BELGIAN ADVISORY COMMITTEE ON
Bioethics

Opinion no. 57 of 16 December 2013 on the ethical aspects of the freezing of eggs in anticipation of age-related infertility

Request for an opinion from Mrs Laurette Onkelinx, Federal Minister for Social Affairs and Public Health [*Ministre fédéral des Affaires Sociales et de la Santé Publique*], by letter of 24 October 2011 addressed to the Belgian Advisory Committee on Bioethics [*Comité consultatif de Bioéthique*].

The Advisory Committee on Bioethics, in its plenary session of 12 December 2011, deemed the request admissible and set up a select committee responsible for studying the issue of "social freezing", which began its work on 4 September 2012.

Content of the opinion

REFERRAL

This request is primarily concerned with the following question:
"What are the ethical problems relating to the preservation of human gametes for the purpose of differed[1] autologous use, without medical indication, including the "social freezing"[2] of eggs?
The Minister is therefore requesting an opinion on this new application relating to reproductive medicine and, more specifically, is seeking an opinion on:
- the social significance
- the special conditions for the donor
- any limitations, conditions or requirements for the centres for reproductive medicine and the doctors who envisage offering this option
- the content of the procedures which the informed consent must satisfy
- the accessibility
- the secondary use of the reproductive material.

The Committee examined this question in terms of its medical and technical, societal, legal and ethical aspects.

[1] See certain definitions in the Law of 19 December 2008 on the procurement and use of human biological material intended for medical human applications or for scientific research, Article 2(22): "autologous use": the use of human biological material on or in the same person as the person from whom this material was collected; Article 2(31) "differed use": any use differed in time which, from the moment of procuring the human biological material, is intended for a specific recipient.
[2] Freely translated from the English: the "freezing of eggs for social reasons".

I. Definition, rephrasing the question and defining the scope

In general, "social freezing" is defined as the freezing and the preservation of eggs desired by the woman in order to preserve her fertility for when she is older.
In the text that follows, it will always be the **vitrification technique** that is concerned whenever frozen or cryopreserved eggs are mentioned.

This opinion deals, among other things, with three questions:
1. Can a distinction be made between the medical applications of egg freezing and the non-medical applications ("social freezing")?
2. Is the freezing of eggs for non-medical reasons (or "social freezing") ethically acceptable?
3. Should the freezing of eggs for non-medical reasons (or "social freezing") be reimbursed under sickness and disability insurance?
During the discussions initiated in the select committee, it became quickly apparent that there were diverging opinions:

- some members adopt the term "social freezing" in the same sense as that used by the Minister in order to draw a clear distinction with the freezing of gametes for medical reasons, for example to protect the fertility of the person against exposure to mutagenic risks (irradiation, toxic substances, etc.);
- other members do not wish to introduce any distinction. Where the woman chooses to freeze her eggs for later use, this is not, in their view, a medical or a social reason but rather a biological reason, given the definite decline in fertility linked to age.
  In the light of the above, it is therefore preferable to talk of "freezing gametes for the purpose of preserving fertility".

Although the name "social freezing" raises questions for some people, this is because they feel it has a connotation of a preconceived value judgement, whereas, in fact, this term, which is very common in international scientific circles, does not have such a connotation.
To avoid this problem, the Committee felt it appropriate to rephrase the title as follows: "Opinion on the ethical aspects of the freezing of eggs in anticipation of age-related infertility" (ARI, abbreviation used below in the opinion).

The arguments, among other things, expressed by some members against "the freezing of eggs in anticipation of ARI" as such are as follows: it is not natural; it constitutes an unjustifiable medicalisation of procreation; it fosters the idea that procreation is entirely controllable; and it contributes to maintaining a society dominated by man. The arguments put forward by other members in favour of "the freezing of eggs in anticipation of ARI" as such are that it increases equality between the sexes, it favours the autonomy of women and it allows those involved to

have their children under circumstances which are more favourable to them.

II. Historic evolution

The preservation and freezing of male gametes has been possible for many years. The option of freezing male gametes and of thawing them at a later date means that male fertility can be controlled over time. The Advisory Committee has already given an opinion on this subject[3].
By contrast, the freezing of female gametes was impossible until recently. Any fertility technique involving female gametes was considered experimental and with little chance of success, except in the case of freshly collected gametes. Advances in the technique of freezing eggs has enabled the same possibilities for preserving female gametes as for male gametes and raises some new questions.
It should be also be specified, moreover, that the freezing of *embryos* is possible and has been applied for a very long time already. However, the embryo is frozen only if a process aimed at having a child in a case of infertility has already been started or will be started by the partners. To date, in the context of a medically assisted procreation (MAP) treatment, given that there was a practical advantage in freezing the embryos rather than the eggs, some embryos have been frozen for later use. This is how surplus frozen embryos have been accumulated.
The freezing of eggs does present an advantage, namely that of avoiding the freezing of surplus embryos, which makes it possible to avoid any arguments between the partners concerning the use of the embryos.

III. Medical and technical aspects

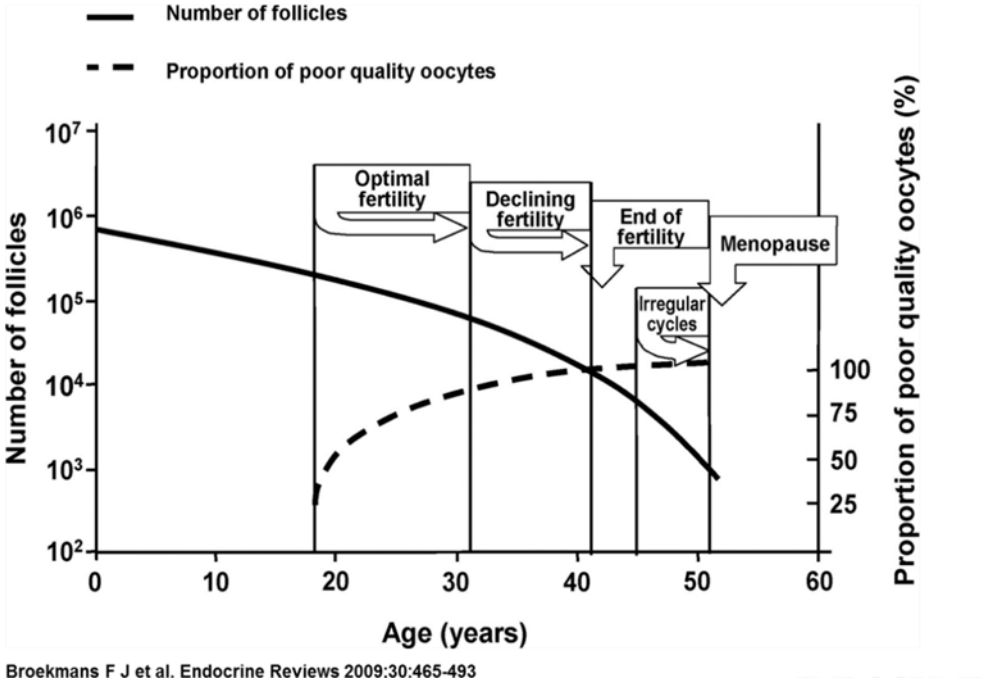
3.1. General introduction

Under normal circumstances, a woman produces "fertilisable" eggs from puberty to the menopause. In order for her to become pregnant and to be able to have a child, these eggs must, of course, be fertilised.
Fecundity[4] declines with age.
Social changes (contraception, women being more highly educated, etc.) have greatly reduced the fertility rate[5] (number of births per woman). The decision to defer pregnancy means that an increasing number of women are moving into the category of infertile women (who are not

[3] Opinion no. 28 of 21 June 2004 on procreation after the death of the partner. The opinions of the Advisory Committee are available at www.health.belgium.be/bioeth, under the "Opinions" section.
[4] Fecundity: ability to produce offspring.
[5] Fertility rate = number of children born per woman.

pregnant after 12 months of regular sexual relations) who need help (MAP[6]) to have a child.

As a woman gets older, the number and the quality of her eggs decrease (cf. fig. below). The gradual loss of eggs occurs as early as during fetal development. The 300,000 to 400,000 eggs available at around the time of the menarche[7] will therefore gradually decrease in number until there are only around a thousand at the time of the menopause. Furthermore, as a woman gets older, the quality of the eggs diminishes (in particular, there are more aneuploid[8] eggs).



Figure[9]: left-hand axis: the number of follicles (eggs). Right-hand axis: the proportion of "poor" quality eggs. Horizontal axis: the age of the woman. The bold line indicates the extent to which the supply of eggs dimishes with age. The dotted line shows the increase in the percentage of "poor" quality eggs as the age increases. These observations, in conjunction with others, indicate that women reach their optimal age of fertility between the ages of 20 and 30 and that their fertility decreases between 30 and 40 and usually ends between 40 and 45.

When a woman seeks treatment for her infertility, her ovarian reserve is usually examined by determining the level of Follicle-Stimulating Hormone (FSH) and Anti-Müllerian Hormone[10] (AMH)

[6] MAP: medically assisted procreation; ART = Assisted Reproductive Technology.
[7] Name given to the onset of menstruation.
[8] The term aneuploidy means an abnormal number of chromosomes and, in the case of an egg, more or less than 23.
[9] Broekmans F J, Soules M R & Fauser B C, *Ovarian Aging: Mechanisms and Clinical Consequences*. Endocrine Reviews, 2009 Aug, 30(5):465–493.
[10] The Anti-müllerian hormone (AMH) is, among other things, responsible for the development of the follicles into eggs and is therefore a good marker for ovarian function (around the menopause).

present in the blood and by counting the number of antral follicles on the third day of the menstrual cycle. If there is an increase in the concentration of FSH (more than 10 UI/L) and a low concentration of AMH (less than 1ng/ml) and a small number of follicles, the ovarian reserve is poor, and the chances of pregnancy (spontaneous or after ovarian stimulation) are slim. However, the sensitivity of all these tests is limited. Apart from extreme data values, such as after the menopause, none of these tests offer conclusive evidence of the total absence of any chance of reproduction[11].

Age is far from being the only reason for using MAP. In both women and men there are many causes of infertility for which IVF and/or ICSI[12] may offer a solution: blocked Fallopian tubes, ovarian dysfunction, decline in the ovarian reserve, endometriosis, poor quality sperm, unexplained infertility.

The chances of giving birth to a child after in-vitro fertilisation with transfer of fresh embryos falls from around 40% after the age of 30 to 25% at the age of 38 and 20% at the age of 40. The cumulative chance of one birth per cycle will be higher if the unsuccessful transfer of fresh embryos is combined with frozen embryo transfer[13]. Based on this information, it can be concluded that egg storage or building up an egg bank is recommended preferably before the age of 38. Beyond the age of 40, the freezing process has much less chance of success given the natural decline in fertility which has already occurred[14].

3.2. Description of the medical procedures and actions

3.2.1. General points

In a woman, at the start of each monthly cycle, 4 or 5 eggs start to grow in each ovary. Normally, during the first half of the cycle, one (sometimes two) of these eggs will continue to develop. At around the 14th day, ovulation takes place: the mature egg enters the Fallopian tube where it can be fertilised by a sperm. An embryo may form and implant in the uterus and continue to develop there to become a fetus and eventually lead to the birth of a child. The other possibilities are the absence of fertilisation and menstruation or fertilisation and transfer following by a miscarriage.

Standard IVF (in-vitro fertilisation) begins with ovarian stimulation. Here, a hormonal treatment stimulates egg maturation which results in the presence, at a certain point, of several mature eggs in the ovary.

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[11] *Assisted reproductive technology,* chapter 32*, in: Clinical gynecologic endocrinology and infertility,* Edts Fritz M A and Speroff L, 8th edition, 2011.

[12] In-vitro fertilisation with intra-cytoplasmic sperm injection.

[13] *Assisted reproductive technology*, *op. cit.,* 2011.

[14] Stoop D, Ermini B, Polyzos N P, Haentjens P, De Vos M, Verheyen G, Devroey P*, Reproductive potential of a metaphase II oocyte retrieved after ovarian stimulation: an analysis of 23 354 ICSI cycles*. Hum Reprod. 2012 Jul; 27(7):2030-5.

These eggs are collected and placed in a container in a laboratory. The addition of sperm causes the fertilisation of the eggs and the development of several embryos, one or two of which will be transferred into the uterus on the 3rd or the 5th day. If they implant correctly and continue to develop, they will lead to the birth of a child. The surplus embryos are generally cryopreserved for transfer into the uterus at a later date.

Cryotechnology was previously insufficiently reliable to preserve eggs. Only embryos were able to be preserved. The freezing of oocytes has only recently become a recognised technique in the in-vitro process. A classic example is hyperstimulation syndrome which endangers the health of the woman and makes the transfer of an embryo inadvisable: the available eggs can be frozen and fertilised at a later date for an embryo transfer in an unstimulated cycle. Another reason is the classic medical indication: a woman needs to be treated for cancer and requests collection and preservation of her eggs with a view to IVF treatment at a later date.

3.2.2. Specific procedures[15]

3.2.2.1. Egg collection

A. After ovarian stimulation

There are various (short and long) stimulation protocols which involve, each time, a period of 7-10 days of daily intramuscular injections, daily blood tests and regular ultrasound scans of the ovaries until a sufficient number of follicles (containing the eggs) have reached a sufficient size. The egg collection can then be scheduled. The risks inherent in such stimulation are, in the short term, hyperstimulation syndrome (<1%) which can and must be recognised and treated correctly[16,17,18]. The risk of hyperstimulation has become very low thanks to the professionalism and care provided by the various parties involved[19]. However, the problem of the very long-term effects of this therapy is unknown (see below). The data that exists in the literature concerning the risks of developing ovarian malignancy is negative for the moment. The majority of the studies do not indicate any link, but the interval is without doubt still too short to be definitive on this issue.

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[15] *Assisted reproductive technology, op. cit.*, 2011.

[16] Venn A, Hemminki E, Watson L, Bruinsma F, Healy D, *Mortality in a cohort of IVF patients.* Hum Reprod. 2001 Dec; 16(12):2691-6.

[17] Bodri D, Guillén J J, Polo A, Trullenque M, Esteve C, Coll O*, Complications related to ovarian stimulation andoocyte retrieval in 4052 oocyte donor cycles*. Reprod Biomed Online. 2008 Aug; 17(2):237-43.

[18] Shmorgun D, Claman P, Gysler M, Hemmings R, Cheung A P, Goodrow G J, Hughes E G, Min J K, Roberts J, Senikas V, Wong B C, Young D C, *The diagnosis and management of ovarian hyperstimulation syndrome*: No. 268, 2011 Nov. Joint Society of Obstetricians and Gynaecologists of Canada-Canadian Fertility and Andrology Society Clinical Practice Guidelines Committee. Republished by Obstet Gynaecol Can. 2011 Nov; 33(11):1156-62. Int J Gynaecol Obstet. 2012 Mar; 116(3):268-73.

[19] Melo M, Busso C E, Bellver J, Alama P, Garrido N, Meseguer M, Pellicer A, Remohí J, *GnRH agonist versus recombinant HCG in an oocyte donation programme: a randomized, prospective, controlled, assessor-blind study.* Reprod Biomed Online. 2009 Oct; 19(4):486-92.

B. Egg collection

Under local anaesthetic and with ultrasound monitoring, the ovarian follicles are pierced vaginally using a long needle and the eggs are collected and saved in a Petri dish in the laboratory. The risks inherent in this procedure are bleeding, pain and sometimes infections, but they are rare (<1%)[20,21].

3.2.2.2. Preservation of eggs by freezing

A. Previously (before the 2000s)

In the past, attempts at freezing eggs by cryopreservation for differed use were limited, mainly on account of the fact that the eggs were often damaged. The slow freezing methods were not yet efficient.

B. Today (since 2005)

The results of the vitrification technology (ultra-rapid freezing) are encouraging[22]. The use of a high concentration of cryoprotectant makes it possible to dehydrate the eggs and to immerse them directly in the liquid nitrogen with the result that the oocyte becomes vitreous with no formation of ice crystals. The survival rate for the eggs of women aged under 35 (on average, 26 +/-5 years) was 90% after thawing, the fertilisation rate for these eggs was 77.5% and the development rate of the resulting embryos on the 3rd day was 61%. After these embryos were transferred to recipients aged on average 39 +/- 6 years, ongoing pregnancies were seen in 45% of cases[23].

The chances of survival of frozen eggs after thawing are high (75 to 90% or more)[24]. The rates of fertilisation and embryo development are good and, based on a randomised study, just as good as when fresh eggs are used[25]. One study, which examines the process from egg collection through to birth, describes some good results[26]. Based on still limited data, there is nothing to indicate that children born after fertilisation of frozen eggs are in poorer health at birth other

[20] Venn A *et al*, *op. cit*.

[21] Bodri D *et al, op. cit*.

[22] Dovey S, *Oocyte cryopreservation: advances and drawbacks*. Minerva Gynecol. 2012 Dec; 64(6):485-500.

[23] Stoop D, De Munck N, Jansen E, Platteau P, Van den Abbeel E, Verheyen G, Devroey P, *Clinical validation of a closed vitrification system in an oocyte-donation programme*. Reprod Biomed Online. 2012 Feb; 24(2):180-5.

[24] Cobo A, Garcia-Velasco J A, Domingo J, Remohí J, Pellicer A, *Is vitrification of oocytes useful for fertility preservation for age-related fertility decline and in cancer patients?* Fertil Steril. 2013 May;99(6):1485-95.

[25] Cobo A, Meseguer M, Remohí J, Pellicer A, *Use of cryo-banked oocytes in an ovum donation programme: a prospective, randomized, controlled, clinical tria*l. Hum Reprod. 2010. Sep;25(9):2239-46. Hum Reprod. 2012 Jun; 27(6):1606-12.

[26] Rienzi L, Cobo A, Paffoni A, Scarduelli C, Capalbo A, Vajta G, Remohí J, Ragni G, Ubaldi F, *Consistent and predictable delivery rates after oocyte vitrification: an observational longitudinal cohort multicentric study*. Hum Reprod. 2012 Jun;27(6):1606-12.

children born after straightforward IVF[27,28,29]. However, the technique is so recent that no definitive conclusion can yet be drawn.

C. How many eggs are needed?

The available data seems to indicate that the chances of giving birth to a child using a frozen egg are 4-5%. It is important to be aware that the age of the woman plays a crucial role in obtaining a sufficient number of good quality eggs. However, other factors may also play a role, such as the response to the stimulation, which is variable[30]. Based on the literature and some unpublished data from UZ Brussel [University Hospital Brussels], it can be claimed that 6 to 8 mature eggs can be obtained per stimulated cycle. Of the 6 to 8 frozen eggs, 75 to 80% survive after thawing. After in-vitro fertilisation, one embryo is obtained on average, which develops, after transfer, in 25 to 30% of cases into a pregnancy followed by a birth.

In short, the more frozen eggs there are, the greater the chances of pregnancy. It is up to the woman, based on her financial situation and her psychological disposition, to decide on the number of transfer cycles and, indirectly, the number of eggs to be frozen.

D. Use of frozen and stored eggs

Frozen eggs can be used for the purpose of achieving three objectives:

1. In-vitro fertilisation and transfer into the person from whom the eggs were collected.

Regardless of age, the transfer of an embryo in a natural (unstimulated) cycle seems to increase the chances of pregnancy[31]. (There also appear to be fewer ectopic pregnancies after transfer of frozen embryos[32]).

2. Donation to female recipients

The recipients are, for example, women who no longer have any eggs themselves (following premature menopause or because they are too old) or who are carriers of a genetic risk (in the case of mitochondrial disease, for instance). The eggs may come from women who had had them preserved for themselves but who no longer wish to make use of them and deliberately donate

[27] Pfeifer S, Goldberg J, McClure R, Lobo R, Thomas M, Widra E, Licht M, Collins J, Cedars M, Racowsky C, Vernon M, Davis O, Gracia C, Catherino W, Thornton K, Rebar R, La Barbera A, *Mature oocyte cryopreservation: a guideline*. Practice Committees of American Society for Reproductive Medicine; Society for Assisted Reproductive Technology. Fertil Steril. 2013 Jan; 99(1):37-43.

[28] Noyes N, Porcu E, Borini A, *Over 900 oocyte cryopreservation babies born with no apparent increase in congenital anomalies*. Reprod Biomed Online, 2009; 18:769–76. Level II-3.

[29] Chian R C, Huang J Y, Tan S L, Lucena E, Saa A, Rojas A, *Obstetric and perinatal outcome in 200 infants conceived from vitrified oocytes*. Reprod Biomed Online 2008; 16:608–10. Level II-3.

[30] Stoop *et al*, *op. cit*., 2012.

[31] Glujovsky D Pesce R, Fiszbajn G, Sueldo C, Hart R J, Ciapponi A, *Endometrial preparation for women undergoing embryo transfer with frozen embryos or embryos derived from donor oocytes*. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006359.

[32] Shapiro B S, Daneshmand S T, De Leon L, Garner F C, Aguirre M, Hudson C, *Frozen-thawed embryo transfer is associated with a significantly reduced incidence of ectopic pregnancy*. Fertil Steril. 2012 Dec; 98(6):1490-4.

them to other women.
The donors undergo a screening procedure.
The eggs are of better quality when they are collected from a young donor (<35). After fertilisation, the embryos have more chance of implanting. The risks of aneuploidy are lower, such that there are fewer miscarriages and it is less frequently necessary to carry out a termination.

3. Donation for scientific research purposes

In this instance, there is the possibility of carrying out scientific research both on the gamete, in the strict sense, and on the embryo which appears after fertilisation.
The intention is not to describe, here, all the possible research on frozen eggs. This may involve research on the condition of eggs or embryos, for example for the purpose of studying cellular differentiation. This second possibility is strictly regulated and governed by the law on embryos.
The eggs used for research purposes often come from women who have preserved eggs for themselves but who are not able or who no longer wish to use them subsequently. Women also offer their eggs for research where it is established unexpectedly, during IVF treatment, that the partner is unable to produce sperm.

IV. Legal context

There is no legal provision that specifically governs the issue studied in this opinion. In general, reference can be made to the international laws which have been mentioned, among other things, in the context of drafting the Law of 6 July 2007 on medically assisted procreation and the use of gametes and supernumerary embryos and the Law of 22 August 2002 on patients' rights. The underlying elements have already been fully developed in the previous opinions of the Advisory Committee on Bioethics[33]. We will limit ourselves, in this section, to mentioning several pertinent provisions contained in Belgian legislation[34].

[33] In general, see in particular the following Opinions of the Advisory Committee on Bioethics: Opinion no. 54 of 10 December 2012 on consent for post-mortem collection of human biological material intended for human medical applications or for scientific research purposes;
Opinion no. 53 of 14 May 2012 on refusal of medical care by a pregnant woman which has an impact on the fetus; Opinion no. 52 of 12 March 2012 on the ethical aspects of certain provisions contained in the European and Belgian regulations on human tissues and cells used in the context of reproductive medicine; Opinion no. 50 of 9 May 2011 on certain ethical aspects of the amendments made by the Law of 25 February 2007 to the Law of 13 June 1986 on the collection and transplantation of organs; Opinion no. 49 of 20 April 2009 on the use of pre-implantation genetic diagnosis (PGD) to detect healthy carriers of a mutation causing a serious hereditary disease which may lead to an increased risk for the offspring; Opinion no. 30 of 5 July 2004 on gestational surrogacy; Opinion no. 29 of 21 June 2004 on embryo donation; Opinion no. 28 of 21 June 2004 on procreation after the death of the partner; Opinion no. 27 of 8 March 2004 on sperm and egg donation.
[34] This section is inspired by the contribution of G. Schamps, "*L'autonomie de la femme et les interventions biomédicales sur son corps en droit belge* [The autonomy of the woman and biomedical interventions on her

4.1. The law of 22 August 2002 on patients' rights

4.1.1. The scope of the law

It may be considered that health care procured in the context of activities related to medically assisted procreation falls, in particular, within the law on patients' rights. This legislation applies to health care dispensed by a professional practitioner to a patient.

Health care refers to the services dispensed by a professional practitioner for the purpose of promoting, determining, preserving, restoring or improving the state of health of a patient, of altering his or her physical appearance primarily for aesthetic purposes or of providing end-of-life care[35].

The term professional practitioner[36] covers doctors, midwives, nurses, dentists, pharmacists, physiotherapists, first responders or any person carrying on a paramedical profession. It also covers practitioners who have a non-conventional practice in the medical, pharmaceutical, physiotherapy, nursing and paramedical fields[37], and also acupuncturists, chiropractors, homeopaths and osteopaths. The patient is the physical person to whom health care is dispensed, at his or her request or otherwise[38].

4.1.2. Self-determination of the patient and dialogue with the doctor

A number of rights already existed before the adoption of the Law of 22 August 2002, in particular through the application of the rules of common law relating to criminal and civil liabilities. However, this legislation specified the scope of these rights and established some new ones[39]. Its provisions reflect the concern that the self-determination of the patient be respected, in the context of a dialogue with the practitioner.

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body in Belgian law]", *in*: *Le corps de la femme et la biomédecine*, Brussels, Bruylant, 2013, pp. 41-70; see also the authors cited in this contribution.

[35] Art. 2(2) of the Law on patients' rights.

[36] Art. 2(3) of the Law on patients' rights.

[37] Within the meaning of the Law of 29 April 1999 on non-conventional practices in the medical, pharmaceutical, physiotherapy, nursing and paramedical fields.

[38] Art. 2(1) of the Law on patients' rights.

[39] See assistance by a trusted person (Arts. 7 and 9), direct access to and obtaining a copy of the file (Art 9), the ability for the family to have access to the file, to a certain degree, after the death of the patient (Art. 9) and the ability to file a complaint with the competent mediation service (Art. 11). A central liability of the hospital has also been established for breaches of patients' rights committed by the practitioners who work there, even if they are self-employed, provided that no disclaimer has been put forward by the hospital in respect of these individuals (Art. 30 of the law on hospitals and other health care establishments, coordinated on 10 July 2008). Moreover, a specific representation mechanism for incapable adult patients has been established (Art. 14) and the provision relating to the communication of medical certificates in the context of insurance has been reworked (Art. 95 of the Law of 25 June 1992 on terrestrial insurance contracts).

The same can be said regarding the right to high quality services which respect human dignity and the self-determination of the patient, where no distinction of any sort can be made[40]; the right to a free choice of practitioner, subject to legal limits[41]; the right to information regarding one's state of health and how it is likely to change[42]; the right to (refusal of) free and informed consent concerning any intervention[43]; the right to treatment or to pain relief[44]; the right to privacy and protection of one's private life[45], and the right to access one's file directly and to obtain a copy of it not later than fifteen days from receipt of the request[46].

Like any patient, a woman is thus entitled to obtain all the personal information which affects her and which may be required in order for her to understand her state of health and how it is likely to change[47]. Her free and informed consent must be obtained in order to carry out any intervention proposed by the doctor in the context of his freedom of therapy.

4.2. The Law of 6 July 2007 on medically assisted procreation and destination of supernumerary embryos and gametes

Medically assisted procreation[48] is defined, by the Law of 6 July 2007, as being "all the of procedures and implementation conditions relating to the new medical techniques for assisted reproduction in which the following are carried out: 1) either artificial insemination, 2) or one of the in-vitro fertilisation techniques, in other words techniques in which, at a given moment in the procedure, access is provided to the oocyte and/or to the embryo"[49].

4.2.1. Access to medically assisted procreation activities

According to this legislation, the originator of the parental project is "any person who has taken

[40] Art. 5 of the Law of 22 August 2002.
[41] Art. 6 of the Law of 22 August 2002.
[42] Art. 7 of the Law of 22 August 2002.
[43] Art. 8 of the Law of 22 August 2002.
[44] Art. 11*bis* of the Law of 22 August 2002.
[45] Art. 10 of the Law of 22 August 2002.
[46] Art. 9 of the Law of 22 August 2002.
[47] Art. 7(1) of the Law of 22 August 2002.
[48] On the subject, see inter alia G. Schamps and M.-N. Derese, "*L'anonymat et la procréation médicalement assistée en droit belge. Des pratiques à la loi du 6 juillet 2007* [Anonymity and medically assisted procreation in Belgian law. Practices under the Law of 6 July 2007]", *in Procréation assistée et Anonymat - Panorama international*, B. Feuillet (Ed.), Brussels, Bruylant, 2008, pp. 125-152; M.-N. Derese and G. Willems, "*La loi du 6 juillet 2007 relative à la procréation médicalement assistée et à la destination des embryons surnuméraires et des gamètes* [Law of 6 July 2007 on medically assisted procreation and the use of gametes and supernumerary embryos ", *Rev. trim. dr. fam.*, 2008/2, pp. 279-359 ; H. Nys and T. Wuyts, "De wet betreffende de medisch begeleide voortplanting en de bestemming van de overtallige embryo's en de gameten", *R.W.*, 2007-2008, pp. 762-776; G. Genicot, "*La maîtrise du début de la vie: la loi du 6 juillet 2007 relative à la procréation médicalement assistée* [Controlling the start of life: the Law of 6 July 2007 on medically assisted procreation]", *J.T.*, 2009, pp. 17-27.
[49] Art. 2(a) of the Law of 6 July 2007.

the decision to become a parent by means of medically assisted procreation, whether or not it is carried out using his or her own gametes or embryos"[50]. Unlike other countries, the legislature has not established any criterion regarding the profile of the individuals seeking access to medically assisted procreation. It is, therefore, not necessary to be married or to be living as a couple, whether heterosexual or homosexual[51].

In addition to the insemination of gametes from her partner or the transfer of embryos created from their own biological material, an adult woman may also receive a donation of sperm or of embryos. In the event of the death of her partner, she may also request, subject to certain conditions, that the cryopreserved embryos be implanted in her or that she be inseminated with the cryopreserved gametes of the deceased person. In Belgium, gestational surrogacy practices exist, given that this is not forbidden by law[52].

A procedure is drawn up (in the form of a written protocol) for each activity linked to medically assisted procreation. This consists, among other things, and with variations depending on the type of action undertaken, in providing clear information in advance on medically assisted procreation and psychological support for the interested parties, before and during the medically assisted procreation process, in addition to concluding an agreement between the fertility centre and the individuals involved[53].

If the fertility centre responds favourably to the request for medically assisted procreation treatment, it must verify, "for the cases where this is indicated", that the causes of the sterility, the infertility or the hypofertility of the requesting woman or couple have been determined and treated in accordance with the established scientific data and with the customary practices of the profession[54].

The centres are obliged to demonstrate the greatest possible transparency regarding their options relating to treatment accessibility. They are allowed to invoke a conscience clause and therefore have discretion as regards accepting or turning down the requests they receive. They must advise the requester(s) of their refusal to accept the request, within one month of the decision taken by the doctor consulted.

If it refuses the request, the centre must express this decision in writing and must indicate either the medical reasons for the refusal or the fact that the conscience clause is being invoked. If the

[50] Art. 2(f) of the Law of 6 July 2007.
[51] In Belgium, two people of the same sex are allowed to marry or adopt a child.
[52] On the subject, see inter alia the contributions from the work *La Gestation pour autrui: vers un encadrement* [Gestational surrogacy: towards a framework]*?*, G. Schamps and J. Sosson (Eds.), Brussels, Bruylant, 2013, 458 pp.
[53] See Articles 6-8, 12-14, 20, 29-32, 41-43, 49, 58-62, 66-69 of the Law of 6 July 2007.
[54] Art. 6 of the Law of 6 July 2007.

requester(s) so desire, the centre must send them the contact details of another fertility centre which they can approach[55].

Gamete collection and requests for embryo transfer or gamete insemination are available to adult women of a maximum age of 45. Embryo transfer and gamete insemination cannot be carried out in women aged over 47[56]. Nevertheless, the collection, for cryopreservation, of gametes, surplus embryos, gonads or fragments of gonads may be carried out, if medically indicated, on a minor[57].

Access to medically assisted procreation is facilitated by the fact that health insurance reimburses, under certain conditions, the pharmaceutical products administered in connection with in-vitro fertilisation treatment.

An allowance is also granted to hospitals which offer an approved "reproductive medicine B" care programme. At present, this involves a fixed sum[58] per cycle (for a maximum of six cycles), awarded where the woman concerned is of a maximum age of 42[59]. Discussions are ongoing to bring down to 41 the age at which health insurance applies[60], by fixing a transition period. In order to receive this funding, the care programme must comply with the rules which lay down the number of embryos to be implanted per attempt. This varies according to the age of the woman and the nature of the cycle[61]. The funding covers the costs of the reproductive medicine laboratory, such as staff costs, equipment, hardware and indirect costs.

4.2.2. Concluding an agreement

Prior to any medical process, an agreement is drawn up between the originator(s) of the parental project and the fertility centre. It includes information relating to the identity, the age and the address of the parties concerned. Where a couple is involved, it is signed by both the originators

[55] Art. 5(3) of the Law of 6 July 2007.
[56] Art. 4(1) to (3) of the Law of 6 July 2007.
[57] Art. 4(4) of the Law of 6 July 2007.
[58] See Royal Decree of 16 September amending the Royal Decree of 6 October 2008 establishing a fixed-price reimbursement for female infertility treatments. *Cf.* http://www.vvog.be/docs/2013/09/30080403.pdf
[59] The term "cycle" is understood to mean all the laboratory activities required for egg insemination by means of IVF/ICSI (Art. 74*bis* of the Royal Decree of 25 April 2002 on fixing and settling the financial resources budget of hospitals).
[60] A Royal Decree of 10 January 2013 had been adopted in this sense but it was then withdrawn by a Royal Decree of 11 February 2013 since it did not provide for any temporary measure (Royal Decree of 10 January 2013 amending Article 14(g) of the Annex to the Royal Decree of 14 September 1984 establishing the nomenclature for healthcare services as regards compulsory health insurance and benefits; Royal Decree of 11 February 2013 withdrawing the Royal Decree of 10 January 2013 amending Article 14(g) of the Annex to the Royal Decree of 14 September 1984 establishing the nomenclature for healthcare services as regards compulsory health insurance and benefits).
[61] See Annex 15 to the aforementioned Royal Decree of 25 April 2002.

of the parental project[62]. The instructions of the originator(s) of the parental project may be amended up until the completion of the final instruction given, subject to the expiry of the preservation deadline for the surplus gametes or embryos. These amendments are the subject of a written document, signed by all the signatory parties to the agreement. Where a couple is involved, the amendments must be made by mutual consent[63].

This agreement concluded with the fertility centre must stipulate the intended use of the surplus embryos and gametes. It must, therefore, mention the choice available by law to the requester(s)[64]: cryopreserving the embryos or gametes for the purpose of a parental project, destroying them, integrating them into a research protocol or allocating them to a donation programme. The surplus embryos and gametes may not under any circumstances be allocated to a use which is different to that stipulated in the agreement[65].

The time limit for cryopreservation of surplus embryos for the purpose of a parental project is five years, with effect from the day of cryopreservation[66].
It is ten years for surplus gametes[67]. A reduction or extension[68] of the period may be requested from the fertility centre.
Unless medically indicated, no new collections of gametes may be carried out in order to form other embryos while the originator(s) of the parental project still have cryopreserved surplus embryos, provided that these embryos satisfy the required health standards.
The assessment of the health safety of the surplus embryos is carried out by the fertility centre consulted[69].

If surplus embryos are cryopreserved, the agreement must stipulate how they will be used should one of the following situations arise: separation, divorce, permanent inability to make decisions of one of the originators of the parental project, irreconcilable difference of opinion between them, the death of one of them or the expiry of the cryopreservation deadline[70]. As far as cryopreserved surplus gametes are concerned, the agreement must mention how they will be used in the event of the permanent inability to make decisions or the death of the person who requested the cryopreservation or upon the expiry of the cryopreservation deadline[71].

Thus, provided that the agreement stipulates it, a separated or divorced woman may, where

[62] Art. 7 of the Law of 6 July 2007.
[63] Art. 8 of the Law of 6 July 2007.
[64] Arts. 10, 13, 20, 30, 37, 40, 42, 49 and 59 of the Law of 6 July 2007.
[65] Arts. 11 and 38 of the Law of 6 July 2007.
[66] Art. 17 of the Law of 6 July 2007.
[67] Art. 46(1) of the Law of 6 July 2007.
[68] Arts. 17, 18, 46 and 47 of the Law of 6 July 2007. The fertility centre may or may not give its consent.
[69] Art. 9 of the Law of 6 July 2007.
[70] Art. 13 of the Law of 6 July 2007.
[71] Art. 42 of the Law of 6 July 2007.

appropriate[72], give birth to a child through the transfer of the cryopreserved embryo or through the insemination of the cryopreserved[73] gametes of her former partner.

4.3. Law of 19 December 2008 on the procurement and use of human biological material intended for medical human applications or for scientific research

The law of 19 December 2008 governs the donation, collection, procurement, control, treatment, preservation, storage, distribution and use of human biological material intended for human applications and also for scientific research. It may involve any human biological material, including human tissues and cells, gametes, embryos, fetuses, and the substances extracted from them, whatever the amount of processing involved[74]. The collection and all the operations carried out using stem cells, whatever their origin, particular those from the cord blood, the peripheral blood, the bone marrow or of mesenchymal origin, are also subject to this law. A number of royal decrees have been adopted to ensure its execution.

Without prejudice to the aforementioned Law of 6 July 2007, this legislation applies to donation, collection, operations and use in relation to gametes, gonads, fragments of gonads, embryos or fetuses[75].

However, certain provisions contained in the Law of 19 December 2008 are not applicable. These are Article 7(4) (laying down the quality standards), Article 8(1)(1)(4) (the ban, subject to exceptions, on the collection and storage of human biological material intended for a differed, autologous or allogenic use, for a particular, identified recipient), Article 8(2) (relating to the operations carried out by the production establishment), and Article 10(4) (concerning the consent for the collection of stem cells from the cord blood, and of the placenta and the related residual biological material)[76].

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[72] In the event of subsequent disagreement between the originators of the parental project, the question does, however, arise of reconciling Article 12 and Article 14 of the Law of 6 July 2007. Under Article 12(2), the fertility centre must ensure the effective consent of the two originators to the transfer of the cryopreserved surplus embryos. Article 14(2) states, however, that in the event of a disagreement between the originators of the parental project after the signing of the agreement, regarding the use of the surplus embryos, the fertility centre consulted will take account of the most recent instruction given by mutual consent by the two originators of the parental project.

[73] According to Art. 41(2) of the Law of 6 July 2007, in the event of a request for insemination of cryopreserved gametes at the request of couple who are planning a parental project, the fertility centre consulted must, prior to any medical step, ensure the effective consent of the two originators to this new insemination.

[74] Art. 2(1) of the Law of 19 December 2008.

[75] Art. 8(4) of the Law of 19 December 2008.

[76] The Law of 19 December 2008 does not apply to other scenarios (see the cases set out in Art. 3(4) of the law), which concern the collection of male gametes (Art. 4(1) and Art. 13(1) and (3)), the donation between partners of male gametes which are immediately applied on site to the female partner for the purpose of procreation (Art. 4(2)), the issue of consent for the use of residual biological material for scientific research,

Fertility centres, within the meaning of the Law of 6 July 2007, are treated in the same way as human biobanks. Operations involving gametes and embryos can be carried out solely by fertility centres[77].

The Law of 19 December 2008 includes, in particular, some specific provisions relating to free and informed consent and the procedures for this consent, and to the tasks and responsibilities of the various parties involved, including the biobanks. However, these provisions are not applicable where the collection and any operation carried out using human biological material are performed solely with a directly preventive, diagnostic or therapeutic objective, which is scientifically accepted, in favour of the donor (Article 9). Some particular provisions also deal with the donor's consent for any secondary use of the human biological material (in other words, other than that for which the donor has given his or her consent in the context of the collection) and for the use of residual human biological material for scientific research.

We can conclude that, from the legal point of view, there is no provision in Belgian law which prohibits the freezing of eggs in anticipation of ARI and there is nothing to limit the possible indications in a way which would point towards one solution rather than another.
What is more, the autonomy of the parties involved, which is defined in the aforementioned laws, confirms their freedom to seek this option. But the centres for reproductive medicine may, nevertheless, refuse treatment on the basis of a conscience clause.
Moreover, there is no provision in international law which prohibits the freezing of eggs in anticipation of ARI nor is there any directive that advises against it[78].

in accordance with Art. 20(2), where it is a question of using embryos or fetal human biological material or gametes or gonads for the purpose of creating embryos.

[77] Nevertheless, the capacitation of male gametes may take place in an approved clinical biology laboratory, under Article 63(1) of the law on compulsory health insurance and benefits, which is at the same time approved as an intermediary establishment for human biological material and which has concluded a collaboration agreement with a fertility centre with a view to evaluating the quality of the medical activity in question.

[78] "*En France, pendant près de trois ans, cette nouvelle technique a été considérée comme une forme de recherche indirecte sur l'embryon, et a donc été proscrite par les lois de bioéthique en vigueur. Il a donc fallu attendre le 27 janvier 2011 pour que la commission chargée de la révision de ces lois vote l'autorisation de vitrifier des ovules* [In France, for nearly three years, this new technique has been regarded as a form of indirect research on the embryo, and has therefore been proscribed by the bioethical laws in force. It was therefore necessary to wait until 27 January 2011 for the commission responsible for revising these laws to approve the authorisation of egg vitrification]" [for autologous use] (See Law no. 2011-814 of 7 July 2011 on bioethics). E. Lecomte *in:* Sciences & Avenir, 6-09-2013.

V. Social and psychological aspects

The methodology of preserving eggs for personal use in the event of ARI raises a number of questions of a psychological and societal nature.

5.1. Increase in the age of first-time motherhood and its consequences

In the majority of countries in the West, the demographics of parenthood have undergone a huge change while the proportion of people using in-vitro fertilisation has increased greatly. The age of the parents when their first child is born has risen sharply in recent decades. In the United Kingdom, the average age of a mother when she has her first child has risen from 23 in 1968 to 30 to 31 in 2009[79]. For Belgium, the change can be determined on the basis of the tables entitled "Live births by gender, by civil status, age at the birth and year of birth of the mother", which are available, per year, up to 2009 inclusive (Source: *Direction générale des Statistiques et Information Economique – Direction Thématique Société* [General Directorate for Statistics and Economic Information – Society Thematic Department]). On that basis, a calculation has been carried out on the number of children born to a mother aged 45 or over in 1998, 2004 and 2009 and, here too, a large increase can be seen: 0.63 per 1000 births in 1998 (in absolute figures: 72/11,4259), 0.9 per 1000 in 2004 (116/11,7295) and 1.35 per 1000 in 2009 (172/12,7198). In the space of 12 years, the proportion of children born to a mother aged 45 or over has doubled. However, on the basis of these tables it is not possible to determine how many of these children were first-borns. The proportion of children who are born to mothers aged 45 and over following in-vitro fertilisation treatment and who are first-borns is not known. This observation raises the question of whether "older" mothers are an asset for the upbringing and the care of the child.

Some of the literature mentions a negative effect on the children due to the older age of their parents. However, we have little empirical data on this subject. There is a lot of recent literature which suggests a relationship between autism and older parents[80]. In addition, there are studies which demonstrate that later parenthood may also offer some advantages. Late parenthood is associated with many advantages for the parents (and with certain advantages for the children), including "smaller losses of income and shorter career breaks for mothers[81]", "greater stability for

[79] Office for National Statistics of the United Kingdom (UK) (ONS, 2007) *in:* Boivin J, Rice F, Hayle D, Harold G, Lewis A, van den Bree M B, Thapar A, *Associations between maternal older age, family environment and parent and child wellbeing in families using assisted reproductive techniques to conceive*, Social Science & Medicine 68 (2009) 1948–1955.

[80] Frans E M, Sandin S, Reichenberg A, Långström L, Lichtenstein P, McGrath J J, Hultman C M*, Autism risk across generations,* Jama Psychiatry, Vol 70 (N°5): 516-521, 2013 May.

[81] Miller A R, *Motherhood delay and the human capital of the next generation*. The American Economic Review 2009, 99(2): 154-158.

the couple[82]", "better situations in terms of finance and housing", "a stronger feeling of having the necessary skills to become a parent[83]" and, even, "higher happiness levels among the parents[84]". These factors give an indication only indirectly of the effect of an older age on the children.
A more stable couple relationship between the parents is, therefore, a positive point. Poverty, for example, has a negative effect on the general development of a child; consequently, a more comfortable financial situation will be a positive point.

On the other hand, it must be noted that older parents reduce the chances of assistance and support from grandparents in the upbringing of the child.
According to some studies[85], the presence of grandparents is sometimes important for the upbringing of children. The older age of the mother when the child is born will, under certain circumstances, lead to less contact with the grandparents. This aspect must be considered in the light of the Griggs et al. study[86], in which it is clearly demonstrated, on the basis of both qualitative and quantitative elements, that support from grandparents is considered an important factor in the general well-being of the child in the context of normal family relations.

5.2. Consequences of IVF on the upbringing and the psychosocial development of the child

A number of studies have been carried out concerning the consequences of in-vitro fertilisation on the upbringing and the psychosocial development of children. The longest monitoring period appears in the H. Colpin study (2012)[87]. In the context of a longitudinal study, this research followed a group of children conceived by in-vitro fertilisation, and their parents, until they reached adolescence. For this study, data was gathered relating to the period in which the child was an infant (age 2), was in primary school (age 8 to 9) and during his or her period of adolescence (age 15 to 16). None of these three periods revealed any notables differences in terms of upbringing and psychosocial development between the children born by in-vitro fertilisation and the children in a comparison group who were conceived naturally. As far as the first two periods are concerned, the findings are in line with other studies. The interesting point about the Colpin study is that the children were followed over a longer period, until adolescence,

[82] Sobotka T, *Oocyte cryopreservation as an insurance strategy: a socio-demographic viewpoint. Proceedings of the 1st International Symposium on Social Egg Freezing*, Barcelona, 5-28, 2013.
[83] Mills M, Rindfuss R R, McDonald P, te Velde E & on behalf of the ESHRE Reproduction Society Task Force. (2011). *Why do people postpone parenthood? Reasons and social policy incentives*. Human Reproduction Update, 17(6), 848-860.
[84] Myrskylä M and Margolis R, workpaper, Max Planck Institute for Demographic Research 2012: *Before and after the kids.*
[85] Griggs J, Tan J-P, Buchanan A, Attar-Schwartz S, Flouri E, *'They've Always Been There for Me': Grandparental Involvement and Child Well-Being.* Children & Society, Volume 24, (2010) pp. 200-14.
[86] *Ibid.*
[87] Colpin H, *Anders (of toch niet)? Opvoeding en ontwikkeling van kinderen verwekt door medisch begeleide bevruchting*, in 'Gezinnen in soorten' (éditions Garant, 2012).

and that, here too, no significant difference was noted during this period. The results of this study and of other studies published on this issue must be interpreted with a degree of caution as this type of longitudinal study is characterised by a number of conceptual and methodological limitations.

Boivin e.a. (2009[88]) studied the association between, on the one hand, the age of the mother at the birth of children born through IVF and, on the other, the well-being of the children and the parents. This involved a group of first-born children who were aged from 4 to 11 at the time of the study. To examine the association with the age of the mother, the mothers were classified in three groups: young mothers (31 and under), a median group (over 31 but under 38), and older mothers (38 and over).
This study revealed that the well-being of the children, as reported by the parents in the questionnaires, was not significantly different in the three age groups, despite some marked differences being observed in the warmth of the relationship between the parents and despite the significantly higher number of symptoms of depression reported by the mothers and fathers who were in the older age group. It is, of course, necessary to bear in mind that social opportunity may play a role if the well-being of the children is measured solely by means of the reports provided by the parents.

The findings of the study among mothers who used in-vitro fertilisation at older age on account of an infertility problem do not demonstrate any negative consequence for the psychosocial well-being of the children and are reassuring. Further studies focusing on the experiences of the children prove absolutely essential.

5.3. Data relating to the freezing of eggs and the position of the reproductive medicine centres which already apply the technique at present

For some time now, eggs have been frozen for purely medical reasons in the context of IVF treatment (for example, in the event of hyperstimulation or absence of available sperm after the collection of the egg) or in anticipation of IVF treatment (for a probable premature menopause or after cancer treatment, for instance).
It is worth mentioning the possible comparison with the freezing of sperm in men suffering from cancer, for the purpose of possible later use in order to satisfy a desire for a child. The data from the literature based on eight studies tells us that, out of 629 patients involved, 3.6 to 16.3% of the patients made use of their frozen sperm. Of those, between 40 and 50% became fathers in

[88] Boivin J, Rice F, Hayle D, Harold G, Lewis A, van den Bree M B, Thapar A, *Associations between maternal older age, family environment and parent and child wellbeing in families using assisted reproductive techniques to conceive*, Social Science & Medicine 68 (2009) 1948–1955.

this way[89].

More recently, eggs are also being preserved at the request of women (often aged 35 or over) who do not yet have children (often through lack of a partner).
Before commencing any egg freezing, the Reproductive Medicine Centre at UZ Brussel sent out an electronic questionnaire to 1,914 women in Belgium in order to survey their intentions regarding a possible preservation of eggs in order to guarantee their possibilities of having a child. Out of all these women, 1,049 responded. Only 3.1% of the women said that they would consider freezing their eggs for social reasons; 28.4% replied that they might do so[90]. Between July 2009 and December 2012, 243 candidates for egg freezing came to this same Centre. These women were interviewed and the followed data was collected: 64% of the women were university graduates, 80% had a job and 50% were from the Netherlands. Out of all these women, 72% were single, 98% had already had a relationship and 2% already had a child; 84% of them expressed a clear desire to have a child and wanted above all to find a partner. For more than half (57%), the reason for freezing their eggs was the absence of the right partner whereas, for 4%, this freezing was motivated by the priority given to their professional career.

When asked about their intentions with a view to satisfying their desire for motherhood after finding a partner, 80% of them responded, in order, that (1) they would choose natural conception, (2) if necessary, they would use IVF, (3) they would use frozen eggs. The remaining 20% said that they would choose, in order, (1) to use their frozen eggs immediately on account of their old age, (2) to seek advice from a doctor, (3) to do nothing, as they did not know what to do in the immediate future.

Finally, if they did not need to use their frozen eggs, 31% of them would donate them to research, 17% would donate them to third parties, 13% would ask for them to be destroyed and 27% were undecided.

Of these 243 women who came to the Centre with the intention of freezing their eggs (in July 2009), 124 eventually had them frozen and 119 did not do so or had not yet done so (in December 2012). Of these 119 women, 35 had their request refused because they were already over the age of 40 or on account of a poor ovarian reserve, 29 abandoned their plan for various reasons: they had found another solution to their problem (8), had found a partner (7), were pregnant (4), considered the cost too high (5) or mentioned various other reasons (5). In the end, 55 out of 119 women at the start remained potential candidates for egg freezing (17 undecided and 28

[89] Van Casteren N J, van Santbrink E J P, van Inzen W, Romijn J C, Dohle R*, Use rate and assisted reproduction technologies outcome of cryopreserved semen from 629 cancer patients,* Fertil. Steril, 2008, 90, 2245-2250.
[90] Stoop D, Nekkebroeck J, Devroey P, *A survey on the intentions and attitudes towards oocyte cryopreservation for non-medical reasons among women of reproductive age*. Hum Reprod, Mar 2011; 26(3):655-6.

who had not yet indicated their intentions)[91].

The principle of egg freezing is already recognised by the European Society of Human Reproduction and Embryology (ESHRE, ref. 2011[92]) but with the recommendation to provide sound information to candidates, to be seen to be selective with the centres where the intervention can be carried out and to collect accurate data. A comparable position has been adopted by the good practice committees of the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART[93]) in the USA. It will be noted that, even though the majority of the groups take a positive view on this new treatment, they all include the need to collect data for the future.

5.4. Medicalisation of a societal problem?

Some members consider that the social pressure on young women to succeed first and foremost in their professional career and only afterwards to fulfil their role as a mother is unavoidable. It will be noted in this regard that the majority of the current candidates for egg freezing come from the higher social classes. This seems fairly obvious since no reimbursement is provided for the freezing and storing of eggs. It is therefore reasonable to wonder whether the reimbursement which enables this methodology will increase this social pressure even more, with the consequence that the children to be born will have parents and grandparents who are even older.

Both the report from the *Reageerbuisdebat* in the Netherlands[94] and the article by Shkedi-Rafid and Hashiloni-Dolev (2012)[95] address the issue of whether it is truly desirable to solve a societal problem by medical means (medicalisation). Is there not the risk of a negative effect from egg freezing, in order to enable differed procreation, on the social desire to change the factors which cause women to have children increasingly late? What are the consequences for the social position of women?

Will the social pressure to delay procreation not be felt excessively, to the point of taking

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[91] Nekkebroeck J, UZ Brussel, *Opting for oocyte cryopreservation for prevention of age related fertility loss or 'Social Freezing'*. Oral presentation during the 29th meeting of the European Society of Human Reproduction and Embryology (ESHRE), on 7 July 2013 - London, United Kingdom.

[92] ESHRE Task Force on Ethics and Law, Dondorp W, de Wert G, Pennings G, Shenfield F, Devroey P, Tarlatzis B, Barri P, Diedrich K, *Oocyte cryopreservation for age-related fertility loss,* Hum Reprod. 2012 May; 27(5):1231-7.

[93] Pfeifer S *et al, op.cit.,* 2013.

[94] Dondorp en de Wert, *Het reageerbuisdebat: een rituele dans*, 28 juni 2012, V. http://www.zonmw.nl/nl/publicaties/detail/reageerbuisdebat-over-de-maakbaarheid-van-de-voortplanting/?no_cache=1&cHash=1c8d9a0a150c2a513278cc40c1c05f1c
Dondorp W J, De Wert G M, *Fertility preservation for healthy women: ethical aspects*, Human Reproduction, Vol.24, No.8 pp. 1779–1785, 2009.

[95] Shkedi-Rafid. en Hashiloni-Dolev Y, *Egg freezing for non-medical uses: the lack of a relational approach to autonomy in the new Israeli policy and in academic discussion*, Journal of Medical Ethics 38 (3):154-157 (2012).

precedence over the individual autonomy of the woman in practice? To what extent does the freezing of eggs in order to differ a pregnancy meet a real need of women or, rather, a need created entirely by the fertility centres? Should we not learn to live with greater awareness of the fixed time limits available to us to make our choices? Even if there is not a unanimous response to all these questions, everyone is agreed that egg freezing cannot be presented as a simple means of differing one's desire for a child, and that the information campaigns must emphasise the fact that it is always preferable not to differ one's pregnancy too long. Some members point out that our society ought to make more effort to create collective facilities (in universities and businesses, for example) in order to enable young women to reconcile their plans for motherhood with their education or career plans.

Other members consider that there is no proof, at present, of the assertion whereby career considerations or the difficulties that exist in reconciling work and family life are the major reasons which motivate women to delay procreation. In addition to many other factors, the heavy demands imposed on parents probably represent an explanation which is just as important. Consequently, these members wish to raise the question of whether the current pressure from society to have children earlier leads to procreation under conditions which will be far from ideal for the well-being of the unborn child.

According to these members, denying women the possibility of freezing their eggs means that their desire to have, at a later date, children created from their own genetic material is being overlooked. They therefore consider it very important to curb this infantilisation of women and this paternalistic attitude through campaigns to make women aware of the decline in fertility from a certain age and of the possibility of cryopreserving their eggs.
Treating women who freeze their eggs in the same way as women who are solely committed to their career is not only gratuitous and without scientific basis, it is also deduced directly from the idea that the primary role of the woman must be that of a mother.

5.5. The issue of health economics

Egg freezing is expensive. Women undergo the necessary treatments, in other words, preparatory examinations (doctor, psychologist, laboratory), ovarian stimulation and the collection of the eggs from the ovary (single or multiple). Then comes the cryopreservation of the eggs (8 units or more). Later on, there is the possible use of the eggs 1) by the person who entrusted them for preservation (successfully – with the birth of a child – or otherwise), 2) through a donor or 3) for science. What are the financial consequences of this technique for the person concerned and for society?
At the moment, two models have been developed to evaluate the costs. Van Loenderschoot *et al*

(2011)[96] concluded that, provided that one is willing to pay around 20,000 euro for an additional birth, egg freezing was more cost-effective than IVF if at least 61% of the women intend to actually use their eggs. This hypothesis was compared with three strategies: freezing at the age of 35 and IVF at 40, natural conception, and IVF at 40 without freezing. The study by Hirshfeld-Cytron *et al* (2012)[97] came to the conclusion that egg vitrification is not cost-effective, but they compared other strategies, namely no action at the age of 25, egg vitrification at 25 and freezing of ovarian tissue. Further studies using the same parameters are needed in order to be able to reach a definitive conclusion on the issue.

VI. Ethical considerations

6.1. Can a distinction be made between the medical applications of egg freezing and its non-medical applications (in other words, "social freezing")?

Today, the vitrification or freezing of eggs is practised for two kinds of motivation. The first concerns patients who are preparing to undergo a treatment (drug, surgery, other therapies) which risks making them sterile. For these women, egg freezing is a solution to increase their chances of having a child after the treatment. The medical indication, here, is unquestionable. The second kind of motivation for using this technique concerns women who, for various personal reasons (establishing a professional career, absence of a stable partner, ongoing studies, limited financial means) wish to or are obliged to delay their pregnancy.

Some people see this as a social rather than a biological indication, linked to age, and they dispute the medical nature of these indications given that, at the time they are mentioned, they are totally independent of any medical problem. They therefore use the expression "social freezing", but they do agree with the expression "age-related infertility" (ARI).

Other members of the Committee do not make any distinction between egg freezing due to medical indications and egg freezing for age-related reasons. For this reason, they do not wish to talk of "social freezing" on the one hand and "medical freezing" on the other. The major problem inherent in the terminology which distinguishes freezing of a social nature and freezing for medical reasons is that it immediately introduces a normative structure into the discussion. However, one must start from a position whereby the reason which motivates the cryopreservation is relevant for the debate. It is therefore appropriate to put forward arguments

[96] van Loendersloot L L, Moolenaar L M, Mol, B W J, Repping S, van der Veen F & Goddijn M (2011). *Expanding reproductive lifespan: a cost-effectiveness study on oocyte freezing*. Human Reproduction, 26(11), 3054-3060.

[97] Hirshfeld-Cytron J, Grobman W A & Milad, M P (2012). *Fertility preservation for social indications: a cost-based decision analysis*. Fertil Steril, 97, 665-670.

rather than suppositions. Consequently, the proposal from these members is to adopt a position of neutrality which acknowledges the coexistence of various motivations. Their position is that cryopreservation always takes place to counter a risk of ovarian failure linked to four possible causes: 1) a medical treatment, 2) a disease or condition, 3) irradiation and 4) aging in general. In all four cases, a measure is taken in order to preserve or increase the possibility of the woman having, in the future, a child created from her own genetic material. A particular effect of the current dichotomy (medical vs. social) is, they say, that is transfers the responsibility onto the woman. It also shows that the medical reasons are clearly deemed legitimate, whereas the age-related motivations require additional justification.

However, when one examines the current list of medical indications, it is difficult to detect any common characteristics. It includes patients suffering from a genetic condition (Turner syndrome, for example[98]), patients presenting an increased risk of premature ovarian failure, cancer patients, patients with endometriosis, and women who are exposed to environmental factors presenting a possible mutagenic effect. The risks of infertility are very varied. In certain cancers and oncological treatments, there is the issue of a low probability of permanent sterility. In conditions such as premature ovarian failure (POF), there is no absolute certainty regarding future infertility nor any concerning the number of years during which the woman will remain fertile. A woman aged 20 who presents an increased risk of POF may nevertheless, in principle, also decide to have a child since she is young and, for her, therefore, cryopreservation and delaying pregnancy also fall within age-related reasons. Consequently, we can say that the distinction between the medical reasons mentioned above and the age-related reasons is far from being distinct and that it is more a question of a continuum.

6.2. Is the freezing of eggs for non-medical reasons ("social freezing") ethically acceptable?

For the use of this technique to be considered ethically acceptable, the principle condition is that of the absence of harm caused to the woman and to the child who is created from a frozen egg. However, based on the current data mentioned in Section III, no proven harm to the woman or to the child has been clearly established to date. However, the information on the short-term and long-term effects is still limited today. The collection and monitoring of data remains, therefore, strongly recommended.

In addition to the risks linked to the freezing technique, consideration should also be given to the safety factors specific to using in-vitro fertilisation. On this subject, Opinion no. 52 of the Advisory Committee on Bioethics[99] should be consulted. Society does not have to judge, from a

[98] Premature ovarian failure is one the characteristics of Turner syndrome.

[99] Opinion no. 52 of 12 March 2012 on the ethical aspects of certain provisions contained in the European and Belgian regulations on human tissues and cells used in the context of reproductive medicine.

moral point of view, the reasons why a woman does or does not wish to have her eggs frozen. Individuals should be free to organise their reproductive lives as they wish, provided that they do not commit an unlawful act. The situation of a woman who refuses to consider pregnancy before the age of 35, or even later, for personal reasons is not morally significant.
Some members consider that the freezing of eggs motivated by social reasons is also acceptable from an ethical point of view, but they express a number of reservations, because they are of the opinion that, initially, measures should be taken to facilitate motherhood at a younger age. This group also wishes to highlight the fact that the natural process must be attempted before any use of highly technical procedures.

6.3. Should egg freezing applications for non-medical reasons (in other words, "social freezing") be reimbursed under compulsory health insurance?

Before detailing the different positions regarding reimbursement, we wish to clarify the reasoning behind the fair distribution of resources. At the moment, some people are of the opinion that the egg freezing technique is not equally accessible to all women in society but only to women who have sufficient financial resources. Equality in the distribution of the resources needed for health care is a crucial factor in the context of the ethical evaluation of insurance intervention in health care. The resources are dedicated to the formation of a "basic package" of health care. This basic offer varies from one country to another. Belgium, for example, has decided to include IVF in this offer. People who claim that "social freezing" is the result of a personal convenience choice (which is not, therefore, part of the basic offer) favour non-reimbursement. Like the reimbursement rules regarding cosmetic surgery, it is accepted that people can have this type of operation done without any community intervention being provided. The issue of fairness arises, therefore, only for those who argue that "social freezing", just like IVF, must be part of the basic offer contained in the INAMI [*Institut National d'Assurance Maladie Invalidite* – Belgium Health Insurance Agency] list of services.

The Committee is very divided on the issue of reimbursement. Two positions have emerged.
Supporters of the first position argue in favour of a total absence of reimbursement for "social freezing". By contrast, the second group considers that reimbursement must be made for all fertility preservation applications which satisfy the criteria (see below), whether medical or social indications are involved.

6.3.1. Arguments against health insurance intervention in meeting the costs of egg freezing for social reasons (position 1)

The proponents of this position (social control position) argue in favour of a much more restrictive

attitude inspired by the distinction mentioned above relating to the medical reasons and the personal (social) reasons. In their view, there are, on the one hand, individuals who are involuntarily exposed to the consequences of a disease and, on the other, other people who are making a life choice for which they should assume responsibility. Such a difference in context could therefore constitute an objective criterion for the reimbursement of egg freezing: only women for whom there are clear medical reasons for this procedure will be entitled to it. These members draw attention to the importance of a fair distribution of the very limited resources in the context of financing the most difficult healthcare procedures, and wonder whether people will be able to support the reimbursement of social freezing knowing that the costs of other more vital therapies or techniques remain the responsibility of the patient.

Furthermore, the supporters of this position do not regard as ethically neutral the life choices that lie behind the requests for egg freezing for social reasons. The difficulties which the children born to older parents may encounter (cf. above) are regularly mentioned to support the idea that having children late in life should not be encouraged socially.

In this regard, some members of the Committee note that, today, medicine is increasingly mandated by society to solve problems of a societal nature (place of women in society, difficulties in balancing work life and private life, etc.). This trend is perhaps inevitable, but it may be that medicine is not necessarily the most effective or the most efficient tool for solving these societal problems. The proponents of this position, therefore, argue in favour of reimbursement of this egg freezing technique only in cases which meet some strictly medical criteria.

6.3.2 Arguments in favour of health insurance intervention in meeting the costs of egg freezing for social reasons (position 2)

A variety of arguments can be put forward here in the context of health insurance intervention, but the most convincing is probably that of seeking consistency in terms of medically assisted procreation (MAP). Although freezing is recognised as occupying a special place within the current MAP measures, there is no reason not to reimburse the use of this technique. Such reimbursement would be all the more justified if it was possible to demonstrate that it is more efficient to carry out freezing (see paragraph 4.5). Some people even mention the idea that egg freezing could be regarded as preventive medicine, avoiding the risks linked to the aging of eggs, and consequently should be reimbursed in this context.

A treatment with frozen eggs comprises two parts: the first involves ovarian stimulation and the collection and freezing of the eggs. The second involves the thawing and the fertilisation of the eggs, followed by the transfer of the embryos. This segmentation also suggests several possibilities as regards reimbursement. The positions are as follows: 1) nothing is reimbursed; 2) everything is reimbursed; 3) only the second phase is reimbursed and 4) the first phase is

reimbursed only if the woman returns to the MAP centre to use her eggs for the purpose of having a child herself. There are arguments for and against for each of these propositions[100]. It is important to carry on the discussion in the Belgian context, namely a context in which full reimbursement of 6 cycles of stimulation is provided for IVF. Given the difficult budgetary situation, preference could be given to the fourth proposition: reimbursement if the woman returns to use her own eggs. This solution avoids wasting public funds, it is efficient, and it is also the most consistent with the reimbursement provided for IVF. Some more elaborate systems, which also take account of the age of the woman at the time of the freezing, are also possible.

The members who consider that no category distinction should be made between medical and social reasons feel that all instances of egg freezing must be evaluated on the basis of the same criteria. Today, there is a tendency to believe that cryopreservation for medical reasons is always acceptable, but this is far from being this case. We can illustrate our remarks with a realistic example: a woman is suffering from a form of cancer for which the treatment leads to infertility in 40% of patients. Does it, therefore, go without saying that all these women should be offered a cycle of IVF at health insurance expense? There is also the question of a gradual process. What happens if it turns out that only 30% of these 40% actually make use of this material for their own reproduction? And what happens if, afterwards, only 30% of them actually fall pregnant? Based on the studies relating to the freezing of gametes to preserve fertility in so-called medical cases, we know that a very limited percentage of patients also use their own material subsequently.
These members also claim that reimbursement of all cases of freezing must be evaluated according to the following criteria: probability of infertility, probability of having a child with the frozen eggs (efficiency), and probability of using the eggs (use rate). As indicated above, the interventions for medical reasons do not meet all these criteria. Likewise, the "social" indications do not satisfy all these criteria: a woman aged 41 who still wishes to freeze her eggs may gain a few years at most and her chances of success are very low on account of her age (few eggs and poor quality). This would, moreover, be consistent with the law on reimbursement of IVF. Conversely, studies will have to demonstrate whether freezing at a young age is also sufficiently effective. Let us imagine that it is established that only 10% of the women who use cryopreservation before the age of 27 also make use of their frozen eggs. It seems perfectly acceptable to permit such applications, but not to reimburse them.
In a broader context, reimbursement may also be permitted even if the woman decides at the end of a certain period not to use her eggs for herself. Where she donates her eggs to third parties, she is then in a comparable situation to that of egg donors, who are also compensated in full for the costs they agree to and for the treatment they undergo. In some countries, women are also compensated where they donate their eggs to science. This compensation cannot be treated like a payment, a practice, moreover, which is prohibited by law in our country.

[100] Mertes H, Pennings G, Dondorp W, de Wert G, *Implications of oocyte cryostorage for the practice of oocyte donation,* Human Reproduction, 2012 27 (10): 2886-2893.

All the members of the second group agree that, given the lack of financial resources (particularly for this possible additional reimbursement) and the ever-increasing needs, it will be necessary, in terms of reimbursement of freezing, whatever the indication in question, to give constant consideration to the "efficacy, effectiveness and efficiency" criteria clearly described in Opinion no. 56 of 8 July 2013 on the issue of the financing of expensive drugs.

Efficacy[101] indicates the result (success) of the technique under experimental conditions. This is clearly present in the case of freezing in anticipation of ARI.

Effectiveness[102] is the benefit/risk ratio when this technique is applied on a large scale, outside any research context. This is still to be demonstrated, given the short period of time that the technique has existed.

Efficiency is evaluated on the basis of the cost/benefit ratio.

It can be said in this regard that, beyond a certain age, the chances of success of the freezing technique are greatly compromised: consequently, the members consider that any collection carried out after this age is hard to justify.

Although it is true that the members of the first group are opposed to reimbursement of egg freezing for social reasons, the fact remains that they share the opinion of the members of the second group in the case of strictly medical indications, namely that the freezing must be in accordance with the three criteria mentioned.

VII. Conclusions and Recommendations

1. The ***term "social freezing"*** is, for some members, controversial at the semantic level and was immediately the subject of discussion.

- One group of members do not accept any difference between egg freezing for classic medical reasons – such as early menopause resulting from a genetic condition or from a medical treatment – and egg freezing for the purpose of differing pregnancy for various other reasons (absence of a stable partner, priority given to the career, etc.). The risk of infertility for a classic medical reason forms a continuum with age-related infertility (ARI) (which indicates the decline in fertility or the natural infertility which appears in women from the age of 35-40). For this reason, its members would like to abandon the terms "social freezing" and "medical freezing", which induce a normative structure into the debate, and only use the term "age-related infertility" in the title of the opinion.
- A second group does, however, make a distinction between the two indications and has no objection to using the term "social freezing", which, as it happens, is used in the international

[101] General definition in "Oxford dictionaries": *"the ability to produce a desired or intended result".*
[102] General definition in "Oxford dictionaries": *the degree to which something is successful in producing a desired result; success: the effectiveness of the treatment*.

literature. In their view, women who delay a pregnancy due to the fact that they have not yet found a stable partner, for example, or because they want to devote themselves to developing their career as a priority, have their eggs frozen for social reasons and do so, at the moment, *irrespective* of any medical problem.

However, the members of this group do not raise any objection to the title of the opinion containing the phrase "in anticipation of age-related infertility" instead of the term "social freezing".

2. ***Concerning the substance of the issue***, none of the members consider that "social freezing" is fundamentally unacceptable from the ethical point of view. Two lines of thought emerge in this context:

- One group regards the "freezing of eggs in anticipation of age-related infertility" as a totally separate right of an independent woman, enabling her to make decisions about her fertility regardless of any pressure.
- The second group regards the "freezing of eggs in anticipation of age-related infertility" as the excessive medicalisation of a natural process or the use of medicine for the purpose of solving a social problem which could be solved by other means. These members are of the opinion that, initially, measures should be taken aimed at both men and women in order to facilitate motherhood at a younger age.

3. All the members of the Committee agree that treatment of age-related infertility (ARI) can take place when it presents ***no health risk*** for the woman and offers an ***acceptable degree of safety*** for the unborn child. At the moment, there is no evidence to suggest the existence of a risk for the woman or the child. However, since the short-term and long-term information is, even today, still limited, the collection and monitoring of additional data is very highly recommended.

4. Concerning ***social security reimbursement of the costs of egg freezing***, two orientations have emerged from within Committee:

- one group thinks that, given the limited budgetary resources, the community must never reimburse egg freezing for social reasons;
- a second group does not wish to make any distinction between medical and social indications, and would like an identical reimbursement decision to be made whatever the indication. Given the limited resources and the increasingly pressing needs, it is always necessary to take into account the "efficacy, effectiveness and efficiency" arguments"[103] in

[103] Clinicians and decision-makers often make a distinction between the efficacy and the effectiveness of an intervention. Efficacy trials (explanatory trials) determine whether an intervention produces the desired result under ideal conditions. Effectiveness trials (pragmatic trials) measure the degree of beneficial effect in a "real" clinical environment." (Freely translated from the English), *Criteria for Distinguishing Effectiveness From Efficacy Trials in Systematic Reviews. Technical Reviews*, No. 12, Gartlehner G, Hansen R A, Nissman D *et al*. Rockville (MD): Agency for Healthcare Research and Quality (United States); 2006 Apr. V. http://www.ncbi.nlm.nih.gov/books/NBK44024

the context of reimbursement of egg freezing, whatever the indication that motivates it.

- Although it is true that the members of the first group are opposed to reimbursement of egg freezing for social reasons, the fact remains that they share the opinion of the members of the second group in the case of strictly medical indications, namely that the freezing must be in accordance with the three criteria mentioned.

5. As for the ***"age-related" criterion,*** the Committee adheres to the rules established by the legislature.
The members consider that reimbursement of a collection beyond the age of 40 is very hard to justify from the social point of view.

6. Given that the technology requires a ***specific infrastructure***, egg freezing can be implemented only in duly approved centres for reproductive medicine. These centres must offer excellent information to patients and psychological monitoring, and they must have a gamete bank.
The doctors in the centres must also have ***freedom of conscience*** in this regard, as determined by the law of 6 July 2007.

An ***agreement*** which clearly describes the use that will be made of the gametes, how long they will be preserved and what will happen to them when the preservation period ends (end of the agreement, woman aged over 47, death of the woman) must be given to all patients when this treatment starts. Four possibilities should be provided for here: continuation of the preservation (if it is still possible), destruction, donation to other individuals for the purpose of procreation or donation to scientific research (with or without fertilisation).

7. Some members consider that society must take ***steps aimed at avoiding increased pressure*** on adult women to delay motherhood. Other members of the Committee argue that the social pressure on an adult women to have children earlier does not cause her to have children in unfavourable social and psychological conditions.

8. All the members of the Committee consider it necessary for ***information campaigns*** to be carried out, with the following objectives:

- informing women and men about the decline in fertility with the age of the woman;
- informing them of the possibilities and the limitations related to IVF, so that they have realistic expectations of it;
- informing them of the possibility of vitrifying eggs to reduce the risk of age-related infertility caused by delaying pregnancy for an extended period.

All the members of the Committee stress the need to introduce the necessary social measures, for the men and the women concerned, aimed at ***reducing the obstacles to carrying out***

parental projects at the time the originators of these projects decide to do so.

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The opinion was prepared in the select commission 2012/1, consisting of:

Joint chairmen	Joint reporters	Members	Member of the Bureau
R. Rubens	G. Evers- Kiebooms	H. Alexandre	P. Devroey
G. Schamps	I. Liebaers	M. Dumont	
	L. Ravez	N. Gallus	
	R. Rubens	G. Pennings	
	G. Schamps		

Member of the secretariat
B. Orban

Experts interviewed
Prof. Dr Diane De Neubourg, *Chef de clinique de Gynécologie obstétrique* [Head of Obstetrics and Gynaecology], *Centre universitaire de la fertilité* [University Fertility Centre] of KULeuven.
Dr Petra De Sutter, *Chef de la clinique de la fertilité* [Head of Fertility] at the University Hospital of Ghent.
Julie Nekkebroeck, Psychologist CRG/CMG [Centre for Reproductive Medicine/Centre for Medical Genetics], University Hospital Brussels (VUB).
Prof. Dr Luc Roegiers, Child Psychiatrist, In-vitro fertilisation, Child-psychiatry/Perinatology (St-Luc University Clinics).
Dr Dominic STOOP, IVF Clinic (VUB).

The working documents of the select commission 2012/1 – request for opinion, personal contributions of the members, minutes of the meetings, documents consulted – are stored as Annexes 2012/1 at the Committee's documentation centre, where they may be consulted and copied.

This opinion is also available at www.health.belgium.be/bioeth, under the "Opinions" section.