayed with a gray background color if no images are acquired from the well. If you click on a well ID, the background color of the well ID changes to light blue. You can open the **Annotate** page with a specific well loaded by double-clicking on the well ID. Alternatively, if you want to annotate more wells, click on the desired well IDs and then click the **Annotate** button (this feature is not available if you use the Guided Annotation tool).
- **Dec.:** Displays the current decision made for the embryos, i.e. transfer fresh , freeze , transfer after freezing , avoid  or pending decision . You can change the decision by using the selection tool after you have chosen the relevant embryo from the **Compare & Select** table.
- **Current score:** Displays how the embryo is currently scored by the chosen model. The score returned by the model (either a number or a letter) will appear as **NA** (not available) if some or all of the variables included in the model have not yet been annotated for the embryo. If no model has been chosen, this column will be empty.
- **Last stage:** Displays at which cell stage the last annotation was made, e.g. B (blastocyst) or HB (hatching blastocyst).
- **Morph. grade:** Displays the morphological grade entered on the **Timeline** or **Annotate** page (see sections 5.2.3 and 5.3.5).
- **Last image:** Contains an icon that links to the latest time-lapse image of the embryo. If you click on the icon, a magnified version of the latest image of the embryo is displayed. In the magnified image, you can use the scroll wheel on your mouse or the up and down arrows on your keyboard to change image focal planes.
- **Saved score:** Displays the last saved score of the embryo, if any. The score (either a number or a letter) will appear as **NA** (not available) if some or all of the variables included in the model had not yet been annotated for the embryo when the model was applied.

5.4.2.2 Variable columns in the Compare & Select table

In addition to the fixed content columns, the **Compare & Select** table contains a number of flexible content columns. These columns contain information about the specific variables included in the currently chosen model. These variables will vary from one model to the other.

You can include a maximum of ten variables in each model. Each variable will be listed in a separate column.

Columns displaying variables used for calculating the score of the embryos have a light gray color whereas variables that are strictly informational have a medium gray color. Exclusion variables (used only in hierarchical models) are displayed in a dark gray color.



The timing variables used in the model will be displayed in green or red color: 54.5 45.5. The green color indicates that the embryo is within the time range specified for the model. The red color indicates that the embryo is outside the time range specified for the model.

When the variable has a positive weight, the green color indicates that the embryo is within the time range specified for the model. The red color indicates that the embryo is outside the time range specified for the model.

When the variable has a negative weight, the colors are reversed: The green color indicates that the embryo is outside the time range specified for the model, and the red color indicates that the embryo is within the time range specified for the model.

The following illustration shows how the colors are used on the **Compare & Select** page:

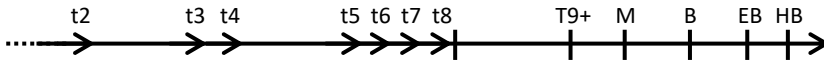
Well	Dec.	Current score	t2	t2
1		NA	?	?
2		0	43.9	43.9
3		NA	?	?
4		NA	?	?
5		NA	?	?
6	✓	NA	?	?
7		NA	?	?
8		NA	?	?
9		NA	?	?
10		NA	?	?
11		NA	?	?
12		NA	?	?
Min			10.0	10.0
Max			20.0	20.0
Weight			1	-1

A question mark indicates that a variable included in the model has not yet been annotated for this particular embryo. In this case, the model score for the embryo will always be **NA** (not available) if the variable has been given a weight (used only in additive and multiplicative models). If the

variable has been given a weight of 0 in an additive model or a weight of 1 in a multiplicative model, the score will not be affected.

5.4.2.3 Missing or coinciding timing variables

The normal development pattern of an embryo is illustrated in the following figure (see section 7.4.3 for a description of the variables):



If any timing variables up to t8 have not been annotated or coincide when the model is applied, this will be handled as follows by the EmbryoViewer software:

- If, for example, t3 and t4 coincide (i.e. the embryo divides directly from two to four cells), no explicit annotation will exist for t3. The model will then assume that $t3 = t4$, which will be correct in this particular case.
- If, for example, *only* t8 is annotated, the model will return an incorrect score because the model will assume that $t2 = t3 = t4 = t5 = t6 = t7 = t8$.

Annotations ranging from t9+ to HB will only be taken into account by the model if explicit annotations exist for such observations.

5.4.2.4 Logical variables

For logical variables, i.e. variables with only two possible values (e.g. present or not present), a green dot (●) indicates that the requirement is met, a red triangle (▲) indicates that the requirement is not met, and a question mark indicates that the variable has not yet been annotated. If you use the Guided Annotation tool, user-defined comments can be included in models as information variables. In this case, the name of the user-defined comment will be listed at the top of the column, and a white square (□) will be shown to indicate that this comment is true (i.e. has been annotated) for a specific embryo.

If an embryo has been marked to be avoided, the green, red and white icons will turn grey as shown for well AA-6 below.

Well	Dec.	Current score	UNEVEN2	Frag-2	MN-2 Cells	Coll. Count	Vacuoles							Last stage	Morph. grade	Last image	Saved score
AA-1		NA	●	5.0	0.0	?	□							B			
AA-2		NA	●	10.0	0.0	?								B			
AA-3		NA	●	10.0	NA	?								B			
AA-4		NA	●	10.0	NA	?								B			
AA-5	✗	NA	?	?	?	?							-				
AA-6	✗	NA	?	?	?	?	□						-				
AA-7		NA	●	20.0	0.0	?								B			
AA-8		NA	▲	5.0	2.0	?								B			
		Min															
		Max															
		Weight															

5.4.2.5 Embryos with the highest score in the model

Below the table on the **Compare & Select** page, images of the first four embryos that have obtained the highest score in the model can be found. The embryo with the highest score is displayed first, the embryo with the second highest score is displayed second, etc.

This does not imply that the embryos that are left out are unsuitable for transfer, nor that the embryos displayed are the ones best suited for transfer. All embryos must be assessed by the user before a decision is made to either transfer, freeze or avoid a given embryo.

If you have applied a model that contains only information variables, no embryos are displayed. In this case, you must actively select the embryos in the **Well** column to display them.

5.4.2.6 Applying a model to a culture dish

Follow these steps to apply a model to the embryos:

1. On the **Annotate** page, ensure that the variables included in the chosen model have been annotated.
2. In the navigation panel, click the **Compare & Select** button.
3. On the **Compare & Select** page, choose the desired model from the **Current Model** drop-down list.

The **Compare & Select** table is now populated with the variables from the chosen model.

The embryo scores are displayed in the **Current score** column.

4. In the **Saved Model** group box, click the **Save Score** button. Note that saving a new score overwrites a possible pre-existing score for the embryos in the current culture dish.

After scoring the embryos, you can decide which embryos to transfer, freeze, avoid or mark for later decision. During this procedure, you may decide either to take the saved score into consideration or to disregard it. Click the **Save** button at the bottom of the page if you want to save your new selection.

5.4.2.7 Viewing embryos side by side

Before making a decision for the embryos, you may view up to six embryos side by side in order to compare their characteristics:

Score assigned by the currently active model

Embryo details: Selected parameters, e.g. presence of multinucleation, score assigned by the model of your choice, etc.

Selection of side-by-side view

Annotation comments

A maximum of four different embryo details can be displayed. The clinic can freely choose which details to display, e.g. the presence of multinucleation, fragmentation, the score assigned by a model, etc. The embryo details are set up locally on each EmbryoViewer client from the **Embryo Details** tab (see section 7.6).

The comments displayed above the embryo details are the comments entered on the **Annotate** page.

To display embryos side by side:

1. Go to the **Compare & Select** page.
2. Select up to six embryos by clicking their well IDs.
3. Select the **Side-by-Side View** radio button at the bottom of the page:



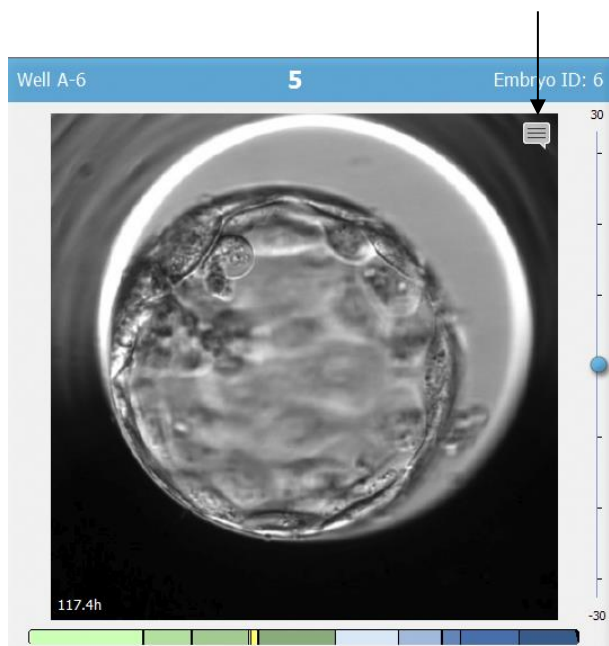
The selected embryos will now be displayed next to each other.

4. *Optional step:* If you only want to display the annotation comments and *not* the embryo details, deselect the **Embryo Details** check box:



Once you have removed the embryo details, you will be able to see more embryos at the same time. You can still access the annotation comments by clicking the comments icon in the top right corner of the image:

Click this icon to see the annotation comments

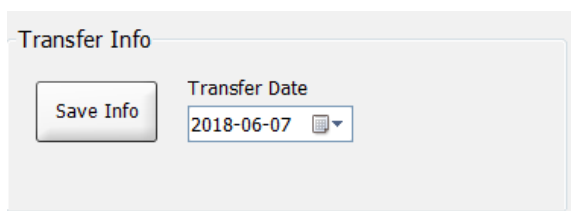


5. *Optional step*: Use the decision buttons to indicate which embryo to transfer fresh, freeze, transfer after freezing or avoid.
6. Select the **Model View** radio button to return to the **Compare & Select** table.

5.4.3 Selecting fresh embryos and registering the outcome of embryos transferred on a specific date

To register the outcome of one or more embryos transferred on the same date, follow the below procedure:

1. Annotate all embryos in a treatment on the **Annotate** page.
2. Go to the **Compare & Select** page.
3. If desired, apply a model to the embryos.
4. Select the embryo(s) you want to transfer to the patient. Use the embryo selection buttons for this purpose.
5. In the **Transfer Info** group box, enter the date when the embryo will be transferred to the patient and click **Save Info**:



The screenshot shows a software interface titled "Transfer Info". Inside this box, there is a "Save Info" button on the left. To the right of the button is a "Transfer Date" label above a date input field. The input field contains the text "2018-06-07" and a small calendar icon to its right.

NOTE

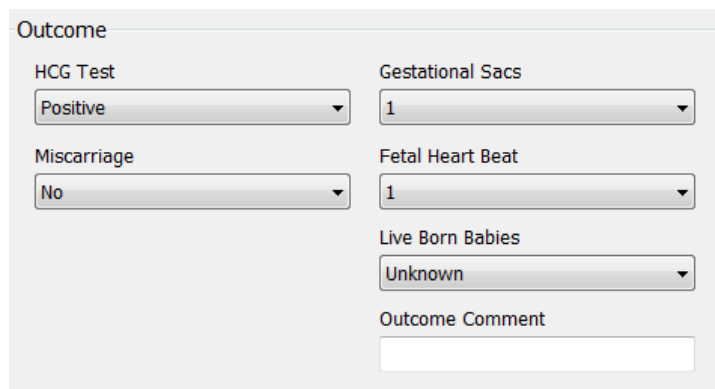
- Once you have clicked **Save Info**, it is no longer possible to revert your choice.

6. Using the embryo selection buttons, make your choice for the remaining embryos (avoid or freeze).

It is important to indicate your choice for *all* of the embryos. This will ensure the quality of your data and enable you to verify the fate of each embryo at a later time. We therefore recommend this as a standard procedure.

7. To register the outcome of the transferred embryos when a pregnancy test has been performed, go to the **Patient Details** page and select the **Transfer** tab.

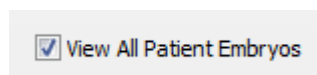
8. In the **Outcome** group box, register the result of the transfer:



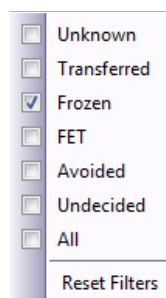
The screenshot shows a form titled "Outcome" with several dropdown menus and a text input field. The fields are arranged in two columns. The left column contains "HCG Test" (set to "Positive"), "Miscarriage" (set to "No"), and "Live Born Babies" (set to "Unknown"). The right column contains "Gestational Sacs" (set to "1") and "Fetal Heart Beat" (set to "1"). Below these is an "Outcome Comment" text input field.

5.4.4 Transferring a thawed embryo from an existing treatment without culturing the embryo further


1. On the **Patient Details** page, select the desired patient.
2. Go to the **Compare & Select** page.
3. Select the **View All Patient Embryos** check box to display all of the patient's embryos from all treatments.



4. In the header named **Dec.**, filter the embryos by selecting **Frozen**. Only frozen embryos will now be displayed on the page.



5. If desired, apply a model to the embryos.

6. Use the embryo selection button  to select which thawed embryo(s) you want to transfer to the patient:

Well	Dec.	Current score	NOT2PN	t2	t3	t4	t5	tB	ICM	TE	Last stage	Morph. grade	Last image	Saved score
AA-1		3.8	●	26.6	37.9	38.0	51.8	118.9	B	C				
AA-2		9.1	●	23.3	33.0	35.3	45.1	96.3	A	A				
AA-3		3.1	●	21.7	31.4	41.2	41.7	110.7	C	C				
AA-4	✗	NA	?	?	?	?	?	?	?	?				
AA-5	✖	8.4	●	26.0	36.6	37.2	48.9	102.4	A	A				
AA-6	✗	NA	?	?	?	?	?	?	?	?				
AA-7	✗	NA	?	?	?	?	?	?	?	?				
AA-8	✗	NA	?	?	?	?	?	?	?	?				
AA-9	✗	NA	?	?	?	?	?	?	?	?				
AA-10		4.9	●	28.4	40.0	40.4	52.8	106.9	B	C				
AA-11		6.7	●	25.2	37.2	37.9	54.5	101.6	B	B				
AA-12		3	●	28.2	29.0	38.0	38.5	109.6	C	B				

Current Model

KIDScoreD5 v3

Created 2018-11-01 by Vitrolife

Saved Model

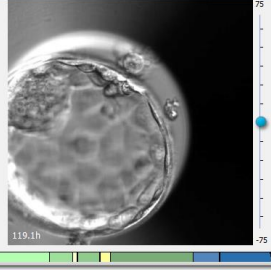
Save Score No saved model

Transfer Info

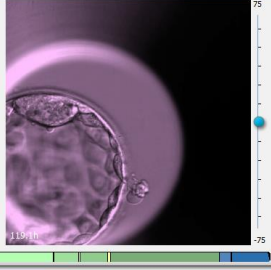
Save Info Transfer Date 2019-04-29

☐ View All Patient Embryos

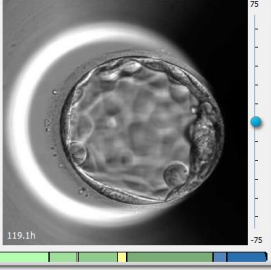
Well AA-2 9.1 Embryo ID: AA2



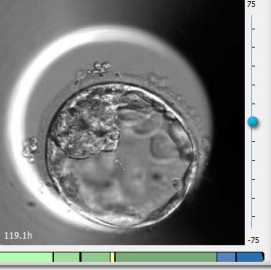
Well AA-5 8.4 Embryo ID: AA5



Well AA-11 6.7 Embryo ID: AA11



Well AA-10 4.9 Embryo ID: AA10



Compare & Select View


☒ Model View

☐ Side-by-Side View

Film Speed

Normal

Save



Frozen embryo selected for transfer

7. Click **Save Info**.
8. To register the outcome of the transferred embryo(s) when a pregnancy test has been performed, go to the **Patient Details** page and select the **Transfer** tab:

Treatment
Transfer

All Transfers

2018-04-01, Fresh Transfer

2018-04-01, Cryo Transfer

Delete Transfer

Transfer Details

Transfer Date 2018-05-01

Transfer Type Cryo Transfer

Embryos from Other Sources

Transfer Comment

FET Stimulation

Medication Protocol Natural / Unstimulated

Stimulation Comment

Transfer Media

Transfer Media EmbryoGlue

Transfer Media Comment

Outcome

HCG Test Positive

Miscarriage

Gestational Sacs 1

Fetal Heart Beat 1

Live Born Babies Unknown

Outcome Comment

Treatment ID	Slide ID	Well	Embryo ID	Decision
Unknown	D2000.01.01_51002_1000	9	AA5	FET

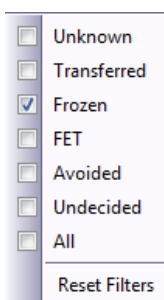
5.4.5 Continuing culturing thawed embryos and selecting one or more embryos for transfer

Follow this procedure if you want to continue culturing thawed embryos before selecting an embryo for transfer:

1. On the **Patient Details** page, select the relevant patient.
2. Go to the **Compare & Select** page.
3. Select **View All Patient Embryos** to display all of the patient's embryos from all treatments.



4. In the header named **Dec.**, filter the embryos by selecting **Frozen**. Only frozen embryos will now be displayed on the page.



5. If desired, apply a model to the embryos.
6. Determine which embryos to thaw. To ensure data integrity, do not use the embryo selection buttons for this purpose. Instead, manually register in which wells the embryos reside in the new culture dish. Then thaw the embryos.
7. On the **Patient Details** page, create a new treatment to continue culturing the embryos.
8. Insert the culture dish into the EmbryoScope or CulturePro incubator and start the cultivation.
9. Go to the **Compare & Select** page. Use the embryo selection buttons to indicate which embryo(s) to transfer.
10. Go to the **Annotate** page. On the last image of the thawed embryo, insert a comment that this embryo has been thawed and further cultured. Also, note in which culture dish and well ID the embryo has been further cultured.

Alternatively, enter the frozen transfer date on the original culture dish and comment that the embryo has been further cultured and in which treatment and culture dish ID.

This procedure will ensure that the embryo is only marked as transferred in one treatment.

5.5 Report page

From the **Report** page, you can generate reports based on the information obtained from both the EmbryoScope incubator and the EmbryoViewer software. The reports can be either saved as a PDF file or printed directly from the **Report** page.

You can open the **Report** page by clicking the **Report** button in the navigation panel. When you click the button, the EmbryoViewer software automatically generates a patient treatment report based on the data from the selected culture dish.

Running

View Running

Patients

Patient Name
Anna Hansson

Patient ID
013

View All Patients

Patient Details

Slides

Treatment ID
2172-2020

Slide ID
AA-D2000.01.01.S10013.0000.P

View Slide

Timeline

Annotate

Compare & Select

Report

Video

Incubation

Database

View All Slides

Instrument

User: ADMIN

Logout

Settings

2021-07-20 12:11

Patient Information - Patient Treatment Report

Patient Name Anna Hansson

Patient ID 013

Slide ID D2000.01.01.S10013.0000.P

2021-07-20

Embryo Summary

Procedure	Number
Embryos Transferred	1
Embryos Frozen	8

First Embryo for Transfer

20 hrs 32 hrs 44 hrs Last

Second Embryo for Transfer

Frozen last image

1 of 4

Display of images of transferred embryos

Time 1 20.0 hours

Time 2 32.0 hours

Time 3 44.0 hours

Time last Last hours

Display of images of frozen embryos

Time Last hours

Report types:

PatientReport

Generate

Print

Save as PDF

Generate report

Report type selection drop-down box

The patient treatment report consists of four pages:

- Page 1 – **Patient Information** – contains:
 - Metadata from the chosen culture dish.
 - A specification of the how many embryos have been selected for transfer and freezing.
 - Four images of each of the first two embryos selected for transfer. Images 1-3 are from the time intervals specified in the boxes under **Display of images of transferred embryos**. Image 4 is the last recorded image of the embryos. The lower part of the page displays the last image of the first three embryos selected for freezing. The images of frozen embryos are from the point in time entered under

Display of images of frozen embryos. If you do not enter any specific time, the software will display the last image taken of the frozen embryos.

- Page 2 – **Laboratory Data** – contains:
 - The last image of the embryos selected for transfer and freezing and a specification of their position in the culture dish.
- Page 3 – **Laboratory Data** – contains:
 - The results of performed annotations.
 - Fields for adding signatures and date and time of selection.
- Page 4 – **Instrument Data** – contains:
 - Information on the running conditions of the EmbryoScope incubator during the incubation of the culture dish.

5.5.1 Generating a patient treatment report

Follow these steps to generate a patient treatment report:

1. From the navigation panel, select a patient, a treatment and a culture dish.
2. Click the **Report** button.

The EmbryoViewer software will now generate a report for the chosen culture dish.
3. Specify the three time intervals under **Display of images of transferred embryos**.

This indicates from which time intervals the images of transfer embryos will be taken. The images will appear on the second page of the report.
4. Click the **Generate** button.

This updates the report with the selected time intervals.

5.5.2 Generating an annotation and evaluation report

Follow these steps to generate an annotation and evaluation report:

1. From the navigation panel, choose an annotated culture dish to which a model has been applied on the **Compare & Select** page.
2. In the navigation panel, click the **Report** button.

A report is now generated.
3. On the **Report** page, select **AnnotationAndEvaluationReport** from the **Report types** drop-down list.
4. On the **Report** page, click the **Generate** button.

A report based on the parameters from the model is now generated.

5.5.3 Printing a report

Follow these steps to print the report:

1. Generate the report as specified in section 5.5.1 or 5.5.2.
2. On the **Report** page, click the **Print** button.

5.6 Video page

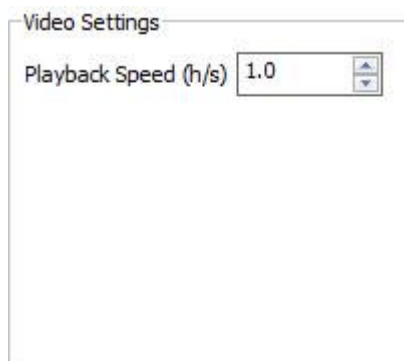
The **Video** button becomes active when you have selected 1-12 embryos from either the **View Slide** page or the **Timeline** page.



5.6.1 Generating a video of the embryos

Follow these steps to generate a video of the embryo development:

1. In the navigation panel, click the **Video** button to open the **Video** page.
2. Specify the desired parameters for your video:
 - a. From the **Video Settings** group box, you can specify the playback speed of the video (hours per second).



The screenshot shows a dialog box titled "Video Settings". Inside, there is a label "Playback Speed (h/s)" followed by a text input field containing the value "1.0". To the right of the input field is a small vertical spinner control with up and down arrows.

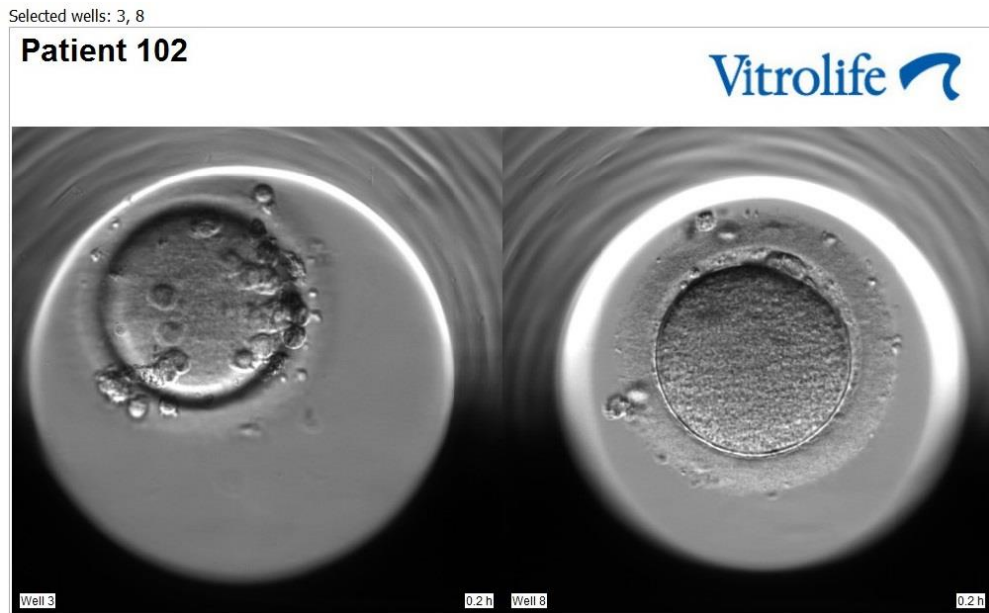
The higher the number you enter, the faster the video will be played.

- b. In the **Video Header** group box, you can insert your own clinic logo. Click the **Select Logo File** button and select a logo file from Windows Explorer. The file must be in JPG format. To have the logo displayed as a header on your video, make sure to select the **Display Logo** check box.



The screenshot shows a dialog box titled "Video Header". It contains several controls: a "Display Header" checkbox (unchecked), a "Height of Header (pixels)" label with a text input field containing "100" and a vertical spinner, a "Label" text input field, a "Select Logo File" button, and a "Display Logo" checkbox (checked). To the right of these controls is a large rectangular preview area showing the "Vitrolife" logo in blue text with a stylized blue swirl icon to its right.

- c. You can also adjust the height of the header in pixels and insert a label next to your logo. **Label** is a free text field where you may enter both letters and numbers. You may need to adjust the height of the header to display both the logo and the label correctly:



3. In the **Generate** group box, indicate at which point in time you want the video to start (hours after fertilization) and end.

Generate

Start Time (h) 5.4

End Time (h) 67.7

Generate Video ☒

Generate Images ☐

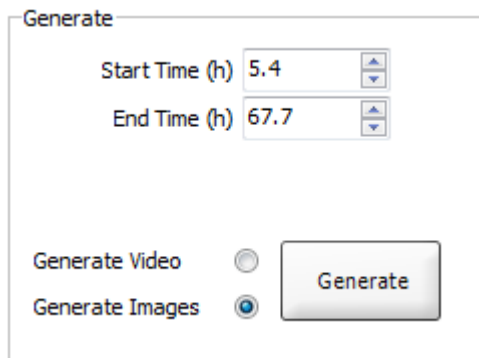
Generate

4. Select the **Generate Video** radio button to indicate that you intend to create a new video.
5. Click **Generate** to create the video.
Windows Explorer opens.
6. Specify a name and location for the file you are about to create, and click **Save**.
You can play the video by double-clicking it in Windows Explorer.

5.6.2 Generating images of the embryos

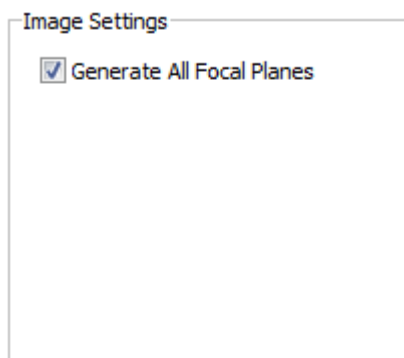
Follow these steps to generate images of the embryos:

1. In the navigation panel, click the **Video** button to open the **Video** page.
2. In the **Generate** group box, select the **Generate Images** radio button to indicate that you intend to create new images:



The 'Generate' dialog box contains two time input fields: 'Start Time (h)' with a value of 5.4 and 'End Time (h)' with a value of 67.7. Below these fields are two radio buttons: 'Generate Video' (unselected) and 'Generate Images' (selected). To the right of the radio buttons is a 'Generate' button.

3. In the **Image Settings** group box, select the **Generate All Focal Planes** check box if you want to create images from all focal planes of the selected embryo:



The 'Image Settings' dialog box contains a single checked checkbox labeled 'Generate All Focal Planes'.

4. Click the **Generate** button to create the images. Images of the selected embryo will now be created in JPG format. Windows Explorer will automatically open.
5. Specify a name for your file and the location where you want to save the images on your computer.

5.7 Incubation page

You can check the running conditions of each EmbryoScope or CulturePro incubator installed in your clinic. You may want to inspect the conditions either during a run or as a final quality check (QC).

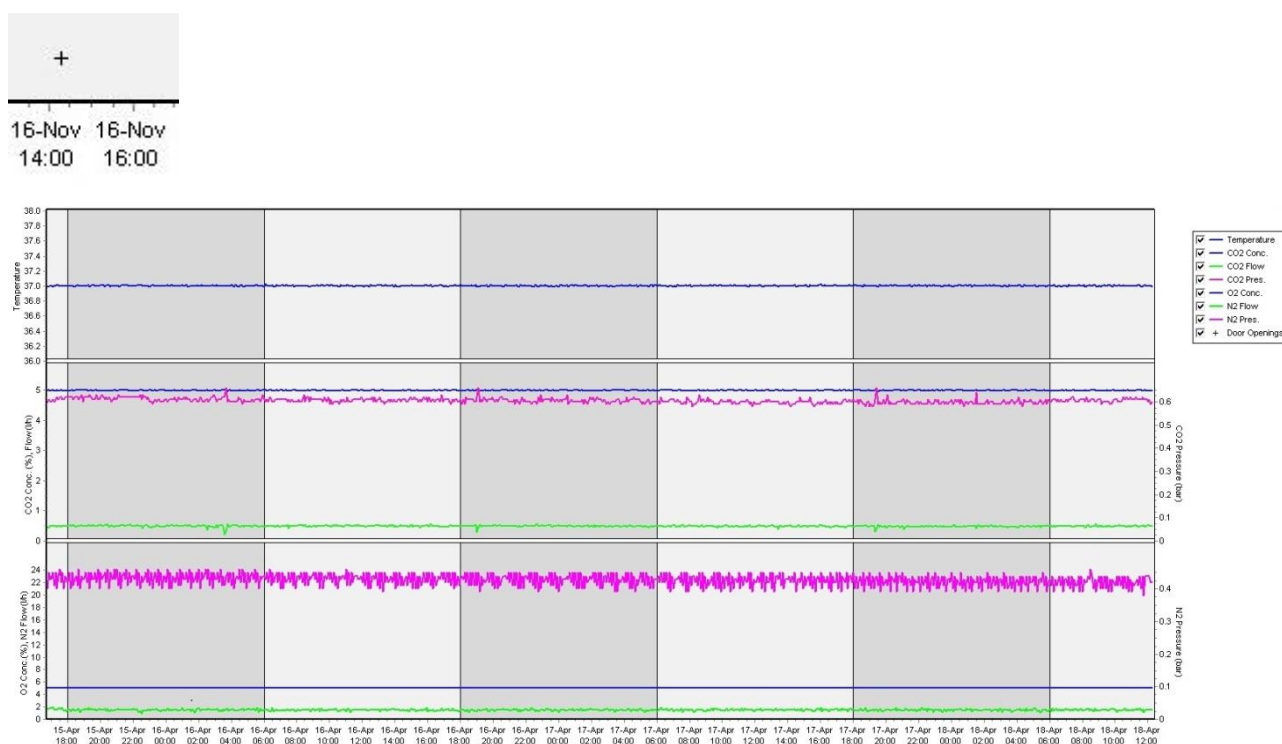
From the **Slides** menu of the navigation panel, click the **Incubation** button.

Alternatively, click the **Instrument** button in the navigation panel. Then double-click on the desired culture dish in the instrument overview table.

This will display a graphical representation of the running conditions of a given culture dish.

The running conditions for CO₂ and O₂ will only be represented if you have set up the EmbryoScope or CulturePro incubator to run with CO₂ and O₂ regulation. The graphs will always show the running conditions for temperature and gas.

Door openings are indicated by a black cross on the graph (bottom of the image):



Top graph: Displays the incubation temperature (blue).

Middle graph: Displays the CO₂ concentration (blue), the CO₂ flow (green) and the CO₂ pressure (pink).

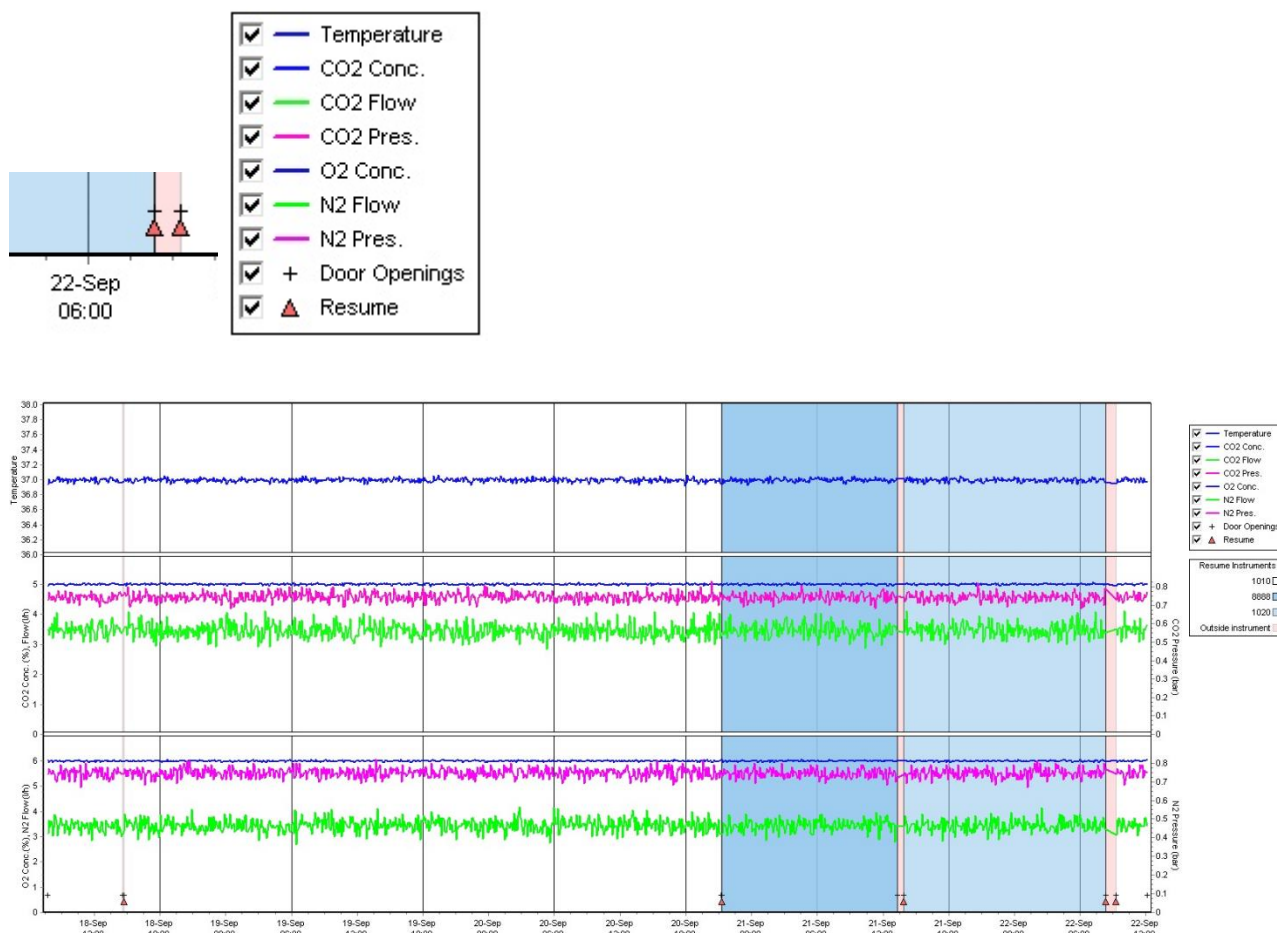
Bottom graph: Displays the O₂ concentration (blue), the N₂ flow (green) and the N₂ pressure (pink).

For all graphs, you can include or exclude parameters shown by selecting or deselecting the appropriate check box:

<input checked="" type="checkbox"/>	Temperature
<input checked="" type="checkbox"/>	CO2 Conc.
<input checked="" type="checkbox"/>	CO2 Flow
<input checked="" type="checkbox"/>	CO2 Pres.
<input checked="" type="checkbox"/>	O2 Conc.
<input checked="" type="checkbox"/>	N2 Flow
<input checked="" type="checkbox"/>	N2 Pres.
<input checked="" type="checkbox"/>	+ Door Openings

The axes on the graph will automatically rescale according to the chosen parameters.

If culture in the selected culture dish has been resumed in the same or another compatible incubator, this is indicated by different background colors. White and blue colors indicate periods of incubation in different incubators, and the pink color indicates periods during which the culture dish was not inserted in an incubator. Resumed culture will be indicated by a red triangle below the door opening symbol if you select it in the parameter box.



The instrument numbers represented by the blue and white colors are displayed in the box on the right, which is only visible if culture in the selected culture dish has been resumed.

Resume Instruments	
1010	<input type="checkbox"/>
8888	<input checked="" type="checkbox"/>
1020	<input type="checkbox"/>
Outside instrument	<input type="checkbox"/>

5.7.1 Summary tab

Click the **Summary** tab to display the running conditions for the incubation temperature and gas concentrations (set point, average, minimum, maximum and standard deviation).

Summary	Alarms	Warnings	Log	Other		
Variable	Unit	Average	Min	Max	StdDev	Set-Point
Temperature	C	37.00	36.98	37.02	0.008	37.0
CO2 Concentration	%	5.98	5.89	6.04	0.018	6.0
CO2 Flow	l/h	0.47	0.11	0.86	0.066	0.0
CO2 Pressure	bar	0.52	0.48	0.54	0.012	0.0
O2 Concentration	%	5.00	4.97	5.22	0.007	5.0
N2 Flow	l/h	2.90	2.04	11.43	0.259	0.0
N2 Pressure	bar	0.49	0.47	0.53	0.012	0.0

5.7.2 Alarms tab

Click the **Alarms** tab to display information about incubator alarms, e.g. deviations of the incubation temperature and gas concentrations from their set points.

Summary	Alarms	Warnings	Log	Other
Date	Time	Warning		
2015-08-24	16:04:15	Temperature alarm		
2015-08-24	16:04:15	CO2 concentration alarm		
2015-08-24	16:04:19	EGS audible alarm is inactive		
2015-08-24	16:04:31	EGS audible alarm is inactive		
2015-08-24	16:04:42	EGS audible alarm is inactive		
2015-08-24	16:04:44	CO2 concentration normal		
2015-08-24	16:04:54	EGS audible alarm is inactive		
2015-08-24	16:05:07	EGS audible alarm is inactive		
2015-08-24	16:05:14	CO2 concentration alarm		
2015-08-24	16:05:19	EGS audible alarm is inactive		
2015-08-24	16:05:23	Temperature normal		

5.7.3 Warnings tab

Click the **Warnings** tab to display information about incubator warnings, e.g. motor, barcode and camera errors, lost connection between the EmbryoScope or CulturePro incubator and the EmbryoViewer software and door openings.

Summary	Alarms	Warnings	Log	Other
Date	Time	Warning		
2016-09-18	13:24:07	Error in micro controller data block checksum		
2016-09-18	13:24:07	The micro controller transmission of the data block was not completed before a new block was initiated		
2016-09-19	13:09:30	User did not respond to dialog. Normal operation has stopped.		

5.7.4 Log tab

Click the **Log** tab to display a number of incubation parameters related to the EmbryoScope or CulturePro incubator. The parameters are grouped into the following categories, which are available from a drop-down list:

- **Default:** Displays information about when a culture dish was loaded, the position of each image, etc.

- **Description:** Displays information about the embryos, when the culture dish was started/ended, program version, etc.
- **Incubator Settings:** Displays O₂, CO₂ and temperature settings.
- **Instrument Parameters:** Displays information about all instrument-specific parameters (calibrated during reset).
- **Well Position:** Displays information about where the well was found.

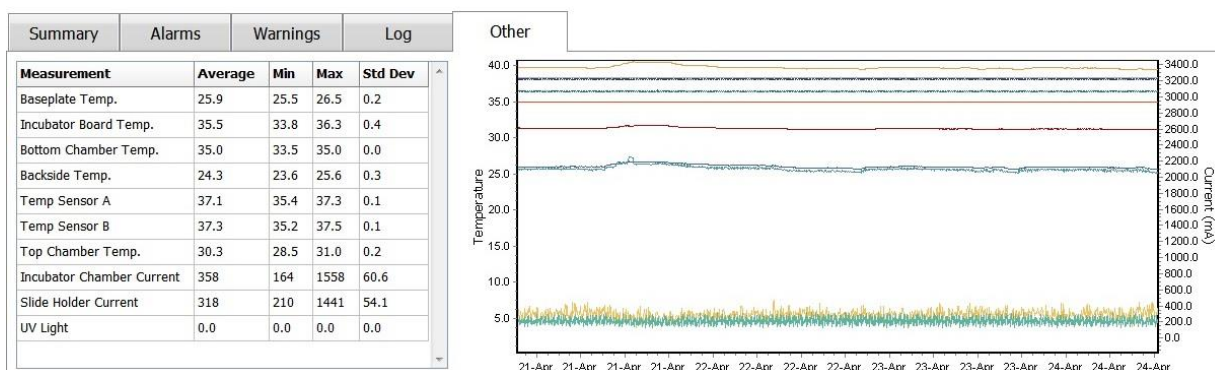
These logs are primarily used for troubleshooting any problems that may have occurred in the EmbryoScope or CulturePro incubator.

Summary	Alarms	Warnings	Log	Other
---------	--------	----------	-----	-------

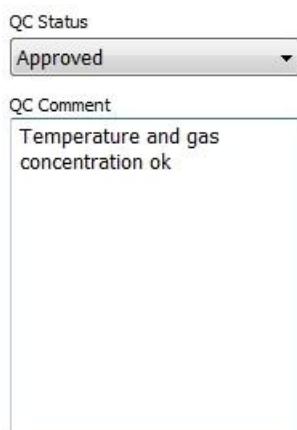
Date	Time	Log
2019-08-28	10:22:06	No detectable barcode on inserted dish.
2019-08-28	10:22:11	Slide 1, Cross found in stack 1. Fit 0.00
2019-08-28	10:22:11	Slide 1, Cross coordinates (x, y, z): 380, 100, 1
2019-08-28	10:22:13	Patient found in database.
2019-08-28	10:23:14	Estimated dish offset: -0.40 degrees.
2019-08-28	10:23:14	Slide 1, Well 1 estimated focus: -400 micro meters (focal index = 1).
2019-08-28	10:23:14	Slide 1, Well 1 estimated well position (X, Y): 400, 544.
2019-08-28	10:23:14	Slide 1, Well 2 estimated focus: -400 micro meters (focal index = 1).
2019-08-28	10:23:14	Slide 1, Well 2 estimated well position (X, Y): 400, 544.
2019-08-28	10:23:14	Slide 1, Well 3 estimated focus: -400 micro meters (focal index = 1).

5.7.5 Other tab

Click the **Other** tab to display a list of average values, minimum values, maximum values and standard deviations for a number of different running conditions, e.g. the temperature within the EmbryoScope or CulturePro incubator and the electronic current usage of the various parts of the system. A graphical representation of the parameters is also available. You can freely choose which parameters to include or exclude by selecting or deselecting the check boxes available to the right of the graphs.



5.7.6 Saving QC status and comments



The screenshot shows a web form for quality control. It has two main sections. The first section is labeled 'QC Status' and contains a dropdown menu with 'Approved' selected. The second section is labeled 'QC Comment' and contains a text area with the text 'Temperature and gas concentration ok'.

When a quality check (QC) of the running conditions has been performed, the name of the user performing the QC is automatically saved. It is possible to add the QC status (**Approved**, **Disapproved**, **Not Checked**) and a comment.

Click the **Save** button to save the entered data. The QC status and any added comments are also displayed on the **Instrument** page, which you can open by clicking the **Instrument** button.

6 Database menu

From the **Database** menu of the navigation panel, you can open the **View All Slides** and **Instrument** pages.

6.1 View All Slides page

Click the **View All Slides** button to open the **View All Slides** page. The page lists data for all culture dishes, e.g. insemination time and instrument quality control status.

You can click on the column headers to sort the data by the column of your choice. By default, the culture dishes are listed in chronological order with the oldest culture dishes at the top. If no culture dish is selected, the view will automatically scroll to the bottom to show the most recent culture dishes. You can also filter the data based on some of the columns. Place the cursor over the column header and click on the arrow to the right of the header. You can now select or deselect different filters. If you would like to set a standard by which the data will be filtered, set the filters and click the **Save Standard Filters** button. The data will now be filtered by the standard filters every time you open the **View All Slides** page. Setting a standard will overwrite the previous standard. Click the **Apply Standard Filters** button to apply the standard filters, or click the **Reset All Filters** button to reset all filters.

When you select a culture dish, the row containing the culture dish will be displayed in blue color. The selected culture dish as well as the patient and treatment associated with it will now be active and highlighted throughout the EmbryoViewer software.

From the **View All Slides** page, you can export data on each culture dish in an EmbryoScope incubator to an Excel or a CSV file. You may also delete all data related to a specific culture dish from this page.

6.1.1 List of culture dishes

For each culture dish, the EmbryoViewer software displays the following parameters:

- Patient ID, patient name and treatment ID
- Insemination time
- Start and end time of incubation in the EmbryoScope or CulturePro incubator (relative to the insemination time)
- Instrument and culture dish number
- Use or non-use of time-lapse
- Annotation status of embryos in the culture dish
- Culture dish type
- Annotation comments and QC status.

Patient ID	Patient Name	Treatment ID	Insemination	Start (h)	End (h)	Instrument	Slide	Timelapse	Annotations	QC Status	Slide Type	Annotation Comments
345678-9012	Rachel Oldie	CP Treatment	2018-03-27 16:00	1.5	17.1	316	10429	No	Not Applicable	Not Checked	Unknown	
234567-8900	Maria Niotre	Second Treatment	2009-11-06 14:00	1.1	69.1	4	965	Yes	Annotated	Approved	Human Clinical	21/03/2013 KLF
520000-2345	Jo Nielsen	Unknown	2011-03-21 13:20	0.6	69.5	16	411	Yes	In Progress	Approved	Other Test	?
570000-1111	Else Olesen	Unknown	2010-02-15 17:00	0.3	137.0	11	194	Yes	In Progress	Not Checked	Human Test	awaits annotation
560000-1111	Karen Hæklestrup	Unknown	2010-04-28 14:00	0.6	67.2	16	143	Yes	Annotated	Not Checked	Human Clinical	annotated by KLF
580000-1111	My test	Unknown	2010-10-12 12:00	0.4	69.9	22	127	Yes	Annotated	Approved	Human Clinical	NN Comments
550000-1111	Dorte Jensen	Unknown	2010-03-22 15:00	0.9	115.8	16	112	Yes	Annotated	Approved	Animal Test	Annotated by KLF
510000-1234	Hanne Hansen	Unknown	2009-09-23 13:00	3.3	68.3	11	60	Yes	In Progress	Approved	Human Clinical	awaits annotation
134567-1234	Helle Lykke	First Treatment	2009-07-29 16:00	0.4	67.1	11	29	Yes	Annotated	Disapproved	Animal Test	KLF

View Only Recent Slides

1 out of 9 slides selected

Delete

Export

Save Standard
Filters

Apply Standard
Filters

Reset All Filters

The block next to the list of culture dishes displays the last image taken of each well in the current culture dish. The colors of the images or their frames indicate whether the embryo is selected to be transferred fresh, transferred after freezing, frozen for use in a later treatment, avoided or pending decision.

6.2 Instrument page

To get an overview of all instruments, running parameters and quality check statuses, click the **Instrument** button. The table lists average incubation details for all culture dishes in the database:

- Average incubation temperature, gas concentration and flow
- QC status and comments on the QC.

Slide ID	Instrument /	Slide	Patient ID	Start	Temperature	CO2 Conc	CO2 Flow	O2 Conc	N2 Flow	QC	Comment
D2010.05.25_50130_1007	7	130	2456	2010-05-25 14:06	37.019	5.351	0.145	4.573	2.373	Approved	
D2010.05.25_50131_1007	7	131	5673-8954	2010-05-25 14:07	37.136	3.963	3.870	8.665	24.561	Approved	
D2010.05.25_50132_1007	7	132	4562-8654	2010-05-25 14:08	37.136	3.963	3.870	8.665	24.561	Approved	
D2010.05.25_50133_1007	7	133	2457-8754	2010-05-25 14:25	37.155	3.731	4.508	8.665	24.561	Approved	
D2010.05.25_50134_1007	7	134	4631-9535	2010-05-25 14:26	37.155	3.731	4.508	8.665	24.561	Approved	
D2010.05.25_50135_1007	7	135	4710-9271	2010-05-25 14:27	37.156	3.639	4.808	8.665	24.561	Approved	
D2010.05.25_50128_1007	7	128	547689-543275	2010-05-25 13:20	37.012	5.302	0.078			Approved	
D2010.05.25_50129_1007	7	129	125648-875367	2010-05-25 13:29	37.014	5.310	0.077			Approved	
D2010.05.25_50130_1007	7	130	2456	2010-05-25 14:06	37.019	5.351	0.145	4.573	2.373	Approved	
D2010.05.25_50131_1007	7	131	5673-8954	2010-05-25 14:07	37.136	3.963	3.870	8.665	24.561	Approved	
D2010.05.25_50132_1007	7	132	4562-8654	2010-05-25 14:08	37.136	3.963	3.870	8.665	24.561	Approved	
D2010.05.25_50133_1007	7	133	2457-8754	2010-05-25 14:25	37.155	3.731	4.508	8.665	24.561	Approved	
D2010.05.25_50134_1007	7	134	4631-9535	2010-05-25 14:26	37.155	3.731	4.508	8.665	24.561	Approved	
D2010.05.25_50135_1007	7	135	4710-9271	2010-05-25 14:27	37.156	3.639	4.808	8.665	24.561	Approved	
Average					37.05	4.75	1.84	7.98	20.86		

6.2.1 Average incubation conditions for all culture dishes

The average incubation temperature, gas concentration and flow for all instruments, several instruments or a specific instrument are calculated at the bottom of the list. The average incubation conditions for a specific instrument are calculated by selecting the instrument in the header row **Instrument**.

By clicking on the header row, you can also indicate whether you want to sort the parameters in ascending or descending order.

7 Settings menu

In the **Settings** menu of the navigation panel, click the **Settings** button to open a page containing tabs for various settings.

7.1 General tab

On the **General** tab of the **Settings** page, you can configure the barcode printer options and specify how you want embryo decisions to be displayed visually.

In the **Barcode Printer** group box, you can select which barcode printer to use when printing labels for the culture dishes and how many labels you want to print at the same time. The labels

are printed from the **Patient Details** page (see section 4.2). You can also set the number of days after insemination after which a barcode reprint warning will be displayed when you reprint the barcode label of a culture dish that has already been running.

Barcode Printer

Selected Printer
Microsoft Print to PDF

Number of labels
1

Show barcode reprint warning after (days)
10

If you enable the barcode reprint warning, a dialog box with a warning will appear when you attempt to reprint the barcode label of a culture dish that has been running for the defined number of days. Click **Yes** to reprint the label or **No** to close the dialog box without reprinting the label.

In the **User Interface** group box, you can select whether you want embryo decisions to be shown as a color overlay covering the entire embryo image (**Color Overlay**) or as a colored frame around the image (**Frame**). This setting is stored in the EmbryoViewer software and can thus be changed individually on each EmbryoViewer client.

User Interface

Embryo Decision Visual Style

Color Overlay

Color Overlay

Frame

7.2 User tab

From the **User** tab on the **Settings** page, you can create, edit and delete users and change the automatic logout and screen saver settings.

NOTE

- Only users having the roles of **Editor** or **Administrator** can edit data.

7.2.1 Creating, editing and deleting users

On the **User** tab, click the **New User** button to create a new user. A dialogue box is opened in which you can specify the user name, user password and user type. If you create a user with an invalid user name, or if you need to change a user name, you will have to delete and recreate the user.

A user name will be invalid if it is a duplicate of an existing user name. The name will also be invalid if the first character is a numerical character or if the name exclusively consists of either numerical or special characters.

A screenshot of a 'User Details' dialog box. It has a title bar with 'User Details' and standard window controls. Inside, there are three input fields: 'User Name' with the text 'William', 'User Password' with masked characters (dots), and 'User Type' with a dropdown menu showing 'Editor'. At the bottom are 'OK' and 'Cancel' buttons.

To edit an existing user, select the user on the list of users and click the **Edit User** button. Edit the user information as required, and click **OK** to save your changes.

To delete an existing user, select the user on the list of users and click the **Delete User** button. Click **Yes** to confirm the deletion.

Note that only users having the **Administrator** role can create new users and edit or delete existing users.

7.2.2 User roles

Users can have four different roles. In addition to the rights specified below, all four user roles can also log in from an external mobile device such as a tablet, provided that the clinic has purchased a separate web service from Vitrolife:

- **Administrator:** Administrators can change all settings in the software. This includes performing annotations, carrying out QC tasks, handling patients and culture dishes, designing **Compare & Select** models and adding or deleting users.
- **Editor:** Editors can perform the same tasks as administrators, except for carrying out user administration tasks and creating models.
- **Reader:** Readers cannot make any changes to the data in the EmbryoViewer software.
- **Web:** Web users are only relevant if you are using an external mobile device. Web users have read-only rights to the available data.

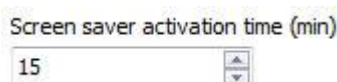
7.2.3 Automatic logout and screen saver settings

On the **User** tab, users having the **Administrator** role can set the idle time period after which users will be automatically logged off or disable the automatic logout function by selecting the **Turn Off Autologout** check box:



The screenshot shows a settings interface for 'Autologout time (min)'. It features a numeric input field with the value '60' and up/down arrow buttons. To the right of this field is a checkbox labeled 'Turn Off Autologout', which is currently unchecked.

They can also set the idle time period after which the screen saver will be activated:



The screenshot shows a settings interface for 'Screen saver activation time (min)'. It features a numeric input field with the value '15' and up/down arrow buttons.

The screen saver will not automatically log users off. This is determined by the automatic logout time.

7.3 Annotations tab

This section describes the **Annotations** tab without the Guided Annotation tool. If the Guided Annotation tool is installed in your clinic, please refer to the description of the **Annotations** tab provided in the separate Guided Annotation user manuals (detailed guidelines and quick guide).

The **Annotations** tab contains facilities that allow you to create your own user-defined annotation variables.

When first opened, the **Annotations** tab will display the user-defined variables that have already been defined, if any (see the following illustration):

The screenshot displays the **Annotations** tab within the software interface. The tab is part of a menu bar that includes General, User, Annotations, Models, Embryo Details, Brands, Export, and About. Below the menu bar, five user-defined variables are listed, each with a text input for the variable name, a list of possible values, and buttons to add or delete values.

Variable Name	Possible Values	Buttons
User defined variable 1: PN	Appear Disappear	Add, Delete
User defined variable 2: MN Type	Binuclear Multinuclear Micronuclei	Add, Delete
User defined variable 3: Blastocyst	B1 b2 b3	Add, Delete
User defined variable 4: cytoplasmic halo	present	Add, Delete
User defined variable 5: General appearance	:) :(;(;)	Add, Delete

Annotations: Saved 2012-07-03 16:56:27

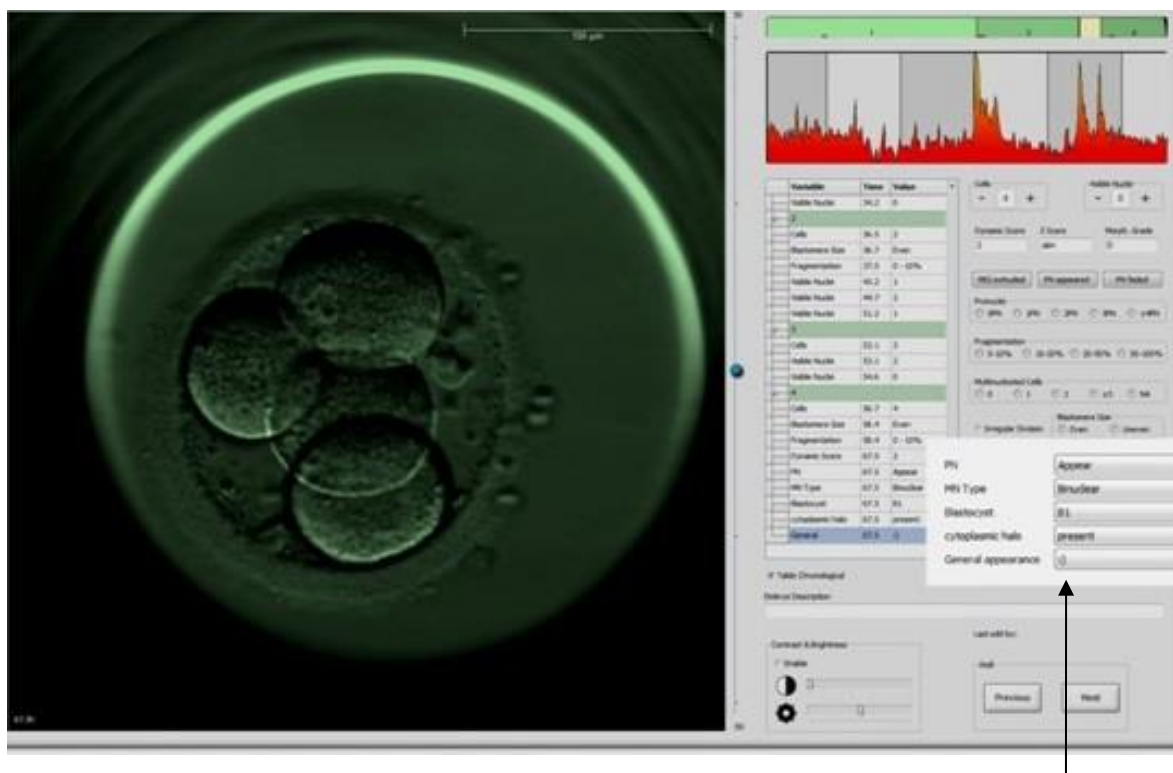
Save

Variable name

Possible values for the variable

Buttons to add or delete values

The variables created here will also appear on the **Annotate** page where you can annotate them for a specific embryo:



User-defined variables on the **Annotate** page

It is possible to add a maximum of five separate variables. A variable consists of a name and up to ten different values.

User-defined variables cannot be included in a model.

For more information on how to annotate user-defined variables, see section 5.3.12.

7.3.1 User rights and user-defined variables

Only users having the **Administrator** role can design and edit user-defined annotation variables, and only users having the **Administrator** or **Editor** role can work with the variables on the **Annotate** page.

See section 7.2.2 for further information on user roles and rights.

7.3.2 Adding a new user-defined variable

To add a new user-defined variable, follow these steps:

1. In the first data entry field of the **Annotations** tab, enter the name of the new user-defined variable.
2. In the **Values** field, add a value to the user-defined variable.

3. To add an additional value, click the **Add** button. Repeat this step until you have added a maximum of ten values.
4. Click **Save**. The user-defined variable is now visible and can be annotated for embryos on the **Annotate** page.

7.3.3 Deleting a user-defined variable

If you delete a user-defined variable, it will no longer be visible on the **Annotate** page and can no longer be used for annotating embryos. The annotations that have previously been made using the deleted user-defined variable will still be kept in the database of the EmbryoViewer software.

To delete a user-defined variable, follow these steps:

1. Highlight the name of the user-defined variable.
2. Press the Delete keyboard button.
3. Click **Save** when the operation is complete.

7.3.4 Redefining a user-defined variable

When you redefine a user-defined variable (adding new or deleting existing values), the annotations that have previously been made using the original definition will still be kept in the database of the EmbryoViewer software. After the redefinition has been performed, no new annotations can be made using the original definition of the user-defined variable.

To redefine a user-defined variable, follow these steps:

1. To add an additional value, click the **Add** button next to the user-defined variable you want to redefine. A maximum of ten values can be included in each user-defined variable.
2. To delete an existing value, highlight the relevant value and click the **Delete** button.
3. Click **Save** when the operation is complete.

7.4 Models tab

On the **Models** tab, you can design models that reflect the experience and data accumulated in your clinic in relation to the assessment of embryo potential.

You can design three different model types on the tab: Hierarchical, additive and multiplicative models. You find a detailed description of these model types in sections 7.4.8, 7.4.9 and 7.4.10.

The EmbryoViewer software lets you choose from multiple types of pre-defined variables when you define a new model. In addition to these pre-defined variables, you can choose variables set up as user-defined comments (this feature is only available if you use the Guided Annotation tool) and define a number of custom expressions that may also be included in your model.

In additive and multiplicative models, you can assign a user-defined weight to each variable that is included. The weight signifies the importance of the variable. If the weight is of the type **Prefer** or

Avoid (i.e. different from 0 in additive models and different from 1 in multiplicative models), you can specify a range for which the weight will apply.

Certain variables can only be applied as information variables (i.e. weight 0 for additive models and weight 1 for multiplicative models). These include variables set up as user-defined comments.

Once the model has been created, you can use it for scoring embryos on the **Compare & Select** page. This serves to facilitate the subsequent embryo assessment and the decision about which embryos to transfer, freeze or avoid.

The **Models** tab appears as follows:

The screenshot shows the 'Models' tab in the EmbryoViewer software. The interface is divided into several sections:

- List of saved models:** A table on the left showing a list of models with columns for 'Active', 'Name', 'Type', 'Creator', and 'Date'. Two models are listed: 'KIDScoreD3 v1.4' and 'KIDScoreD3 v1.3'.
- Model Type drop-down list:** A dropdown menu labeled 'Model Type' with 'Imported' selected.
- Custom Expressions table:** A table with columns 'Name' and 'Expression' for defining custom expressions.
- Model Description box:** A text area containing the description of the selected model: 'KIDScore D3 is defined by Vitrolife A/S based on the knowledge and experience extracted from our available KID data (please see the use manual for the EmbryoViewer software for a definition of KID data)'.
- Save and Clear buttons:** Two buttons labeled 'Save' and 'Clear' at the bottom left.
- Model Definition table:** A table with columns 'Variable', 'Description', 'Min', 'Max', and 'Classification'. It lists variables like 'NOT3PH', '9PH', '12', '13', '14', '15', '18', and 'Cells 69h'.
- Model Provided By:** A section showing the 'Vitrolife' logo and the 'KIDScore D3' model name.
- Model Description box:** A text area containing the description of the selected model: 'KIDScore D3 is defined by Vitrolife A/S based on the knowledge and experience extracted from our available KID data (please see the use manual for the EmbryoViewer software for a definition of KID data)'.
- Model Definition table:** A table with columns 'Variable', 'Description', 'Min', 'Max', and 'Classification'. It lists variables like 'NOT3PH', '9PH', '12', '13', '14', '15', '18', and 'Cells 69h'.

The left part of the **Models** tab contains an overview of all saved models, including information about the type of model and the name of the user who created the model.

If you highlight a model in the list of saved models, the variables included in the model and their specified target intervals will be displayed in the **Selected model** box. Any description or comments added to the model are displayed in the **Model Description** box. More detailed information on the chosen model is displayed in the **Custom Expressions** and **Model Definition** tables.

In the right part of the **Models** tab, you can define new models and create new custom expressions to be included in your models.

See section 7.4.4 for information on how to create custom expressions and section 7.4.7 for information on how to create a new model.

WARNING

- Scoring embryos is a complicated process, and new scientific results are frequently published. Before clinical use, new models should therefore always be subjected to a statistical validation by the clinic in which they will be applied.

NOTE

- The models are simple and may therefore not fully reflect the effect of each variable or of the interaction between two or more variables.
- The examples of models on the following pages contain a number of variables and intervals. These examples are only included for clarification and are not meant as a guideline for designing new models.

7.4.1 User rights on the Models tab

Only users having the **Administrator** role can design, activate and deactivate models.

See section 7.2.2 for further information on user roles and rights.

7.4.2 Variables in models

- **Pre-defined variables:** The EmbryoViewer software contains a number of pre-defined variables. It is possible to include the pre-defined variables in models. See the full list of available pre-defined variables in section 7.4.3.
- **Custom expressions:** Custom expressions are calculated from a number of pre-defined timing variables. Logical variables cannot be used for calculating custom expressions. It is possible to include custom expressions in models. See section 7.4.4 for further information on how to define custom expressions.
- **User-defined variables:** It is not possible to include user-defined variables in models. See section 7.3 for additional information on user-defined variables. If you use the Guided Annotation tool, user-defined variables have been replaced by user-defined comments, which can be included in models as described above.

7.4.3 List of available pre-defined variables

Variable	Description	Values
NOT2PN	Maximum number of pronuclei differs from two	TRUE/FALSE
UNEVEN2	Uneven size of blastomeres at the 2-cell stage	TRUE/FALSE
UNEVEN4	Uneven size of blastomeres at the 4-cell stage	TRUE/FALSE
MN2	Multinuclearity occurs at the 2-cell stage	TRUE/FALSE
MN4	Multinuclearity occurs at the 4-cell stage	TRUE/FALSE
tPB2	Time from insemination until second polar body is extruded	Hours
tPNa	Time from insemination until pronuclei have appeared	Hours
tPNf	Time from insemination until pronuclei have faded	Hours
t2	Time from insemination to complete division to two cells	Hours
t3	Time from insemination to complete division to three cells	Hours
t4	Time from insemination to complete division to four cells	Hours
t5	Time from insemination to complete division to five cells	Hours
t6	Time from insemination to complete division to six cells	Hours
t7	Time from insemination to complete division to seven cells	Hours
t8	Time from insemination to complete division to eight cells	Hours
t9+	Time from insemination to complete division to nine or more cells	Hours
tSC	Time from insemination to start of compaction	Hours
tM	Time from insemination to formation of morula	Hours
tSB	Time from insemination to start of blastulation	Hours
tB	Time from insemination to formation of blastocyst	Hours
tEB	Time from insemination to formation of expanded blastocyst	Hours
tHB	Time from insemination to hatching blastocyst	Hours

7.4.4 Defining custom expressions

When you create a model, it is possible to include one or more custom expressions, which can be set up to reflect the experience and information accumulated in your clinic about the predictive value of the timing and morphokinetics of embryo development.

A custom expression is a variable that is calculated based on some of the pre-defined timing variables delivered with the EmbryoViewer software.

Custom expressions are specific to a particular model. This means that a custom expression can only be included in the model for which it was originally defined and in models subsequently created on the basis of this original model. You can, however, define identical custom expressions for several individual models.

A maximum of ten custom expressions can be defined for each model.

To define a custom expression, follow these steps:

1. Click the **New** button next to the **Custom Expressions** table.

This opens the **Custom Expression** editor.

2. Enter the name of your new custom expression.

The name can consist of a maximum of eight characters. White spaces and special characters are not allowed.

3. Enter the custom expression you want to use for calculating a variable.

The variables that can be included in a custom expression are listed in the editor. Only timing variables are available (not logical variables such as UNEVEN2).

The standard arithmetic operators that can be used in custom expressions are addition (+), subtraction (-), multiplication (*) and division (/).

You may also use parentheses in custom expressions to enclose parts of the formula and thereby change the order of calculation.

In accordance with standard arithmetic rules, multiplication and division is done before addition and subtraction, and the operators are evaluated from left to right, i.e. $a/b*c = (a/b)*c$, which does not equal $a/(b*c)$.

A custom expression can also use the function **cells(t)**, which signifies the number of cells present at a specified point in time expressed as hours after insemination. Thus, the custom expression Cells(48.2) represents the number of annotated cells present 48.2 hours after insemination.

NOTE

- If you enter a time such as *Cells(80)* when the embryo has reached morula or blastocyst stage and the number of individual cells can thus no longer be counted, the **cells(t)** function will use the latest annotated number of cells, even if this annotation was made at an earlier point in time, e.g. 48 hours.

The entered custom expression will be validated as you go along. If your custom expression is valid, a green check mark will appear at the bottom of the editor. If the custom expression is invalid, a red cross will indicate this.

The dialog box titled "Custom Expression" contains a "Name" field with the value "BLAST" and an "Expression" field with the value "tB-tSB". Below these fields is a "Help" section listing variables (tPB2, tPNa, tPNf, t2, t3, t4, t5, t6, t7, t8, t9, tM, tSB, tB, tEB, tHB) and functions (cells(t), with an example: cells(48)). A green checkmark is visible in the bottom left corner, indicating the expression is valid. "Cancel" and "OK" buttons are in the bottom right.

4. Save your expression by clicking **OK**.

The new expression will be inserted in the **Custom Expressions** table and the drop-down list of available variables in the **Model Definition** table, ready to be included in a model.

Custom Expressions

Name	Expression	
BLAST	tB-tSB	
		New
		Edit
		Delete

Model Definition

Variable	Weight	Min	Max	Description	P(Variable)
BLAST					
tB					
t9					
tM					
tSB					
tB					
tEB					
tHB					
BLAST					

7.4.5 Editing custom expressions

You can rename or change the calculation of an existing custom expression. Note that if you have already included the custom expression in the model currently under construction, the changes you make will take effect in the model.

To edit a custom expression, follow these steps:

1. Click the **Edit** button next to the **Custom Expressions** table to open the editor.
2. Click **OK** in the message box.
3. Make your changes to either the name or the formula, and click **OK**.

7.4.6 Deleting custom expressions

If you want to delete a custom expression that has already been included in the model currently under construction, you should take notice that deleting the custom expression (from the **Custom Expressions** table) will also remove it from the new model (in the **Model Definition** table).

To delete a custom expression, follow these steps:

1. Click the **Delete** button next to the **Custom Expressions** table.
2. Click **OK** in the message box.

The custom expression is now removed from the **Custom Expressions** table. If you have already included the custom expression in the model you are currently designing, the expression will also be removed from the **Model Definition** table. Since custom expressions are specific to each model, the expression will not be removed from any other saved models.

7.4.7 Designing a new model

To be able to create a new model, you need administrator rights if user authentication is applied in your clinic.

To create a new model, follow these steps:

1. In the **Model Name** field in the right part of the **Models** tab, enter the name of your new model. The name must be unique. No other restrictions are imposed on the model name, and the name does not need to indicate the model type. We do, however, recommend choosing a name that signifies the intended purpose of the model.
2. From the **Model Type** drop-down list, select the type of your new model (see sections 7.4.8, 7.4.9 and 7.4.10 for a description of the three available types of models).
3. In the **Model Description** field, add a description of the model (optional).
4. In the **Creator** field, add the name or initials of the person who designed the model.

5. In the **Custom Expressions** table, define the custom expression(s) you want to include in the model (optional). See section 7.4.4 for further information on how to define custom expressions.
6. In the **Model Definition** table, specify which variables you want to include in your model. The **Variable** column gives access to a drop-down list from which you can select both pre-defined variables and any custom expressions you may have defined for this particular model. The drop-down list works in two steps:
 - Step 1: Select the type of variable that you want to include, i.e. one of the variable groups from the **Annotations** tab in the **Settings** menu or a user-defined comment (user-defined comments are only available if you use the Guided Annotation tool).

Model Definition						
Variable		Weight	Min	Max	Description	P(Variable)
NOT2PN	▼	0			Info	
tB	▼	0			Info	
	▼					
<div> User Defined Comments Most used Timing Pronuclei 1-cell stage 2-cell stage 4-cell stage Blastocyst Multinucleation Blastomere size Fragmentation Cytoplasm Other All </div>						

- Step 2: Select the specific variable from the drop-down list that now appears in the same column.

Model Definition						
Variable		Weight	Min	Max	Description	P(Variable)
NOT2PN	▼	0			Info	
tB	▼	0			Info	
▼						
Blast Expand						
BS Exp.-Last						
Coll. Count						
Collapse						
ICM						
ICM-Last						
Pulsing						
Re-exp Count						
Strings						
TE						
TE-Last						

- If you are designing an additive or a multiplicative model, specify the weight you want each variable to carry when it falls inside the target interval.
- In the **Min** and **Max** columns, specify the target interval for each variable included in the model (see sections 7.4.8, 7.4.9 and 7.4.10 for further details).
- Save your new model by clicking the **Save** button. The model will now be saved and added to the list of saved models in the upper left corner of the page.

You cannot delete a saved model. When you have designed a new model, you can, however, decide at any given time whether you want the model to be active or inactive by selecting or deselecting the **Active** check box in the list of saved models. Only active models can be used for scoring embryos on the **Compare & Select** page (see section 5.4).

- Before using the new model for scoring embryos, you should validate the model in your clinic (see section 7.5.5).

WARNING

- When a score for embryos is calculated by applying a model on the **Compare & Select** page, the embryos given the highest score will be the ones that best meet the requirements specified in the model. This does not necessarily imply that these embryos are the ones most suitable for transfer. The decision about which embryos to transfer must always be made by the user after an assessment of the quality of all relevant embryos.
- Before clinical use, a model should always be validated by the clinic in which it will be used.

7.4.8 Hierarchical models

Hierarchical models divide the embryos into classes based on their scores. The classes are A, B, C and D (in some cases with the addition of a plus or minus sign if a tertiary variable has been specified) as well as E and F. A is the highest-scoring class that ranks above all others. Embryos that meet the requirements of an exclusion variable will be assigned to class E, and embryos that have been marked to be avoided before the model is applied will be assigned to class F.

The models can include up to three variables and up to seven variables indicative of exclusion of the embryo from a particular class.

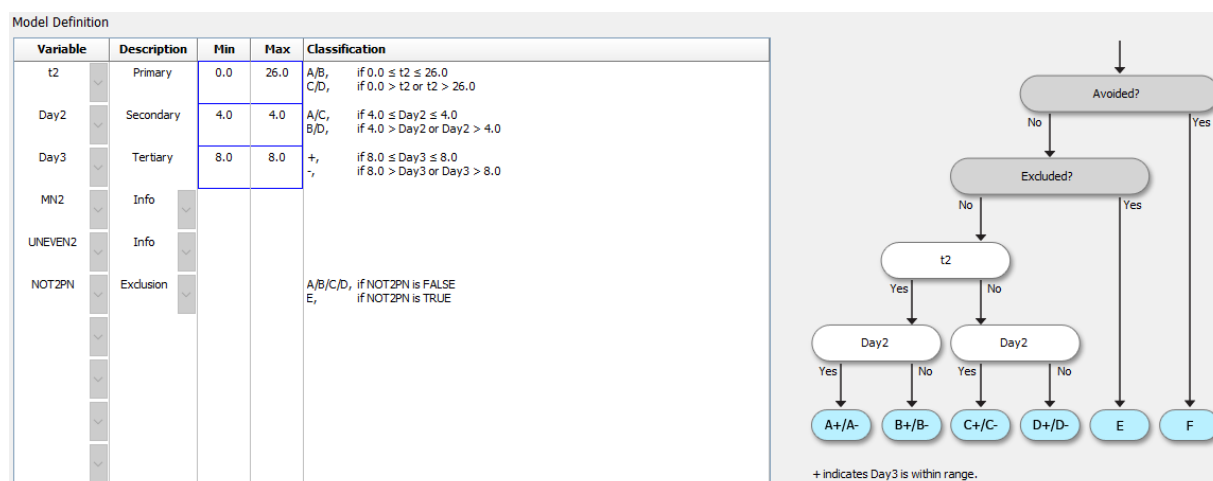
The target interval for a continuous variable is defined by specifying a minimum and a maximum value. If the value of the continuous variable falls inside the target interval (including the minimum and maximum values), the embryo is assigned to a higher-scoring class (to the left in the hierarchical tree shown in the following illustration). If the value of the variable falls outside the target interval, the embryo is assigned to a lower-scoring class (to the right in the illustrated hierarchical tree).

The entered minimum and maximum values are rounded to one decimal. This means that a value of e.g. 24.25 will be rounded to 24.3. When the score is calculated, the rounded value displayed on the screen will be used in the calculation.

If the variable is logical (e.g. multinucleation at the fourth cell stage (MN4)), there is no associated target interval (maximum and minimum values). If the value of the logical variable is **FALSE**, the embryo is assigned to a higher-scoring class (left side of the illustrated hierarchical tree). If the value of the variable is **TRUE**, the embryo is assigned to a lower-scoring class (right side of the illustrated hierarchical tree).

Class A is the highest-scoring class, then B, C and D in descending order. If two embryos are assigned the same letter, an embryo that carries a plus sign will be ranked higher than an embryo that carries a minus sign.

The following is an example of a hierarchical model. A graphical representation of included variables is displayed to the right of the **Model Definition** table:



The five columns of the **Model Definition** table contain the following information for hierarchical models:

- **Variable:** Contains the variables included in the model. In order to save a hierarchical model, you must specify the primary and secondary variables. It is optional to specify a tertiary variable or additional variables used for either exclusion or information. Select either **Info** or **Exclusion** from the drop-down list available from the **Description** column to indicate the purpose of the chosen variable.
- **Description:** Contains a description of the variable (**Primary**, **Secondary**, **Tertiary**, **Info** or **Exclusion**). The first three rows of the **Model Definition** table are reserved for the primary, secondary and tertiary variables. You can specify additional variables as either information or exclusion variables. Variables specified as information will be listed on the **Compare & Select** page. They will, however, not be used for scoring the embryos to which this particular model is applied. An embryo that meets the requirements of an exclusion variable will be assigned to class E (see the preceding figure).
- **Min** (minimum): Specifies the minimum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Max** (maximum): Specifies the maximum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Classification:** Lists a description of the variable outcome within and outside the target interval.

If a variable is annotated as **NA**, the score will be affected as follows:

- Primary, secondary and tertiary variables: The overall score will be **NA**.
- Information variables: The overall score is not affected. The value **NA** will be shown in the column for the variable in question on the **Compare & Select** page.
- Exclusion variables: The overall score will be **NA**.

7.4.9 Additive models

Additive models assign a score to the embryos based on the assumption that the included variables ($v_1, v_2, v_3, \dots, v_n$) have an additive effect on the relative scores of the embryos. Each variable in the model is given a weight that determines the contribution of this particular variable to the additive effect.

The target interval for a continuous variable (v_i) such as t_2 is defined by specifying a maximum (\max_i) and a minimum (\min_i) value for the variable. If the value of the continuous variable falls inside this target interval, the weight (p_i) assigned to the variable will be the user-defined weight (w_i) you have entered for this variable in the **Weight** column of the **Model Definition** table (e.g. 2). If the value of the continuous variable falls outside the target interval, the assigned weight will always be zero. The user-defined weight of a continuous variable should be a number between -1,000 and 100.

The entered minimum and maximum values are rounded to one decimal. This means that the value of e.g. 24.25 will be rounded to 24.3. When the score is calculated, the rounded value displayed on the screen will be used in the calculation.

If the variable is logical (e.g. multinucleation at the fourth cell stage (MN4)), there is no associated target interval (maximum and minimum values). If the value of the variable is **TRUE**, the weight (p) assigned to the variable will be the user-defined weight you have entered in the **Weight** column of the **Model Definition** table. If the value of the variable is **FALSE**, the assigned weight will always be zero. The user-defined weight of a logical variable should be a number between -1,000 and 100.

The scores calculated by an additive model can be any negative or positive number. The embryos are ranked by descending score.

The mathematical formula used in additive models is as follows:

$$Score = \sum_{all\ i} p_i = p_1 + p_2 + p_3 + \dots + p_n$$

For continuous variables (time intervals):

$$p_i = \begin{cases} w_i, & \text{if } \min_i \leq v_i \leq \max_i \\ 0, & \text{else} \end{cases}$$

For logical variables (variables that are **TRUE** or **FALSE**):

$$p_i = \begin{cases} w_i, & \text{if } v_i \text{ is TRUE} \\ 0, & \text{if } v_i \text{ is FALSE} \end{cases}$$

If the user-defined weight given to the variable is more than zero, a value inside the target interval will increase the embryo score (**Prefer**). If the weight given to the variable is less than zero, a value inside the target interval will decrease the embryo score (**Avoid**).

The following is an example of an additive model. The formula for the model you have designed is displayed below the **Model Definition** table:

Variable	Weight	Min	Max	Description	P(Variable)
NOT2PN	-100			Avoid	-100, 0, if NOT2PN is TRUE if NOT2PN is FALSE
t2	1	0.0	26.0	Prefer	1, 0, if $0.0 \leq t2 \leq 26.0$ if $0.0 > t2$ or $t2 > 26.0$
Day2	1	4.0	4.0	Prefer	1, 0, if $4.0 \leq \text{Day2} \leq 4.0$ if $4.0 > \text{Day2}$ or $\text{Day2} > 4.0$
Day3	1	8.0	8.0	Prefer	1, 0, if $8.0 \leq \text{Day3} \leq 8.0$ if $8.0 > \text{Day3}$ or $\text{Day3} > 8.0$
MN2	0			Info	
UNEVEN2	0			Info	

$$\text{Score} = P(\text{NOT2PN}) + P(t_2) + P(\text{Day2}) + P(\text{Day3})$$



The six columns of the **Model Definition** table contain the following information for additive models:

- **Variable:** Contains the variables included in the model.
- **Weight:** Contains the user-defined weight of the variable.
- **Min** (minimum): Specifies the minimum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Max** (maximum): Specifies the maximum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Description:** Contains a description of the variable. The description will automatically be inserted on the basis of the user-defined weight of the variable. Variables with weight = 0 will have the description **Info**, variables with a negative weight (i.e. below 0) will have the description **Avoid**, and variables with a positive weight (i.e. above 0) will have the description **Prefer**.
- **P(Variable):** Lists the additive effect of the variable based on the target interval for continuous variables or the value of logical variables.

If a variable is annotated as **NA**, the score will be affected as follows:

- Variables with a positive or negative weight: The overall score will be **NA**.
- Variables with a weight of zero: The overall score is not affected. The value **NA** will be shown in the column for the variable in question on the **Compare & Select** page.

7.4.10 Multiplicative models

Multiplicative models assign a score to the embryos based on the assumption that the included variables ($v_1, v_2, v_3, \dots, v_n$) have a multiplicative effect on the relative scores of the embryos. Each variable in the model is given a weight that determines the contribution of this particular variable to the multiplicative effect.

The target interval for a continuous variable (v_i) such as t_2 is defined by specifying a maximum (\max_i) and a minimum (\min_i) value. If the value of the continuous variable (v_i) falls inside the interval (including the minimum and maximum values), the weight assigned to the variable (p_i) will be the user-defined weight (w_i) you have entered for this variable in the **Weight** column of the **Model Definition** table (e.g. 2). If the value of the continuous variable falls outside the target interval, the assigned weight will always be one. The user-defined weight of a continuous variable should be a number between 0 and 10.

The entered minimum and maximum values are rounded to one decimal. This means that a value of e.g. 24.25 will be rounded to 24.3. When the score is calculated, the rounded value displayed on the screen will be used in the calculation.

If the variable is logical (e.g. multinucleation at the fourth cell stage (MN4)), there is no associated target interval (maximum and minimum values). If the value of the variable is **TRUE**, the assigned weight will be the user-defined weight entered in the **Weight** column of the **Model Definition** table (i.e. the user-defined weight). If the value of the variable is **FALSE**, the assigned weight (p_i) will

always be one. The user-defined weight of a logical variable should be a number between 0 and 10.

The scores calculated by a multiplicative model will range between zero and infinite. The embryos are ranked by descending score.

The mathematical formula used in multiplicative models is as follows:

$$Score = \prod_{all\ i} p_i = p_1 \cdot p_2 \cdot p_3 \cdot \dots \cdot p_n$$

For continuous variables (time intervals):

$$p_i = \begin{cases} w_i, & \text{if } \min_i \leq v_i \leq \max_i \\ 1, & \text{else} \end{cases}$$

For logical variables (variables that are **TRUE** or **FALSE**):

$$p_i = \begin{cases} w_i, & \text{if } v_i \text{ is TRUE} \\ 1, & \text{if } v_i \text{ is FALSE} \end{cases}$$

If the user-defined weight given to the variable is more than one, a value inside the target interval will increase the embryo score (**Prefer**). If the weight given to the variable is less than one, a value inside the target interval will decrease the embryo score (**Avoid**).

The following is an example of a multiplicative model. The formula for the model you have designed is displayed below the **Model Definition** table:

[illegible]

$$\text{Score} = P(\text{BLAST}) * P(t8) * P(tSB) * P(\text{MN4})$$

III

The six columns of the **Model Definition** table contain the following information for multiplicative models:

- **Variable:** Contains the variables included in the model.
- **Weight:** Contains the user-defined weight of the variable.

- **Min** (minimum): Specifies the minimum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Max** (maximum): Specifies the maximum value of the target interval for continuous variables (one decimal). The column will be empty for logical and information variables.
- **Description**: Contains a description of the variable. The description will automatically be inserted on the basis of the user-defined weight of the variable. Variables with weight = 1 will have the description **Info**, variables with a weight below 1 will have the description **Avoid**, and variables with a weight above 1 will have the description **Prefer**.
- **P(Variable)**: Lists the multiplicative effect of the variable based on the target interval for continuous variables or the value of logical variables.

If a variable is annotated as **NA**, the score will be affected as follows:

- Variables with a weight above or below one: The overall score will be **NA**.
- Variables with a weight of one: The overall score is not affected. The value **NA** will be shown in the column for the variable in question on the **Compare & Select** page.

7.5 Validating models

Before a model is applied, it should be validated in order to determine its predictive capability in your specific clinic.

The model validation quantifies the predictive capability of the model by comparing the scores calculated by the model with a set of clinical data that was *not* used in the original model definition.

The importance of validating the model in relation to the data in your specific clinic is emphasized by the numerous factors that may differ between clinics, e.g. medium type and brand, fertilization method (e.g. ICSI or standard IVF), incubation temperature and oxygen level. These factors may impact the timing of morphological events.

7.5.1 Morphokinetic variables used in models

Three types of morphokinetic variables can be used in models:

- Binary variables, e.g. multinucleation at the fourth cell stage (MN4)
- Pre-defined timing variables, e.g. the timing of the division to two cells (t2) (see section 7.4.3)
- Custom expressions, which are a customized variant of the standard timing variables (see section 7.4.4).

All of the variables used as input in models are the result of manual annotations (see section 5.3). To obtain optimum model performance, it is therefore important to annotate the morphokinetic variables in a complete and consistent manner.

7.5.2 Selecting a data sample

When you validate your model, it may be relevant to exclude certain cycles from the validation process or to include only a sub-set of the available data.

You may want to exclude cycles where the chance of a pregnancy is significantly reduced for reasons other than poor embryo quality (e.g. because the patient has a certain diagnosis) and cycles where division timings are changed for reasons other than embryo quality (e.g. because the embryos are subjected to a biopsy or are grown in a special medium with growth factors).

Depending on the purpose of the model, you may select a specific sub-set of the data for the validation process. The timing patterns differ both between ICSI and IVF treatments and between reduced or ambient oxygen incubation. A model specifically aimed at e.g. ICSI treatments should therefore be validated only against ICSI data. Likewise, a model specifically aimed at low oxygen incubation should be validated only against low oxygen data.

The models should afterwards be applied only to the type of data included in the validation process.

7.5.3 Known implantation data (KID)

You can include the known implantation data (KID) in your model validation.

If you include only embryos that fulfill the KID criteria, specific embryo characteristics can be linked to outcome. The embryos of a particular treatment are KID positive if all of the embryos in that treatment implanted. The embryos are KID negative if all of the embryos in the treatment failed to implant.

KID data can be based on one of three different outcome variables:

- Number of gestational sacs
- Number of fetal heartbeats
- Number of live-born babies.

The outcome variable used for calculating the KID value should be the one most frequently registered in your clinic.

If only a single embryo was transferred and the outcome of the treatment is one, the embryo is KID positive. If the outcome is zero, the embryo is KID negative.

If two embryos were transferred and both of them implanted, both embryos are KID positive. If none of the embryos implanted, both embryos are KID negative. If only one of the embryos in the treatment implanted, no single KID value applies to both embryos, and this treatment should therefore be excluded from the validation.

We recommend that you include in the validation process at least 162 KID embryos of which at least 54 are positives.

7.5.4 Statistical evaluation

A receiver operating characteristics (ROC) curve can be used to evaluate the classification ability of the model. The ROC curve plots the true positive rate (how many out of the total number of positives are contained in this class and in classes with lower scores) as a function of the false positive rate (how many out of the total number of negatives are contained in this class and in classes with lower scores).

The evaluation starts with the classes with the lowest rank and proceeds through the classes in ranked order. The area under curve (AUC) is calculated to evaluate the classification power of the model.

AUC = 1 signifies a perfect model for the retrospective data.

AUC of approximately 0.5 signifies a random model. No classification is possible. This is a poor model for the retrospective data.

We recommend that a minimum AUC of 0.65 should be obtained for the model to be valid when calculated from at least 162 KID embryos of which at least 54 are positives.

7.5.5 How to validate models

To validate a model, follow these steps:

1. Process all clinical cycles in the EmbryoScope time-lapse system without applying a model to the embryos until the required number of embryos that fulfill the KID criteria have been stored in the database.
2. From the **Annotate** page, annotate the morphokinetic variables needed for the model for the KID embryos (see section 5.3).
If creating consistent and complete annotations is already standard procedure in your clinic, the required data may already be available.
3. On the **Models** tab, define the model you are going to validate (see section 7.4).
4. On the **Compare & Select** page, apply the model to the embryos that fulfill the KID criteria (see section 5.4).
5. Export the selected KID data by using the **Export** function available from the **View All Slides** page.
6. In the exported file, delete the data that do not fulfill the KID criteria and are not part of the selected data sub-set.
7. Save the exported file in a location of your choice.

8. Use a standard statistical computer program (SPSS, R, SAS/JMP or similar) to:
 - a) Create an ROC curve based on concurrent KID values and model scores from the **Compare & Select** function and
 - b) Calculate the AUC.

A power calculation performed in the Power Assessment and Sample Size Analysis (PASS) software, version 12 has shown that if the AUC exceeds 0.65 using data from more than 162 KID embryos and more than 54 KID positives, the model is validated with a minimum significance level of 0.05 and a minimum power of 0.9.

7.6 Embryo Details tab

On the **Embryo Details** tab, you can set up which embryo details parameters should be shown in the side-by-side view on the **Compare & Select** page (see section 5.4.2.7). A list of the selected embryo details parameters is shown on the tab. A maximum of four embryo details parameters can be set up.

The screenshot shows the 'Embryo Details' tab in the software interface. The tab is active, and the 'Embryo Details Parameters' table is displayed. The table has four columns: No., Display name, Parameter name, and Parameter type. There are four rows of parameters. The second row is highlighted. To the right of the table are three buttons: New, Edit, and Delete. Below the table is a dialog box titled 'Configure Embryo Details Parameter'. The dialog box has three fields: Parameter type (set to Annotation Variable), Parameter name (set to t2), and Display name (set to t2). There are Cancel and OK buttons at the bottom of the dialog box.

No.	Display name	Parameter name	Parameter type
1	MN-2	MN-2	Calculated Variable
2	t2	t2	Annotation Variable
3	KIDScore D3	KIDScore D3	Model Name
4	My User Var	Blastocyst	User Defined Variable

Buttons: New, Edit, Delete

Dialog Box: Configure Embryo Details Parameter

Parameter type: Annotation Variable

Parameter name: t2

Display name: t2

Buttons: Cancel, OK

7.6.1 Adding embryo details parameters

Click the **New** button to add an embryo details parameter. This opens the **Embryo Details Parameter** dialog box in which you can select the type, name and display name of the embryo details parameter.

Select the parameter type from the **Parameter type** drop-down list. The following parameter types are available:

- **Calculated Variable**
- **Annotation Variable**
- **Model Name**
- **User Defined Variable** (user-defined variables are not available if you use the Guided Annotation tool).

When you have selected the parameter type, the **Parameter name** drop-down list becomes active. The names on the list depend on the type of parameter selected. Select a parameter name from the list.

The **Display name** field is a free-text field in which you can enter the text to be shown on the **Compare & Select** page.

7.6.2 Editing embryo details parameters

To edit an existing embryo details parameter, select the relevant parameter on the list and click the **Edit** button. You can also double-click on the parameter. The **Embryo Details Parameter** dialog box described in section 7.6.1 will open, and you can edit the parameter.

7.6.3 Deleting embryo details parameters

To remove an existing embryo details parameter, select the relevant parameter on the list and click the **Delete** button.

7.7 Brands tab

On the **Brands** tab, you can maintain a list of the medication and media brands used in your clinic. The created list of brands will be available for selection from the **Patient Details** page.

General	User	Annotations	Models	Embryo Details	Brands
<div> <div> Medication brands <ul style="list-style-type: none"> ▶ Gonal F </div> <div> Add Delete </div> </div>					
<div> <div> Media brands <ul style="list-style-type: none"> ▶ G1 G2 EmbryoGlue </div> <div> Add Delete </div> </div>					

To add a brand of medication or medium:

1. Click **Add** next to either the **Medication brands** field or the **Media brands** field. The first row in the list will now become active.
2. Enter the name of the brand that you want to add to the list. It is possible to enter a maximum of 30 keystrokes (including spaces and symbols).
3. Repeat steps 1 and 2 until you have added all relevant brands.
4. Click **Save** at the bottom of the page.

The added brands are now available from the **Treatment** tab of the **Patient Details** page:

Treatment	Transfer
<div> All Treatments <ul style="list-style-type: none"> X6X6 2020 X6X6 2020 </div> <div> New Treatment Rename Treatment Print Barcode Label Reprint Barcode Label </div>	<div> Treatment Comments </div> <div> <input type="checkbox"/> PGT-A / <input type="checkbox"/> PGT-M </div> <div> <div> Medication <ul style="list-style-type: none"> Medication Protocol: Long Agonist Medication Brand: Gonal F Triggering: HCG Total FSH Dose (IU): 1000 <input type="checkbox"/> LH Supplement Medication Comment </div> <div> Oocyte <ul style="list-style-type: none"> Oocyte Source: Autologous Oocyte History: Fresh Oocytes Aspirated: 4 Sibling Embryos in Standard Incubator: No Oocyte Comment </div> <div> Culture <ul style="list-style-type: none"> Media Type: Sequential First Medium Brand: G1 Second Medium Brand: G2 Media Change: Day 3 Culture Comment </div> </div>

Medication

Medication Protocol
Long Agonist

Medication Brand
Gonal-F

Triggering
HCG

Total FSH Dose (IU)
1000.0 ☐ LH Supplement

Medication Comment



Culture

Media Type
Sequential

First Medium Brand
G1

Second Medium Brand
G2

Media Change
Day 3

Culture Comment

Medication Brand, First Medium Brand and Second Medium Brand can be selected from the available list. Brand names can also be entered as free text.

7.8 Export tab

On the **Export** tab, you can create exports that are a collection of pre-defined variables that can be extracted to an Excel or a CSV file for further analysis.

The screenshot shows the 'Export' tab in the EmbryoViewer software. The interface includes a top navigation bar with tabs: General, User, Annotations, Models, Embryo Details, Brands, Export, and About. The 'Export' tab is active.

Available Exports Table:

Active	Name	Default	Creator	Date
<input checked="" type="checkbox"/>	Excel 2003	Default	Vitrolife	2017-03-01
<input checked="" type="checkbox"/>	Guided Annotation CSV		Vitrolife	2017-03-01
<input checked="" type="checkbox"/>	Standard Annotation CSV		Vitrolife	2017-03-01
<input type="checkbox"/>	Validation of annotated		ADMIN	2020-03-11

Export Configuration Area:

Name: Excel 2003
 Display name: Excel 2003
 Description: Backwards compatible Excel 2003 (xls) export set.
 File format: xls
 Included export variables: (List of 84 variables including Slide ID, Patient ID, Patient Name, Birth Year, etc.)
 Export variable count: 84
 Export variable columns: 176

Export Groups and Variables:

Export groups: Patient Group, Treatment Group, Transfer And Outcome Group, Slide Group, Well Group, Morphokinetic Group, Observation Group, Grading Group, User Defined Variable Group, Drawing And Comment Group, Instrument Group, Model Group.

Export variables: Age, BMI, Basal Serum FSH, Birth Month, Birth Year, Diagnosis, Patient Comments, Patient ID, Patient Name.

Only active exports can be used to extract data for an export file

Available exports. Exports marked with a padlock cannot be edited/deleted

Use the **Set As Default** button to determine which export you want to use by default

Variables included in the export

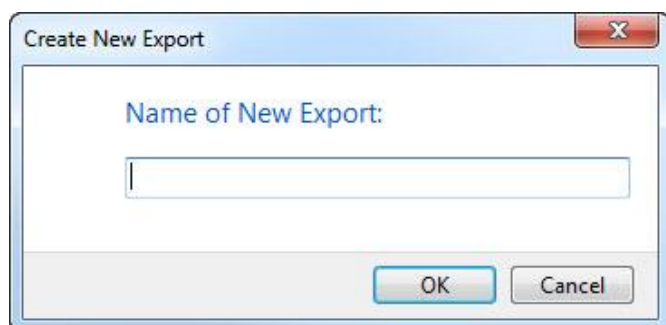
Buttons to include/exclude export items, increase/decrease the number of times a variable is included in the export file and move an item up/down in the export file

Groups from which variables can be included in the export

Variables that can be included in the export

Follow the below instructions to export data:

1. Click either the **New** or the **Copy** button, and enter the name of your new export:



2. If desired, enter a description of the export.
3. From the **File format** drop-down list, select the file format of your export, e.g. CSV (export to a comma-separated text file), XLS (export to Excel) or XLSX (Export to Excel 2007 or later).

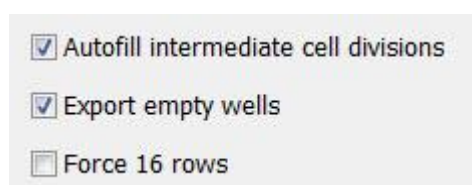


Select **csv** to export to a general, comma-separated text file, which can e.g. be imported into Word. When using this file type, you can export an unlimited number of variables.

Select **xls** to export to Excel (earlier than 2007). This format supports macros. When using this file type, you can export a maximum of 256 variables.

Select **xlsx** to export to Excel (2007 or later). This format does not support macros. When using this file type, you can export more than 16,000 variables.

4. Select the relevant check boxes available in the middle part of the tab:



If you select **Autofill intermediate cell divisions**, the export file will contain columns with auto-completed data for cell divisions that have not been manually annotated by the embryologist. Example: If t2 and t4 have been manually annotated, t3 will automatically be completed in the export file by using the t4 annotations entered by the embryologist.

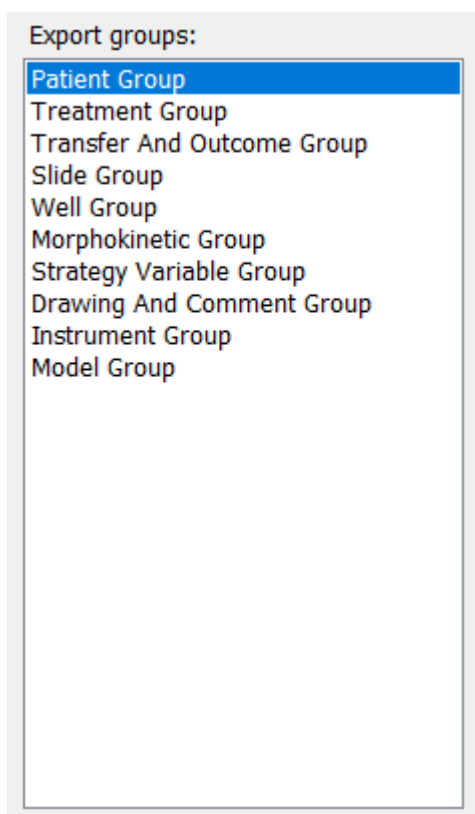
If you select **Export empty wells**, a row will be inserted in the export file if there is an empty well in the culture dish. The row will not contain any data.


If you select **Force 16 rows**, the export file will contain 16 rows for each culture dish included in the file, even if you are also using culture dishes with fewer wells. This may be useful if you

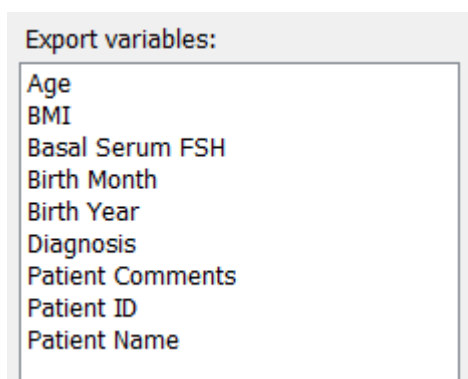
are working with both EmbryoScope D or EmbryoScope Flex and EmbryoScope+ or EmbryoScope 8.

You are now ready to specify which variables you want to include in the export:

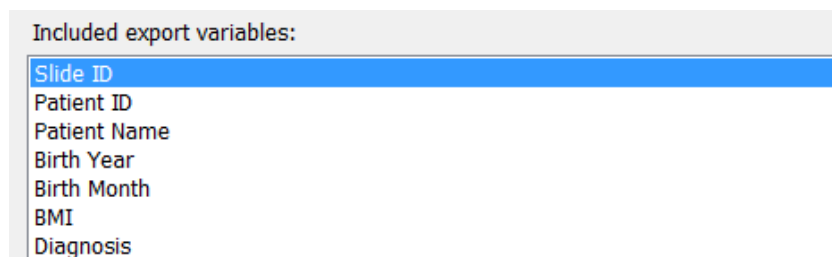
5. From the right side of the tab, select from which group you want to include variables, e.g. **Patient Group** or **Morphokinetic Group**:



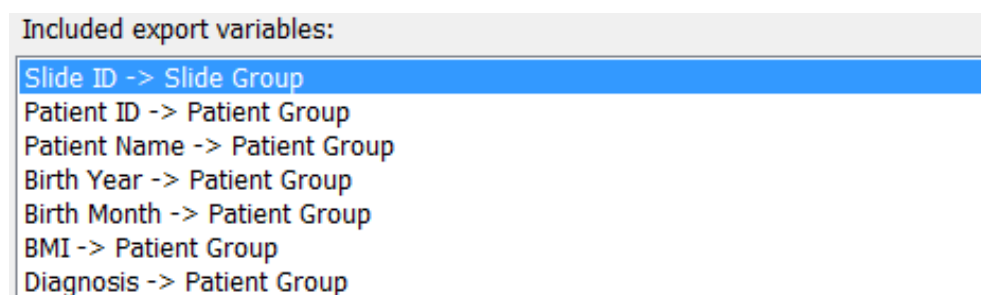
6. Select which variables you want to include from the group, and click on . Press and hold down the Shift or Ctrl key on the keyboard to select multiple variables. You can also double-click on a variable to include it.




The selected variables will now be displayed in the **Included export variables** list (middle part of the tab):

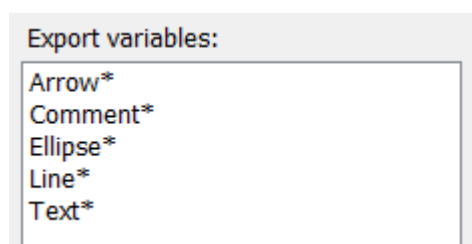




If you select the **Show export groups** check box, the list will display which group the included variables originally came from:



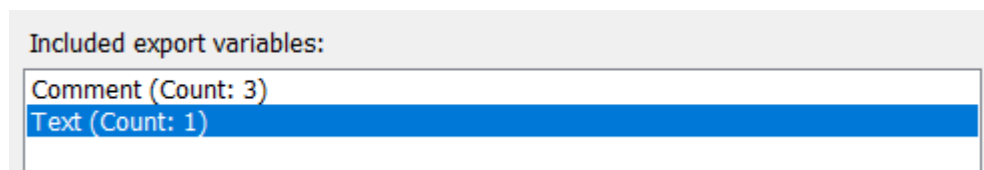
You can remove a variable from the export by selecting it and clicking on . Press and hold down the Shift or Ctrl key on the keyboard to select multiple variables.

7. Repeat the two previous steps to select as many export variables as you want.
8. Export variables marked with an asterisk can be included several times in the export file. This is relevant for variables that can be annotated more than once for each embryo:



To increase or decrease the number of times that one of these variables is included in the export file, select it on the list of included export variables, and click on either  or .

Next to the relevant variables, the list specifies how many columns will represent these variables in the final export file (**Count**):



9. You can move included variables up and down on the list by clicking on either the up or the down button:





The variables will appear in the displayed order when you create the final export file.

10. Click **Save**.
11. Go to the **View All Slides** page, and select one or more culture dishes to export data from. Then click the **Export** button.
12. Enter the name of the export file you are about to create, and select the location of the new file. In the **Save as type** field, select the name of the export you have just created.

The software now generates a file that contains the defined export variables from the selected culture dishes.

7.9 About tab

When you click the **About** tab on the **Settings** page, you can verify the version number and UDI code of both the EmbryoViewer software and the connected ES server and check how much memory is currently used on the ES server:

General	User	Annotations	Models	Embryo Details	Brands	Export	About
<div> <div> EmbryoViewer version 7 <div> <div>REF</div> <div>16622</div> </div> <div> <div>VERSION</div> <div>7.9.5.29564</div> </div> </div> <div> <div>  <div> Vitrolife A/S Jens Juuls Vej 16 8260 Viby J Denmark </div> </div> <div> <div>CE</div> <div>MD</div> </div> </div> </div> <div> <div> <div>UDI</div> <div>(01) 05712714676222 (8012)</div> <div>7.9.5.29564</div> </div> </div>							
<div> <div> ES server version 7 <div> <div>REF</div> <div>16612</div> </div> <div> <div>VERSION</div> <div>7.9.4.29439</div> </div> </div> <div> <div>  <div> Vitrolife A/S Jens Juuls Vej 16 8260 Viby J Denmark </div> </div> <div> <div>CE</div> <div>MD</div> </div> </div> </div> <div> <div> <div>UDI</div> <div>(01) 05712714676123 (8012)</div> <div>7.9.4.29439</div> </div> </div> <div> <div>ES Server Capacity: 33.00 TB free of 33.00 TB</div> <div>ES Server Capacity warning limit at: 500 GB free</div> <div>ES Server Capacity degradation limit at: 25 GB free</div> </div>							

You can also see the upper and lower server memory warning limits. These limits indicate when a warning that the ES server hard disk is running out of space will be displayed. The default values can be changed by Vitrolife upon request and are as follows:

ES server:

- Upper limit (capacity warning limit): 200 GB
- Lower limit (capacity degradation limit): 25 GB

ES server+:

- Upper limit (capacity warning limit): 500 GB
- Lower limit (capacity degradation limit): 25 GB

A warning will be displayed if either of these limits is exceeded. The warning will specify whether the upper or the lower limit is exceeded. Contact Vitrolife for support if you see this warning. You may need to increase your hard disk capacity or free up space on the hard disk.

If the lower limit is exceeded, any connected EmbryoScope and CulturePro incubators will be disconnected until enough free hard disk space is available. During this period, images will only be stored locally on the incubators and not on the ES server. When hard disk space is available again and the incubators are able to reconnect, all locally stored images will be transferred to the ES

server and stored as normal, and complete time-lapse videos will be available in the EmbryoViewer software.

8 Failure of the EmbryoViewer software





If the system crashes, this may have a number of causes, e.g. malfunction of the hard disk, network breakdown, virus infection, crash of the Windows operating system, database corruption, internal failure of the EmbryoViewer software, etc.

While the software is not functioning properly, any running culture dishes can be assessed under a standard microscope or directly from the EmbryoScope incubator.

To solve the problem, restart the EmbryoViewer software. This will not affect the data acquisition for running culture dishes.

If this does not solve the problem, immediately contact Vitrolife for support.

9 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 12.

10 Disposal of waste

In order to minimize 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.

11 Index

- Alarm status; 23
- Annotate page; 36
- Association between various IDs; 14
- Average incubation conditions for all culture dishes; 71
- Blastomere activity; 38
- Brands; 96
- Cell divisions; 39
- Contact information; 106
- Creating or deleting a patient; 24
- Custom expressions
 - defining; 82
 - deleting; 84
 - editing; 84
- Database menu; 69
- Dynamic score, Z score and morphological grade; 39
- Embryo selection on the Annotate page; 42
- Embryo selection on the Timeline page; 35
- Exports; 98
- Formulas; See Custom expressions
- Fragmentation; 40
- General description of the EmbryoViewer software; 12
- Hardware requirements; 5
- Incubation page; 64
- List of culture dishes; 70
- Measuring blastomere size; 43
- Model validation; 92
- Models
 - additive; 88
 - hierarchical; 87
 - multiplicative; 90
- Morphological grade; 36
- Multinucleation; 40
- Outcome, registering; 54
- Overview of the navigation panel; 13
- Patient Details page; 25
- Patients menu; 24
- Printing reports; 60
- Reports; 58
- Running menu; 21
- Saving changes; 34; 46
- Settings; 71
- Side-by-side view; 52
- Slides menu; 30
- Thawed embryos, culturing; 57
- Thawed embryos, transferring; 55
- Timeline page; 35
- User-defined annotation variables; 41
- User-defined variables
 - adding; 77
 - deleting; 77
 - redefining; 77
- Using the annotation table; 38
- Videos; 60
- View All Patients page; 24
- Viewing all slides; 69
- Viewing different focal planes; 32; 36
- Viewing patient treatment information; 26
- Viewing running culture dishes; 23
- Viewing slides; 30
- Viewing time-lapse images of embryo development; 30; 42
- Viewing time-lapse videos
 - jog wheel; 31
 - keyboard; 31
 - mouse; 31
 - navigation buttons; 31
- Visible nuclei; 39

12 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 2 working days)



Vitrolife A/S
Jens Juuls Vej 16
DK-8260 Viby J
Denmark

Telephone: +45 7221 7900

Website: www.vitrolife.com



VITROLIFE A/S, DENMARK