

# IVF and ICSI

# at Spaarne Gasthuis

# **IVF (In Vitro Fertilisation)**

IVF means 'fertilisation in glass'. IVF is also called test-tube fertilisation. Various techniques are used in the laboratory to try to fertilise the eggs with sperm. When fertilisation occurs, embryos are created. These embryos are transferred into the womb. Hopefully, this will then lead to a pregnancy. The steps followed in this treatment are explained in this brochure.

# **ICSI (Intracytoplasmic Sperm Injection)**

ICSI is almost the same as IVF. The only difference is that the sperm is injected into the egg instead of being mixed with it.

The Spaarne Gasthuis works very closely with the Amsterdam UMC IVF Centre, location VUmc, for both treatments. You can watch a webinar about IVF treatment on the website of the IVF Centre: www.vumc.nl/ivf.



# Scientific research

In the Netherlands, approximately 23% of all started IVF treatments result in a live birth ('take home baby rate'). About 60% of all couples who undergo several IVF treatments become pregnant. We are attempting to increase this percentage through scientific research. As a result, the IVF treatment is subject to regular changes. Consequently, the information in this brochure may be outdated during your treatment. We appreciate your understanding in this matter. You may also be asked to participate in a scientific study. You will then receive all the information you need to decide if you want to participate.



# **Reasons for IVF or ICSI treatment**

- severe abnormalities of the fallopian tubes (tubal pathology)
- severe endometriosis
- male subfertility (reduced sperm quality)
- unexplained infertility. If no pregnancy occurs for whatever reason, then, in most cases, IVF will be proposed. IUI (intrauterine insemination) treatment has then usually also been tried unsuccessfully.

### The treatment: summary

- A woman usually only has 1 mature egg (follicle). During an IVF/ICSI treatment, several follicles must ripen. This is possible through the use of medicines that contain the hormone gonadotropins. These hormones are administered via an injection.
- The growth of the follicles are monitored by ultrasound.
- Once the follicles have a diameter of 18 to 22 mm, Ovitrelle® is administered (an hCG injection). This ensures that the eggs are released for egg retrieval.
- The aspiration and emptying of the follicles takes place 34 to 38 hours later. A vaginal ultrasound is made by puncturing the vaginal wall. This is called follicle aspiration or egg retrieval.
- After this, the laboratory phase of the treatment begins. Eggs and sperm are brought together to create embryos.
- If fertilisation occurs, an embryo will be implanted in the womb (3 to 5 days after the egg retrieval).
- A pregnancy test is done about 15 days after egg retrieval.

If there are multiple embryos of good quality, they can be frozen. An embryo that has been frozen is called a cryo. If you do not fall pregnant, the cryo can be transferred to your womb after 1 month. An IVF treatment takes 1 or 2 months, depending on the treatment schedule. If the treatment (including the cryos) does not result in pregnancy, you may restart the IVF treatment (hormone stimulation, follicle aspiration and embryo transfer).

# The treatment: step by step

This section of the brochure describes the procedure at Spaarne Gasthuis and the UMC Amsterdam IVF Centre, VUmc location. We highly recommend that you also watch the webinar on their website www.vumc.nl/ivf.

#### An IVF treatment has seven stages

- 1. Pretreatment
- 2. The stimulation of the ovaries
- 3. The follicle aspiration or egg retrieval
- 4. The laboratory phase
- 5. The transfer of the embryo
- 6. The period after the transfer
- 7. The pregnancy test

# **IVF/ICSI** behandeling schematisch



#### 1. Pretreatment

Ongeveer 2 maanden

Contact the Spaarne Gasthuis Fertility Centre on the first day of your period (= cycle day 1). via e-mail: fertiliteit@spaarnegasthuis.nl

phone: +31 23 224 0918

We will ask for your name, registration number, date of birth, type of treatment (IVF/ICSI) and the phone number on which you can be reached that day. We will then check that all the conditions for starting treatment have been met and discuss the day on which you will start taking the medicine Decapeptyl®. The storage agreement (see appendix at the end of this brochure) for the freezing of embryos must be signed and returned at the start of treatment.

#### 2. Stimulation of the ovaries

In a spontaneous cycle, one follicle usually matures. We try to increase this number using hormones that encourage the ovaries to ripen more than one follicle. For an explanation of the medicines used, see the appendix 'Medicines used during the IVF/ICSI treatment' further on in this brochure. Two stimulation protocols are used. Your doctor will tell you which protocol is suitable for you during the consultation. In most cases, the long protocol is chosen.

#### The long protocol

Start taking the pill on cycle day 3. The pill calms the ovaries. After taking the pill for at least 2 weeks, you will start with Decapeptyl® injections on the agreed day.

A withdrawal bleed almost always occurs after finishing the pill strip. Contact the Spaarne Gasthuis Fertility Centre again on the day of the withdrawal bleeding or after one week if there is no bleeding. You will be given an appointment for an ultrasound scan. If everything is in order, stimulation of the ovaries is then started with either Gonal-F® or Menopur®. You will take this medicine until the follicles have matured.

The IVF treatment following the long protocol takes 2 months. Please take this into account when planning a holiday, for example.

#### The short protocol

Start the Decapeptyl® injections on cycle day 2. The Decapeptyl® injections help a little to stimulate the ovaries in the short protocol. But more importantly, they suppress natural ovulation. Start the stimulation of the ovaries with Gonal-F® or Menopur® on cycle day 3.

You will continue with Decapeptyl® and Gonal-F® or Menopur® until the follicles have matured and the Ovitrelle® injection has been scheduled.

#### Stimulation

The dosage of the medication depends on various factors, including your age and the response to any previous hormone treatments. The way you react to the medication determines how long the stimulation lasts. On average, the stimulation phase lasts about 8 to 14 days. The response to hormone stimulation is assessed by means of 2 tests:

- A transvaginal ultrasound scan: the growth of the follicles is monitored by means of a transvaginal ultrasound scan whereby the transducer is inserted into the vagina. Your bladder does not have to be full for this ultrasound.
- If necessary, a blood sample will be taken after the ultrasound scan. The level of the hormone oestradiol in the blood is measured. This hormone level is a measure of the development of the follicles.

The ultrasound scan and the blood test take place at the Spaarne Gasthuis in Haarlem Zuid. Then an appointment is made for the next step. When the follicles are ripe for aspiration, the VU will call you with the date and time on which you must inject the Ovitrelle®.

#### Concluding the stimulation phase

If the ultrasound reveals that the follicles are large enough (between 18 and 22 mm), Ovitrelle® is administered to end the stimulation. Ovitrelle® initiates the last stages of ripening of the eggs (you will not inject Decapeptyl® or FSH on that day). This vital injection concludes the stimulation phase and must always be given in the evening. There are approximately 36 hours between the Ovitrelle® injection and the egg retrieval.

We will call you in the afternoon to let you know:

- the time of the Ovitrelle® injection
- the date and time of the egg retrieval (at the VUmc)
- the date and time for submitting the sperm sample (at the VUmc)

#### 3. The follicle aspiration (egg retrieval) at the VUmc

The egg retrieval takes place at the VUmc. You must both be able to show proof of identity on the day of the retrieval and you must have your VUmc patient number with you.

#### What this involves for the woman

- The retrieval is an outpatient procedure under local anaesthetic.
- You may have a light breakfast in the morning on the day of the egg retrieval (for example, a rusk and a cup of tea).
- You are expected to report to the IVF Centre at least half an hour before the agreed time for the procedure, and can take a seat in the sitting area with purple chairs near the aquarium. Your partner is welcome to accompany you during the procedure.
- Half an hour before the procedure, you will be given a tablet of Dormicum to calm you down and Pethidine by injection for pain relief.
- The follicles are aspirated via the vagina with the aid of an ultrasound machine.
- The egg retrieval takes about half an hour.
- The number of eggs obtained is known approximately 20 minutes after the aspiration.
- After the egg retrieval, you must lie down for about half an hour.
- Many patients dread the procedure. This is understandable, but, in practice, it is usually not so bad.
- You may not drive after the egg retrieval.
- Working on the day of the egg retrieval is not recommended.
- You may experience vaginal bleeding for a few days afterwards. Do not use tampons.

If the procedure resulted in the retrieval of eggs, you will be given a form with the following information:

- The Utrogestan® capsules schedule: you must insert 2 capsules vaginally 3 times a day, starting on the day of the egg retrieval. The medicine is absorbed quickly, but residue from the capsules will remain, leaving you with a thick, white discharge.
- The date and time the VUmc will contact you to discuss if and when the embryos will be transferred.
- You can take a pregnancy test 15 days after the retrieval. You will be given a telephone appointment to discuss the result.

#### What this involves for the man

You will be asked (before or after the egg retrieval) to produce a sperm sample via masturbation in one of the semen rooms. You will be given an appointment for this. If you think that producing a sperm sample will cause problems, please let us know so that we can look for a solution together.

You may not ejaculate for 3 days prior to the procedure. When you hand in the sperm sample, you must be able to identify yourself, show your VUmc patient number and sign a form.

#### 4. The laboratory phase

Once eggs have been obtained, they are combined with pre-treated sperm or the ICSI procedure takes place. We will know whether fertilisation has occurred and how the further development of the embryos is progressing on the 2nd day after the retrieval. If the development is successful, the VUmc will call you with an appointment for the transfer of the embryo into your womb. This is almost always on the 3rd day after the retrieval.

#### 5. The embryo transfer

- You must both be able to identify yourself for the embryo transfer.
- The embryo transfer into the womb takes place at the outpatient clinic. No anaesthesia is required.
- Just before the embryo transfer, the doctor will tell you how many eggs have been fertilised, how many embryos have been created and which has been selected to be transferred into the womb at that time.
- You will lie on a gynaecological chair with your legs in the leg holders. A speculum is inserted into the vagina to reach the cervix. One or two embryos will be transferred into the womb through a thin plastic tube that is carefully pushed through the cervix into the womb.
- During the embryo transfer, an ultrasound is made via the abdomen. In order to see it properly, you will need to have a full bladder.
- After the tube has been removed and found to be in order after a check by a laboratory employee, you may get up, get dressed and go home.
- You can then resume your daily activities.
- You will be told whether there is a chance that embryos can be frozen. Freezing is done after the embryo transfer and only if the embryos are well divided. A letter will be sent to your home address within 3 weeks stating whether embryos have been frozen (and in how many tubes).

#### 6. The period after the transfer

You will continue to take Utrogestan® capsules vaginally after the transfer. Experience has shown that the period following the embryo transfer should not be underestimated. The tense period of waiting to see whether the treatment has succeeded is very stressful.

#### 7. The pregnancy test

If one or more embryos were transferred, you can take a pregnancy test 15 days after the retrieval. You will be given a telephone appointment to discuss the result of the pregnancy test and to make further arrangements. Even if you start to bleed earlier, you should still take a pregnancy test on the agreed day after the retrieval and continue with the medication according to the schedule. The use of Utrogestan® capsules usually delays menstruation. The absence of bleeding does not automatically mean that you are pregnant.

#### Side effects, risks and complications

For specific side effects of the medicines used, see the section entitled 'Medicines used during IVF/ICSI treatment' later in this brochure.

The most important complications that can occur are:

- The ovaries may react aggressively, causing lots of follicles to mature and the production of a large amount of female hormones. The result is abdominal pain, rapid weight gain and leakage of fluid from the blood vessels, which increases the risk of thrombosis. This can be a very serious complication and need hospitalisation. We always try to prevent this; sometimes stimulation is stopped or the transfer postponed for this reason.
- Multiple births: IVF treatment sometimes involves transferring more than one embryo into the womb. The number of embryos to be transferred depends mainly on the reason for IVF, the quality of the embryos and the woman's age. Approximately 90 to 95% of all pregnancies are single pregnancies. Between 5 and 10% are twin pregnancies. Triplet pregnancies are very rare.
- Bleeding/infection: an infection or bleeding can occur as a result of the aspiration.
- Low response: it can also happen that, despite high doses of FSH, too few eggs mature (low response). In such cases, we might decide not to do the egg retrieval but to proceed with IUI if possible. This can mean that a subsequent attempt is discouraged.
- A recent study shows a slightly increased risk (1.6 vs 0.4) of sex chromosomal abnormalities associated with ICSI. These abnormalities cannot be detected by a NIPT test, but amniocentesis (amniotic fluid puncture) can be used for this purpose. If you are pregnant, the doctor will discuss with you whether you want a consultation about this with the Amsterdam UMC, location AMC in Amsterdam.

#### The cryopreservation cycle

Hopefully, there will be some embryos left over from the IVF or ICSI treatment that are of a good quality to be frozen. If this is the case, you will receive written notification of this within 3 weeks of the embryo transfer. It is, therefore, not 100% certain whether embryos can be frozen on the day of the embryo transfer. In practice, freezing is possible in approximately half of the treatments. Experience has shown that only good-quality embryos can withstand this difficult process. Embryos are frozen in tubes, which usually contain 1, 2 or 3 embryos. These embryo tubes can be thawed at a later stage. If the embryos thaw properly (the chance is about 90%), an embryo transfer can then take place.

There are two possibilities:

- The IVF or ICSI treatment results in a pregnancy. In this case, of course, thawing and embryo transfer can only take place if there is a demand to become pregnant again after the pregnancy. Embryos are stored in tubes and can be kept for years without losing their vitality. Depending on the quality, they are frozen singly or in pairs. All biological processes are halted by the procedure.
- The IVF or ICSI treatment does not result in a pregnancy. A cryo treatment can be started after at least one rest month.

# Cryo treatment

- Just as with IVF or ICSI treatment, you must register for cryo treatment on the first day of your period.
- It regularly happens that you cannot start a cryo cycle because of too many registrations, or that during the cycle, too many people are ready on the same day. Unfortunately, we cannot accommodate everyone.
- In the spontaneous (own) cycle, 1 follicle usually matures. The growth is followed by echoscope, and the Ovitrelle® is injected when the follicle has a diameter of about 18 mm. The Ovitrelle® injection is mainly given for practical reasons. It makes it possible to more accurately determine the optimum time for thawing and transferring the frozen embryos. This increases the chance of pregnancy.
- The tubes are thawed individually. The embryos are then checked to see whether they have survived the freezing and thawing process.
- The IVF laboratory can thaw embryos for a maximum of 6 patients per day (3 at the weekend). Sometimes, however, there are more applications for thawing embryos. The thawing can then be planned with reservation. This means that on the day of the thawing, the laboratory will determine whether there is enough time between the other activities to still perform the thawing. As a rule, about 75% of the thawings that are planned under reservation are still performed. You will only hear whether an embryo transfer will occur (if the thaw took place) when you are called in the morning.
- Some women do not have a menstrual cycle. In this case, the so-called substitution schedule is chosen. This is a combination of the hormones oestradiol (Progynova® tablets) and progesterone (Utrogestan® capsules) that mimics the situation in a natural cycle. If pregnancy occurs, these medicines should be continued until a gestational age of 12 weeks

#### The embryo transfer

- On the morning of the transfer, we evaluate the state of the embryos after the freezing and defrosting process and whether we can do the embryo transfer that day.
- The VU will call you between 9:30 and 10:45 on the morning of the embryo transfer to let you know whether the embryo transfer will take place. If it's happening, you will be told the time you are expected. Embryo transfers usually take place from 11:00. Unfortunately, in about 10% of cases, the embryos do not survive the entire process. In that case, no embryo transfer can take place.

#### The period after the embryo transfer

You can do a pregnancy test from 12 days after the embryo transfer. You will be given a telephone appointment to discuss the result and make further arrangements. You must do a test, even if you have already started to bleed.

# **General information**

#### Is IVF treatment painful?

In the vast majority of cases, IVF treatment is relatively painless. The (self) injection of the hormones can hurt a little, but this is usually not too bad. The hormones may cause a bloated feeling. Some women experience abdominal pain or a heavy feeling in the lower abdomen due to the swelling of the ovaries.

Follicle aspiration under ultrasound control can be a tedious procedure. A needle is pierced through the vaginal wall. It can be particularly unpleasant if the ovaries are positioned unfavourably. This procedure is performed in the outpatient clinic and without anaesthesia.

There are various pain-relieving techniques. As a result, most women find the procedure tolerable. The transfer of the embryos is not medically taxing, but the emotional burden should not be underestimated.

#### IVF and your environment

We advise you to tell a few people that you are undergoing IVF treatment. People will get involved one way or another. Because of the regular visits to the outpatient clinic for injections or ultrasound scans, it is not easy to keep the IVF treatment a secret, for instance, at work. It is also better for family or good friends to be informed. Good friends and close family can give moral support if they know about it.

#### Stress

The influence of tension or stress on the outcome of an IVF treatment has not yet been the subject of scientific research. It is important to know that some things can feel easier when there are fewer factors that cause stress. However, a certain level of stress cannot be avoided during IVF treatment. The best thing to do during the IVF treatment is to continue with life as you normally would, doing as many things as possible that you would normally do. The period following the embryo transfer in particular is experienced as very stressful and difficult. The treatment is then complete, and all that remains to do is to wait and see whether implantation occurs. It is not necessary to give up all normal daily activities and to live as carefully as possible. That only adds to the stress. Normal activities, including physical activities, can continue as usual.

If the IVF treatment did not result in a pregnancy, it means that you will have to start all over again after a rest period. This prospect can be very stressful. A couple must be strong enough to cope. Sometimes outside help is needed. Social workers can offer help. You can also turn to the Stichting Ambulante FIOM. This foundation offers personal support to couples who are in the process of IVF treatment (www.fiom.nl).

IVF often follows a series of tests and treatments that did not lead to pregnancy and a child. There are no other options after IVF. This is why most couples have high expectations of IVF treatment. Unfortunately, in about 40% of all couples, IVF does not result in the birth of a baby. This group can feel lost. After years of trying, examinations, treatments, excitement and hope, all that is left for them is a huge disappointment. At that moment, they need good care from family, friends and perhaps professional counselling. They can then start to process their intense grief about the loss of a long-cherished dream of one or more children. This often leads to a mourning process: the grief about not fulfilling the wish to have children. It might help if those who start IVF can accept in advance that there is a chance they might not fall pregnant.

#### Drugs

The use of drugs (hard drugs and soft drugs) and fertility treatment do not go together. The Amsterdam UMC IVF Centre, location VUmc, does not condone the use of drugs. Soft drugs are also harmful to your fertility treatment and can harm the (unborn) child. We give the effects of cannabis use below. We use this as an example because it is the most widely documented. Scientific research has shown that the use of cannabis has a negative effect on sperm quality. Cannabis use can also affect the DNA in sperm. It lowers the chance of successful fertility treatment because fewer eggs mature, fewer embryos are formed and the chance of fertilisation decreases. It also increases the risk of miscarriage. Children of users have a higher risk of premature birth, lower birth weight, admission to the incubator ward and addiction later in life. If you want to undergo treatment at the IVF Centre, you must stop using

drugs at least three months beforehand. We will stop the treatment if you continue to use drugs.

# **Further information**

Freya, the patients' association for fertility problems, provides information on infertility (causes and possible solutions). This association is actively engaged in combating misunderstandings and taboos surrounding the problem of unwanted childlessness. It consists entirely of volunteers and also promotes the interests of couples who wish to have children in the political arena. www.freya.nl, e-mail: secretariaat@freya.nl

# IVF and health insurance

#### **Reimbursement for IVF**

As of 1 January 2007, 3 IVF treatments are (almost) fully reimbursed, including any embryo transfers from frozen embryos originating from those 3 IVF treatments. IVF treatment is covered by basic health care insurance. If the first 3 IVF treatments are unsuccessful and, in consultation with the doctor, the decision is made to continue, the hospital will charge the patient for the treatment. You will then have to pay for the treatment yourself. You will also have to pay for the medication. The costs: for an IVF treatment, about  $\in$  2050 + medication about  $\in$  1800; for an ICSI treatment, about  $\in$  2300 + medication about  $\in$  1800 and for a cryo cycle, about  $\in$  700. If you have any questions about IVF reimbursement, please contact Zorgverzekeraars Nederland, the umbrella organisation for health insurers, telephone +31 30 698 8911. Freya also has a lot of information about reimbursement for IVF treatments on its website. If you have any doubts or are unclear about reimbursement, you can also contact your health insurer. If you have a disagreement with your health insurer, you can contact the Stichting Klachten en Geschillen Zorgverzekering, Postbus 291, 3700 AG Zeist, telephone +31 30 698 8360.

#### Stopping and then deciding to continue again

Many couples find it difficult to stop the IVF treatment for a while if, for whatever reason, it becomes too much of a burden at some point. It is good to discuss this with your doctor. It does not jeopardise your reimbursement. You are and remain entitled to full reimbursement of the 2nd and 3rd IVF treatment, regardless of when this takes place, up to the age of 43. Medicines used during the IVF/ICSI treatment

#### Microgynon® 30

This pill is used in the long protocol to suppress the ovaries. Start taking this on the 3rd cycle day.

#### Decapeptyl®

Decapeptyl® must be injected under the skin (subcutaneous) once a day. You will start the injections in consultation with the doctor. In the long protocol, this is usually after 2 weeks of taking the pill, but it can also be later; you will be informed when to start. After starting the Decapeptyl®, you will continue taking the pill for at least 7 days. The Decapeptyl® injections are intended to calm the ovaries (reinforce the effect of the pill) and suppress natural ovulation. This prevents the follicles from disappearing before they can be aspirated. With the short protocol, you start on cycle day 2. You should continue with the Decapeptyl® injections until the follicles are 'ripe', until the day of Ovitrelle®.

Side effects: mood swings.

#### Gonal-F®

Subcutaneous injections of follicle-stimulating hormone (FSH). The dose is determined individually and can be adjusted during the stimulation phase according to the findings of the ultrasound scan and blood tests.

Side effects: local skin reactions, headaches and mood swings.

#### *Menopur*®

Subcutaneous injections of follicle-stimulating hormone (FSH) and luteinising hormone (LH). The dose is determined individually and can be adjusted during the stimulation phase according to the findings of the ultrasound scan and blood tests. Side effects: local skin reactions, headaches and mood swings.

#### **Ovitrelle**®

This single, final injection initiates the final egg maturation phase. This injection must always be given in the evening, 34-38 hours prior to the egg retrieval. The VUmc will tell you when.

#### **Utrogestan®**

These are capsules that you must start taking immediately after the egg retrieval. Dosage: 2 capsules 3 times a day, to be taken vaginally. You will continue to take it up to and including the day of the pregnancy test.

#### **Progynova®**

These are tablets that you have to swallow. They contain oestradiol, which helps to build up the endometrium. Side effects: headache, tight breasts.

As of January 2014, almost all medicines used in an IVF or ICSI treatment have come under a new system whereby the medicines are included in the hospital budget. The consequence for you is that the best place to buy medication for IVF or ICSI treatment is at the Spaarne Gasthuis outpatient pharmacy. You may receive a separate invoice for the pill or Utrogestan® (which is sometimes not reimbursed).

#### **VUmc practical matters**

IVF Centre, gebouw Zuid, Amstelveenseweg 601, 1081 JC Amsterdam Reception phone: +31 23 444 3268, www.vumc.nl/ivf

#### How to reach us

For the most recent information, please visit the website of Amsterdam UMC, location VUmc: https://www.vumc.nl/contact-en-route.htm

#### Digital Patient Portal MijnSpaarneGasthuis and Mijn Dossier

- The MijnSpaarneGasthuis patient portal gives you online access to your medical data. This is the digital environment for patients of the Spaarne Gasthuis. You can register via this link: https://spaarnegasthuis.nl/mijnspaarnegasthuis
- **Mijn Dossier** gives you online access to your medical data. This is the digital environment for patients of Amsterdam UMC, location AMC and location VUmc. You can register via this link: https://www.vumc.nl/zorg/mijn-dossier/wat-is-mijn-dossier.htm

In MijnSpaarneGasthuis and Mijn Dossier, you can view your medical file, view appointments and check results. This gives you more insight into your health.

Even if you are already using MijnSpaarneGasthuis, it is also advisable to activate Mijn Dossier so the VU can also pass on important times etc. directly to you.



#### PARKEERLOCATIES VU EN VUmc



The IVF Centre is located here, P1 is the best place to park.

# Appendices

We will ask for your written permission for a number of matters before starting the treatment. You will be given a form to sign for this purpose.

#### Consent for further use of body materials and anonymous medical data

The body materials in question are the residual sperm sample and unfertilised eggs.

#### Residual sperm sample

If a sperm sample is of good quality, there will be a portion left over that is not needed for the IVF treatment. This can be used to carry out essential quality tests in the laboratory. After that, it will be destroyed.

#### Unfertilised eggs

In practice, approximately 60 to 70% of the eggs are fertilised by IVF or ICSI. On the day after the retrieval, we determine which eggs have been fertilised. The unfertilised eggs are no longer needed for the treatment but could be used to practise new techniques or as practice material for new employees. Afterwards, the eggs are destroyed in the usual way.

#### Anonymous medical data

We also collect medical data from the treatments we carry out. This medical data can be used anonymously for scientific research. It is not always necessary to ask your permission to conduct this kind of anonymous research. The researchers will not know your name or any other personal details. The research thus complies with the statutory regulations.

#### Objection

- If you object and do not want the remainder of your sperm sample or unfertilised eggs to be used, you must sign the statement provided at the intake interview and return it to us. If you do not object, you do not have to do anything.
- If you don't want your medical data to be used anonymously for scientific research, you can object. Your data will then not be used. Please send an e-mail to secretariaat.ivf@vumc.nl. In this e-mail, you can inform us that you do not want your data to be used anonymously. Please include your name, date of birth and VUmc patient number.

#### Embryo storage agreement (embryos left over)

With IVF treatment, it is not possible to predict how a person will react to the hormonal stimulation of the ovaries or how well the sperm can fertilise the eggs. This is especially true for a first IVF treatment. It is common for more embryos to develop in the laboratory than are needed for transfer into the womb that month. If no pregnancy occurs after a fresh embryo transfer, embryos can be frozen and then later thawed and transferred into the womb. In practical terms, this means an extra chance of pregnancy without having to undergo the whole complicated treatment. The chance of pregnancy with embryos that have been frozen is slightly lower, but the risk of congenital defects is not higher. The technique of freezing embryos is still improving. Many children have been born, also in the Netherlands, from frozen and later thawed embryos.

Sometimes a couple no longer wishes to claim the remaining frozen embryos. Perhaps because their desire for children has been fulfilled. A couple has the right to dispose of these embryos, which is legally different from the right of ownership. Couples can decide to destroy the remaining embryos or make them available for scientific research.

Donating embryos for adoption has been legal since 20 June 2002 ('Embryo Law').

#### Embryo storage agreement

IVF was introduced in the Netherlands as a method of artificial reproduction in the early 1980s. IVF brought an important increase in treatment possibilities for couples with fertility problems. By keeping the embryos frozen and using them later (cryopreservation), the efficiency of IVF treatment is increased. The embryos that are frozen were created in vitro and not used immediately during transfer into the womb to create a pregnancy. The embryos are left over.

The stored embryos can be used in various ways.

The main purpose is to later transfer the embryos to the womb of the woman of the couple for whom the embryos were created. If a couple no longer claims the stored embryos, then the other purposes for which embryos may be destined and used according to the Embryo Act can be considered.

The embryos can then be made available for:

1. facilitating the pregnancy of another woman (embryo donation)

2. cultivating embryonic stem cells for medical purposes, medical and biological scientific research and education and

3. conducting scientific research that is permitted by law.

The VU Medical Centre (VUmc) does not participate in the option mentioned under 1. Embryos in these cases will be transferred to another IVF Institute that offers this treatment option. VUmc is responsible for the transport.

The Embryo Act includes regulations on control rights for the use of embryos for purposes other than to realise pregnancy in the couple for whom the embryos were created. If donated gametes have been used to create the embryos and the donor has used the option given in Article 6 Paragraph 4 of the Embryo Act, their right of control over the use of the embryos for purposes other than to realise a pregnancy in the couple referred to should also be taken into account. It is important that parties involved in the storage of embryos make proper arrangements regarding the various aspects of storing and transferring the embryos and exercising their right of control. The Embryo Act's basic principle is that those involved must jointly consent to the use of the embryos, that use cannot take place in the event of a difference of opinion between those involved and that any of those involved can revoke such consent at any time without specifying why. This also applies to the storage of embryos for later use. The legal basis for storage lapses if one of the partners no longer wishes to be involved. One should also take into account the possibility of later use post-mortem after the death of one of those with rights of control over the embryos, usually the woman or her partner. The Embryo Act leaves room for such post-mortem use, provided those involved have given their written consent prior to death. At the VUmc, post-mortem reproduction is performed after permission of the Medical Ethics Committee in each individual case. Various consequences of exercising control rights are further elaborated and laid down in the present agreement on the storage and transfer of embryos, as well as the purpose, term, costs and liability in the event of storage. A further explanation of this agreement has been added. Various consequences of exercising control rights are further elaborated and laid down in the present agreement on the storage and transfer of embryos, as well as the purpose, term, costs and liability in the event of storage. A further explanation of this agreement has been added.

# Clarification of the storage agreement for embryos

#### Nature of the agreement

The agreement concerns embryos created as part of an IVF treatment. If a number of embryos are not transferred as part of this treatment, storage of these embryos through cryopreservation may become an option. The primary goal is to use these embryos for a new treatment for the couple involved to realise a pregnancy. If this form of use is no longer relevant, other purposes deemed permissible by law may come into play. Given the context in which the embryos are created, the question may arise as to whether the agreement by which the IVF Institute commits itself to the storage of embryos for the benefit of the couple involved should be considered part of the treatment agreement or as a separate storage agreement. This distinction has consequences in particular for the possibility to include provisions in the agreement aimed at excluding liability. When drawing up this agreement, the VUmc assumed that this was a service to be provided by the IVF Institute which was separate from the (original) treatment agreement. Based on the purpose intended by the parties – storage of the embryos for possible future use – the agreement has the nature of a storage agreement.

#### Parties to the agreement

Control of the embryos belongs to those for whose benefit they were created. This is a control to be exercised jointly, which implies that both partners must be involved as parties to the storage agreement. Without the consent of both partners, no agreement can be established and there is no legitimacy in preserving the embryos. The other party to the storage agreement is the legal entity operating the IVF Institute offering the storage of embryos as a service to couples involved in IVF treatment. The legal entity may appropriately provide for the mandating of one or more officers for the purpose of entering into such agreements. In the case of donation, there is a third party.

#### Commencement of the agreement

Before the agreement can commence, it is necessary to scientifically establish the suitability of embryos to be stored for a subsequent pregnancy. This determination is the responsibility of the medical practitioner. Informing the depositors of the actual storage of embryos is the responsibility of the storage facility. This demarcation of responsibilities is also important to clearly delineate the storage agreement from the treatment agreement. The assessment of the suitability of the embryos for cryopreservation is still considered part of the treatment agreement. The storage agreement will be initiated based on these findings.

#### Duration of the agreement

The choice for an initial duration of the agreement of two years is dictated by the consideration that the depositors must have sufficient time to decide whether to use the embryos to realise a pregnancy or give them another destination. After that period, the storage facility may unilaterally terminate the agreement on certain grounds. The depositors, or one of them, have the authority to terminate the agreement unilaterally at any time – also within the initial period of two years. The chosen maximum duration of the agreement of five years in total is not dictated by scientific considerations but by arguments of a practical nature. In the absence of a term set by legislation, institutes are free to determine this term. The chosen term of five years is generally long enough for the couple concerned to decide if they will use the embryos to realise a pregnancy. Within this term, a final decision on the use or destruction of the embryos can reasonably be taken.

#### Destruction or use for other purposes

The model agreement states that the couple concerned has joint authority over the embryos. This implies that if one of the partners withdraws the permission for (further) storage, the legal ground for storage lapses. In that situation the storage facility must destroy the embryos. In view of the great importance that may be attached to being able to use embryos for other purposes, the model agreement provides for the storage facility to approach the depositors with the question of whether they have mutually decided on another purpose for the embryos. In doing so, attention has also been paid to the position of a possible donor of the gametes with which the embryos were created, in accordance with the requirement of Article 6 Paragraph 4 of the Embryo Act.

#### **Rights of the depositors**

The obligation of the storage facility to deliver the embryos for certain purposes in accordance with the wishes of both depositors is implied in the sense that the applicable laws and regulations (Embryo Act and Act on Safety and Quality of Body Materials) must be observed. It is also important to note that the right of the depositors to request the embryos to realise a pregnancy does not imply that they have a right to assistance in inducing such a pregnancy from the IVF Centre. By taking custody of the embryos, the IVF Centre has not committed itself to this and can verify during each treatment whether those involved (still) fulfil the criteria for that treatment. In light of this, a provision has been made in which the storage facility has the authority to terminate the agreement if it is clear that the couple involved no longer qualify for IVF treatment, given the guidelines used for this purpose.

#### The costs of cryopreservation

The costs for storing frozen embryos are per freezing, per year, depending on the applicable national rate. The invoice date for the storage of the embryos is the day of freezing. The embryos are stored for this fee for part of the year or a maximum of one year. A new invoice will follow (annually, on the invoice date). In the event of early termination of the agreement or the use of the embryos, no refund is possible. After a timely termination of the agreement, no more invoices will be sent. Should you wish to terminate the storage agreement, you must inform the IVF Centre at least two months before the invoice date. To do so, please download the 'Declaration for the cancellation of frozen embryos' form at www.vumc.nl/ivf under 'patients and visitors', fill it in and send it back to the VUmc IVF Centre with a copy of your ID. This can be done by post or by e-mail to the addresses mentioned in the document. If you terminate the storage agreement prematurely, you will, in principle, not be eligible for a new IVF/ICSI treatment at the VUmc for 5 years.

#### **Post-mortem reproduction**

Laws and regulations do not entirely exclude the possibility of embryos being used for postmortem reproduction after the death of one of the partners for whom the embryos were created. Use for other purposes is also a possibility. For use after death, the partner in question must have given explicit and specific permission. The model agreement offers the depositor the possibility to make such a declaration of intent for use other than for reproductive purposes. As far as the use of embryos for reproductive purposes after death is concerned, it was decided to exercise restraint – in line with what was said during the parliamentary debate on the Embryo Act. If the depositors wish to give their permission for this, they must explicitly indicate this in a separate statement. Incidentally, the IVF Centre is not obliged to carry out treatment aimed at post-mortem reproduction. At the VUmc, postmortem reproduction is performed after permission of the Medical Ethics Committee in each individual case. However, based on the storage agreement, there is an obligation to hand over the embryos for purposes determined by the deceased – in accordance with laws and regulations – if the surviving partner requests this.

#### Liability

The state of current cryopreservation technology dictates that the risk of loss of quality of the embryos, as a result of which they may become unsuitable for achieving a pregnancy, must be borne by the depositors. The storage facility can be expected to store the embryos in accordance with the latest scientific standards. The agreement contains important indemnifications (exonerations) for the storage facility, which are not possible within the scope of a treatment agreement but are possible within that of a storage agreement. In some situations, however, invoking the exoneration clause may be contrary to good faith, and the storage facility must demonstrate that the exonerations are not unreasonably onerous and are justified.

On the next page, you will find an example contract containing the agreements made regarding cryo embryos. You will receive a separate storage agreement (storage agreement concerning embryos), which needs to be signed and will be included in the file. If you wish to have data concerning post-mortem reproduction recorded, please sign Article 8 Paragraph 2 and take it with you.

#### **Article 1. Definitions**

Storage facility: the institute where the IVF treatment takes place and the embryos have been created that are eligible for storage and later use and that offers the possibility of cryopreservation of embryos.

Depositors: the people on whose behalf the embryos were created during IVF treatment that are eligible for storage and further use.

IVF: the method of in vitro fertilisation by means of bringing together sperm and eggs or injecting sperm into eggs.

IVF Institute: the institute where the woman is treated for IVF and where embryos can be stored for future use.

Embryos: embryos created during a preceding IVF treatment and not yet used to achieve a pregnancy, for which either eggs and sperm from the depositors or donated eggs or sperm are used.

Cryopreservation: the act of putting and keeping selected embryos in a frozen state for the purpose of using them after thawing, primarily to realise pregnancy in the depositors.

#### Article 2. Purpose of the agreement

The purpose of the agreement is to provide for the storage of embryos created during IVF treatment in such a way that the depositors can use them at a later date – subject to the regulations of the institute – for their own reproduction or for another purpose that is in accordance with the applicable laws.

#### Article 3. Scope of the agreement

#### Paragraph 1. Taking custody of the embryos

The storage facility shall undertake to store one or more embryos suitable for storage according to the method of cryopreservation for the depositors. For this purpose: the IVF Institute has assessed – based on the latest scientific standards – whether the quality of the embryos is such that storage for later use is considered useful. The embryos selected in this manner shall be stored.

within three weeks after commencement of cryopreservation, the IVF Institute shall notify the depositors in writing of 1. how many embryos and 2. in how many containers embryos have been frozen and will be stored.

Paragraph 2. The cryopreservation procedure

The process of cryopreservation shall be performed by a gualified employee at the IVF laboratory of the IVF Institute and in accordance with the latest scientific standards, with the objective of preserving the quality of the embryos as best as possible in order to be able to use them to realise a pregnancy.

Paragraph 3 Use of stored embryos

The IVF Institute undertakes to deliver (a number of) the cryopreserved embryos for the purposes for which the depositors in mutual agreement and with due observance of the applicable laws intend to use the embryos. In certain cases, the IVF Institute shall transfer the embryos to an institute designated by the depositors that meets the legal requirements for the storage or use of embryos.

Paragraph 4 Donor gametes

If donated gametes have been used to create an embryo and the donor/donors have used the option (Article 6 Paragraph 4 of the Embryo Act) to stipulate that the consent of the donor/donors must be obtained by the depositors for any use other than for realising a pregnancy, the storage facility shall ensure that such consent is obtained before surrendering the embryos for such other purposes.

Paragraph 5 Destruction of the embryos

The IVF Institute commits itself to destroy the preserved embryos in the event the consent of one of the depositors for further storage lapses, in the event of the death of one of the depositors - with the exception of the situation referred to in Article 8 - and in the event of termination of the agreement without the depositors having jointly indicated what the embryos will be used for or – in the case of the use of donated gametes – the purpose indicated is not in accordance with the rights of control of the donor(s) of the gametes.

Paragraph 6 Loss of quality

The depositors are aware that despite observing the quality measures required by the latest scientific standards and through no fault of the IVF Institute, the process of cryopreservation may lead to a loss of quality of the embryos.

#### Article 4. Duration and extension of the agreement

#### Paragraph 1. Commencement of the agreement

The agreement regarding the cryopreservation of embryos shall commence after an examination of the embryos by the IVF Institute has demonstrated the suitability of embryos for cryopreservation.

Paragraph 2. Duration of the agreement

The agreement will be entered into for a period of two years, calculated from the day on which it was determined that the embryos are suitable for cryopreservation. The agreement will be tacitly renewed at most three times for a period of one year, up to a total maximum duration of five years, unless terminated prematurely. This maximum period may be extended upon indication.

Paragraph 3 Deviation from the maximum storage period

If the depositors wish to exceed the five-year storage period, they must submit a reasoned written request to the head of the IVF Centre. The head should discuss the request with the IVF team and if no consensus can be reached within the IVF team, submit the request to the Medical Ethics Committee for further review.

Paragraph 4 Termination of the agreement

Upon expiry of the term of the agreement, the storage facility shall give the depositors the opportunity in writing to jointly indicate within three months whether they wish to give the embryos a specific purpose in accordance with laws and regulations. In the event the depositors do not jointly indicate such a use, the embryos in storage will be destroyed.

#### Article 5. Termination of the agreement by the depositors

Paragraph 1. Authorisation of the depositors

Each of the depositors shall at all times be entitled to terminate the agreement in writing – by registered letter with acknowledgement of receipt. After termination, the storage facility shall give the depositors the opportunity in writing to jointly indicate within three months whether they wish to give the embryos a specific purpose in accordance with laws and regulations. If the depositors do not jointly indicate such a use, the embryos in storage shall be destroyed within the period of one month.

Paragraph 2. Use of the embryos in the case of storage termination

The storage facility may upon termination jointly declare to the IVF Institute in writing that the one or more embryos in storage:

- a. must be delivered to another institute authorised to handle embryos in accordance with laws and regulations, for further storage or for use in realising a pregnancy;
- b. can be used for the benefit of another couple with fertility problems;
- c. can be used for the procurement of embryonic stem cells for medical purposes, medical and biological research and education;
- d. can be used for purposes of scientific research that are permitted under the Embryo Act;
- e. must be destroyed.

Paragraph 3 Donor gametes

If the embryos were created with donated material and the depositor chooses destination c or d, Article 3 Paragraph 4 shall apply accordingly.

#### Article 6. Termination by the storage facility

#### Paragraph 1. Authorisation of the storage facility

The storage facility is only authorised to unilaterally terminate the agreement in writing – by registered letter with acknowledgement of receipt – subject to three months notice if:

- the depositors refuse to pay the cost of storage after having been reminded of this in writing by the storage facility by registered letter,
- the woman for whose possible pregnancy the embryos are preserved has reached the age mentioned in the national protocol for egg donation (45 years),
- two years have elapsed, or
- based on new scientific insights, the storage of embryos for a longer period to realise a pregnancy is no longer considered useful.

#### Paragraph 2. Use of the embryos

Upon termination, the IVF Institute invites the depositors to jointly communicate in writing within three months which of the purposes referred to in Article 5 Paragraph 2 sub b, c or d should be given to the embryos. Article 3 Paragraph 4 shall apply accordingly in this situation. Paragraph 3 Termination by the storage facility

After unilateral termination by the storage facility, the embryos will be destroyed, unless the depositors have jointly stated the purpose of the embryos within the set term.

#### Article 7. End of the agreement

Paragraph 1. End of the agreement

Other than by way of unilateral termination, the agreement on cryopreservation shall end:

- by delivery of all embryos by the storage facility for the purpose for which the embryos were mutually intended by the depositors,
- by expiry of the (maximum) duration of the agreement,
- through the death of one or both of the depositors,
- by mutual agreement of the parties, or
- if the depositors' partnership is terminated by other means than death.

#### Paragraph 2. Use of the embryos

If the agreement ends by mutual agreement of the parties, the storage facility shall allow the depositors to specify jointly in writing within three months the intended use of the embryos. Article 3 Paragraph 4 shall apply accordingly in this situation. If the depositors do not jointly designate such a purpose within the said period, the embryos will be destroyed.

#### Article 8. Use after the death of one or both of the depositors

#### Paragraph 1. Destruction if no permission for use after death

The storage facility shall destroy the deposited embryos within 1 month after the storage facility becomes aware of the death of one or both depositors if no permission for use after death has been obtained from the deceased depositor(s) under this agreement. Paragraph 2. Consent for use

#### Depositor 1 \_\_\_\_\_ (name)

gives (by ticking one or more of the options below) consent to the use of the embryos in storage after death for:

- the cultivation of embryonic stem cells for medical purposes, medical and biological scientific research and education,
- scientific research specifically aimed at gaining new insights in the field of: infertility, artificial reproduction techniques, hereditary or congenital diseases or transplantation medicine, or
- scientific research in other fields of medicine.

#### Depositor 2 \_

#### \_\_\_\_ (name)

gives (by ticking one or more of the options below) consent to the use of the embryos in storage after death for:

- the cultivation of embryonic stem cells for medical purposes, medical and biological scientific research and education,
- scientific research specifically aimed at gaining new insights in the field of: infertility, artificial reproduction techniques, hereditary or congenital diseases or transplantation medicine, or
- scientific research in other fields of medicine.

Paragraph 3 Use to realise a pregnancy

If the depositors wish to give their consent to the use of the embryos in storage to realise their own pregnancy after the death of one of the partners or to realise a pregnancy in another couple, they may express this in a separate statement to be kept with this agreement.

#### Article 9. Liability in cryopreservation

#### Paragraph 1. Care obligation of the IVF Institute

The IVF Institute shall ensure a careful manner of cryopreservation of the embryos with due observance of the latest scientific standards. The depositors are aware that the process of cryopreservation may lead to a loss of quality of the embryos through no fault of the IVF

Institute. The depositors accept the risk that the condition of the embryos at the start of the agreement may differ from the condition at the end of the agreement.

#### Paragraph 2. Liability of the IVF Institute

The IVF Institute is not liable to the depositors for damage to the embryos or the loss of the embryos or for damage arising from a violation of the depositors' moral rights, in whatever way caused, unless there is intent or gross negligence on the part of the IVF Institute. Paragraph 3 Exemption from liability

The IVF institute is in any case not liable for the loss of or damage to embryos due to causes in the sphere of force majeure, such as technical shortcomings of the equipment used or external causes, such as fire, burglary and theft.

#### Article 10. The depositors' address

Paragraph 1. Relocation of the depositors

In the event of a change of address during the term of the agreement, the depositors are obliged to send a relocation notice with a new address to the IVF Institute by registered mail with acknowledgement of receipt.

#### Paragraph 2. Addressing

The IVF Institute is obliged to address correspondence (including notices of default and terminations) to the address of the depositors as stated in this agreement unless the depositors have notified the IVF Institute of a new address in accordance with Paragraph 1. The IVF Institute has no obligation to investigate the domicile or residence of the depositors.

#### Article 11. Regulations and protocols at the IVF Institute

The depositors have been made aware of the regulations applicable at the IVF Institute concerning the handling and use of gametes and embryos by the storage facility and have received a written version thereof (IVF information leaflet). They declare to have taken note thereof.

#### Article 12. The costs of cryopreservation

#### Pure costs

The IVF Institute will charge the depositors for the pure costs of storing the embryos. The IVF institute does not charge a storage fee.

For the Dutch folder, click here.

Waar zijn we te vinden?

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