

The best possible start to life

April 2007



A consultation document on multiple births after IVF

Chair's foreword



My main concern as Chair of the Human Fertilisation and Embryology Authority is probably the same as yours – the welfare and safety of women undergoing in vitro fertilisation (IVF) and of the children who are born as a result of those procedures.

Minimising the risks to mother and baby is crucial. The HFEA's licensing and inspection processes are there primarily to ensure that practices are safe. But for all the advances in science and improvements in IVF procedures, the greatest risk to the health and welfare of children is the same as it has always been – being born as a twin or triplet, rather than as a 'singleton' baby.

You will see from reading this consultation document that all indicators for the health of the baby are worse for twins than for singletons. Thankfully the majority of twins are fine in the end. But many have a difficult and sometimes traumatic start to their lives, involving hospitalisation and neonatal intensive care. Mothers, too, are more likely to have dangerous complications during their pregnancy. And a minority of twins and triplets are affected by conditions that can last their lifetime.

Because of these concerns, the HFEA asked a group of experts, including patients and clinicians, to investigate multiple births after IVF. They concluded

that IVF children should be given a better chance to be born as healthy, full-term, normal birthweight singletons.

Their arguments for this view are convincing. Several other countries have introduced procedures for single embryo transfer; and indeed the UK – where 40 percent of babies born after IVF are twins – is out of step with most of northern Europe in this respect.

However, I am acutely aware that abstract statistics are one thing – one's own personal wish to have the best possible chance of having a baby is quite another. How can we balance the concern for the best possible outcome for mother and baby with an anxiety about potentially lowering the chance of a pregnancy?

This is where your views come in. We at the HFEA are keen to move forward with patient groups, practitioners and the professional bodies to see how progress can best be made in changing practice in the IVF sector. We want to know how you think we can move towards a better, safer situation for IVF children and their mothers.

We look forward to hearing from you.

A handwritten signature in black ink that reads "Shirley Harrison". The signature is written in a cursive, flowing style.

Shirley Harrison

Contents

Part 1: Introduction

1. Background to the review
Box 1: The HFEA - who we are and what we do
2. Objective of this policy review and document

Part 2: Background information – what you might need to know in order to answer our questions

3. What is the chance of having twins after IVF?
Box 2: Babies born after IVF/ ICSI treatments from 1991 to 2003
Box 3: Risk – a difficult concept
4. What are the health risks for twins?
5. What are the health risks for mothers of twins?
6. What are the consequences for families of twins?
7. Problems in neonatal and children's services

Part 3: Elective single embryo transfer – methods, problems, international experience

8. Putting back only one embryo during IVF
9. How did other countries introduce the change?
Box 4: Single embryo transfer and multiple birth rates in Sweden 1997 - 2004
10. What effect would single embryo transfers for those patients with the best overall prognosis to conceive have?
Box 5: Predicted outcome and single embryo transfer

Part 4: Reducing multiple births after IVF – options for HFEA regulation

11. Single embryo transfer – who should decide?
Box 6: Current HFEA guidance on embryo transfer
12. Options for HFEA regulation
Box 7: Regulatory options

Part 5: Your views

Part 6: Annexes

- Annex A: Partial regulatory impact assessment
- Annex B: Equality Impact Screening
- Annex C: The independent expert group on multiple births after IVF
- Annex D: Glossary of terms

Executive Summary

In 2005, the Human Fertilisation and Embryology Authority (HFEA) set up an independent expert group, including fertility practitioners, paediatricians, nurses, patients and an NHS commissioner, to review the available data on multiple births after IVF and to investigate the need for change. The Expert Group's Report, *One child at a time*, argued that being born as part of a set of multiples is the biggest risk to IVF children's health and welfare. The negative health outcomes for IVF twins and triplets are mostly due to their frequent prematurity and low birth weight. All the risks of morbidity (ill health) are significantly increased for twins, compared to singleton babies; mothers of twins are at higher risk of complications, health and psychological problems, too. The HFEA concluded that these avoidable risks to IVF children and their mothers are unacceptably high and need to be reduced. IVF practice needs to change in order to give IVF children better chances to be born at full term and with a normal birth weight – a better start to life.

Currently around 1 in 4 IVF pregnancies results in the birth of twins. This is more than 10 times more than the naturally occurring twin birth rate. The high number of twin pregnancies after IVF is caused by the routine transfer of two embryos to the woman's womb during an IVF cycle. The only way the proportion of singleton births after IVF can be increased is by only transferring one embryo to those women who are most likely to conceive – and are therefore also most at risk of conceiving twins (good prognosis patients).

In recent years, some Northern European countries have made the transition towards single embryo transfers for those patients with the best prognosis. They have managed to significantly increase the proportion of healthy, full term, normal birth weight singleton babies born after IVF, while maintaining existing live birth rates. The HFEA is aware that the UK fertility sector is in many ways different from those health care systems where change was successfully introduced. The most important difference is that patients in the UK do not on the whole have access to three NHS funded full IVF treatment cycles, contrary to National Institute for Health and Clinical Excellence (NICE) guidelines in 2004.

All the health care systems that moved towards single embryo transfer for the sub-group of patients with the highest risk of twin birth have generous state provision of IVF services.

The commissioning of NHS fertility services by Primary Care Trusts (PCTs) and charges raised by the private sector are not within the remit of the HFEA. This is because the statutory basis of all HFEA regulation, the HFE Act 1990, creates, but also limits, the HFEA's regulatory powers to deal with laboratory and treatment practices, i.e. the creation and storage of embryos and the requirements for consent and patient safety in IVF.

The HFEA believes that the current twin birth rate after IVF needs to be brought down to below 10% of all births after IVF. This is still much higher than the naturally occurring twin birth rate, but it has been shown internationally to be achievable without damaging patients' chances to conceive.

The HFEA wants to explore, together with practitioners and with patients, how progress towards safer IVF, with better health outcomes for IVF children in particular, could be made in the UK. This consultation document suggests some options for regulation and for joint working with professional bodies, fertility centres and patients in order to increase the proportion of single embryo transfer cycles and therefore the number of singleton babies born after IVF. These options range from more prescriptive to more flexible approaches; their advantages and disadvantages are discussed in more detail in the document itself and in Annex A, the regulatory impact assessment.

The HFEA invites the views of anybody who feels affected by the issues raised in this document.

Part I: Introduction

I. Background to the review

- 1.1 In 2005, the Human Fertilisation and Embryology Authority (HFEA) launched a project on multiple, in particular twin, births after in vitro fertilisation (IVF). The aim of the project was to review whether HFEA guidance on the transfer of embryos during IVF needed to be changed.
- 1.2 The HFEA invited an independent group of experts to review all the available data on this subject. The Expert Group met six times and produced a report entitled 'One child at a time' which was presented to the Authority in October 2006¹. One of the Group's recommendations is that the HFEA should change the current embryo transfer guidance in the Code of Practice for licensed centres with a view to increasing the proportion of single embryo transfer cycles. If this recommendation were adopted, it would mean that the HFEA in future tells clinics that it expects them to work differently in order to reduce the proportion of twin births after IVF and to increase the proportion of singleton babies.

Box 1: The HFEA – who we are and what we do

The Human Fertilisation and Embryology Authority (HFEA) was set up in 1991 by legislation (the Human Fertilisation and Embryology Act 1990) in order to regulate IVF and related treatments and embryo research, and to oversee developments in the science and medicine of human reproduction and embryology. Clinics wishing to perform IVF need to obtain a licence from the HFEA and are subject to regular inspections. One of the main statutory functions of the HFEA is to develop, update and publish a Code of Practice, which sets out what is expected of all licensed centres. **Currently, the Code of Practice contains provisions that women under 40 are expected to have no more than two embryos transferred; women over 40 are allowed a maximum of three.**

The HFEA does not have control over all aspects of fertility services in the UK. Importantly, the HFEA cannot make any decisions about the funding of IVF by the NHS, or about the prices charged by private providers of fertility treatments. This is because the statutory basis of the HFEA's regulatory powers does not extend to questions of funding or service provision. Further, the HFEA does not regulate more 'low-tech' fertility treatments, such as fertility drugs (for example clomifene). Intra-uterine insemination (IUI), where the woman's partner's sperm is placed inside the woman's uterus (womb) in order to help fertilisation, is only partially regulated by the HFEA when the EU Human Tissue Directive comes into force in the UK in spring 2007. This partial regulation is restricted to questions of laboratory safety and quality control and does not necessarily extend to the issue of the welfare of the future child (as is the case for the regulation of IVF).

¹ For more information see Annex C. You can get copies of the report on the HFEA website at www.hfea.gov.uk/multiplebirths

2. Objective of this policy review and document



2.1 The aim of this policy review is to consider whether the HFEA should change its guidance to centres in order to reduce the number of twin pregnancies and to increase the proportion of singleton pregnancies after IVF and related treatments. If new guidance is considered necessary, it should aim to strike the right balance between two overarching policy commitments:

- Achieving public health improvements (by reducing the proportion of IVF twins that are vulnerable due to prematurity and low birth weight)
- Protecting clinical and patient autonomy (by making treatment choices that take account of patients' diverse circumstances and preferences)

2.2 The obvious way in which these two aims can be brought into balance is to restrict single embryo transfer policies to those fertility patients who are most likely to conceive, and who therefore have good chances of getting pregnant, even if only one embryo is transferred. So **all the proposals contained in this document limit the use of single embryo transfer to patients who are the most likely to conceive (i.e. have a good prognosis)**. Later on in this document, this is discussed in more detail, but in short, good prognosis patients are relatively young (up to 35 for example) and have not undergone many previous failed IVF attempts.

2.3 This document sets out possible ways in which the HFEA could change its guidance to clinics, discusses the benefits and risks identified with each approach and asks you for your views. In order to provide readers with the necessary background information, the document contains, in Part Two, a summary of the facts on multiple births after IVF. It summarises the evidence on:

- The incidence and causes of multiple births after IVF
- The increased health risks for twins
- The increased health risks for mothers of twins
- The consequences for families of twins
- The consequences for neonatal services²

2.4 Part Three of this document briefly reviews how a reduction in the proportion of twins born after IVF has been achieved internationally, and discusses whether this experience can be applied to the UK sector. Part Four presents the options for regulation that were identified by the Expert Group in their Report 'One child at a time' and Part Five invites you to give your views on them. All the regulatory options aim to reduce the proportion of twins born after IVF to below ten percent of all births after IVF.

² A more detailed analysis of all these issues, including a full set of references can be found in the Expert Group Report 'One child at a time' on the HFEA website (www.hfea.gov.uk).

Part 2: Background information

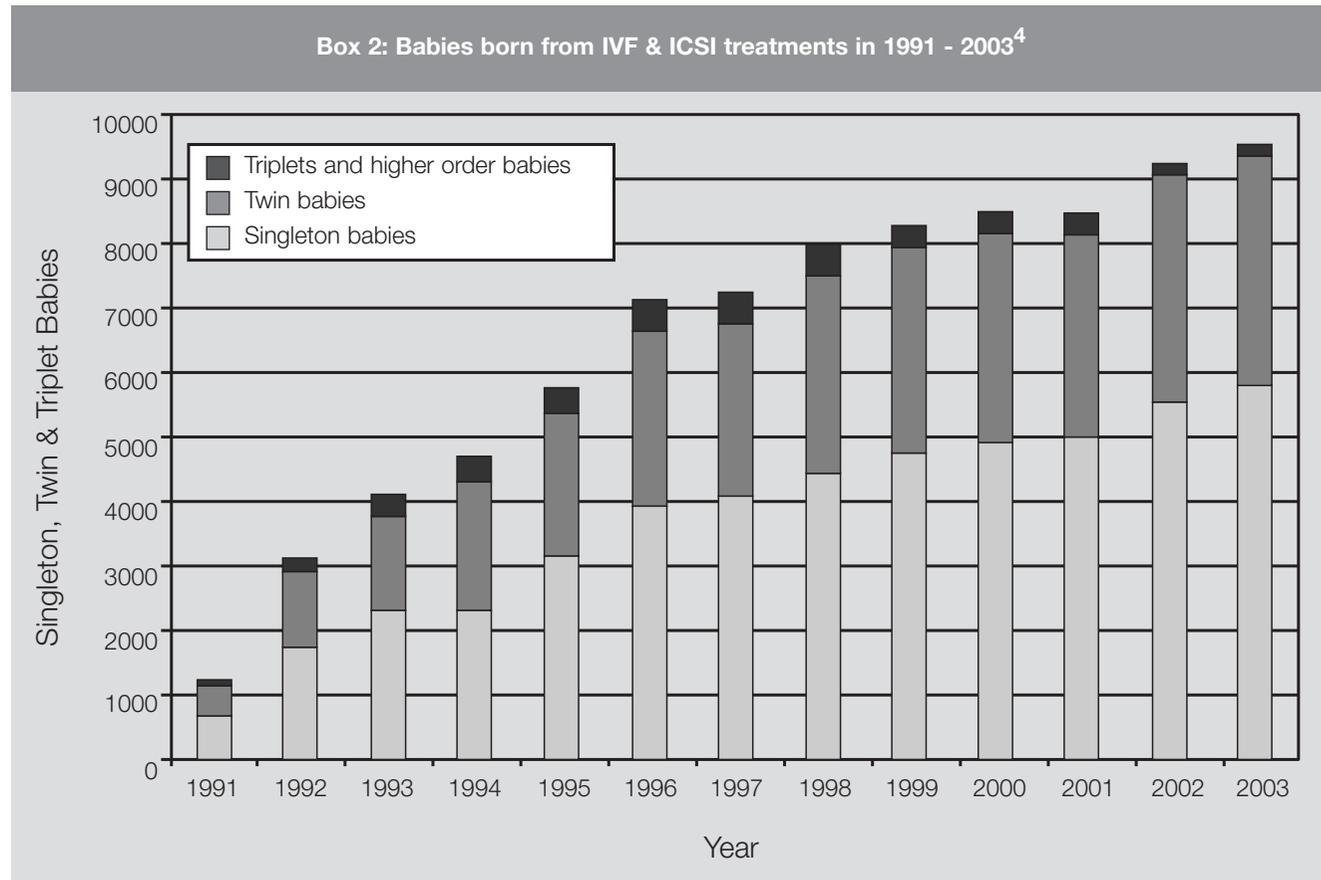
3. What is the chance of having twins after IVF?

3.1 Out of 100 women who give birth after IVF, around 23 will have twins³. After natural conception, only one to two women out of 100 are expected to have twins (one to two percent). We know that nationally, around 25 percent of all the twins in the UK are born to mothers who had IVF treatment.

3.2 The graph (box 2) shows that the number of IVF babies has risen steadily over the years. It also shows that the proportion of triplets was high but is beginning to drop off, partly because the HFEA limited the transfer of three embryos to women over 40. However, the number of twins born after IVF has been unaffected by the two embryo rule for women under 40 and is still very high. The reduction in the proportion of triplet births did not damage overall pregnancy rates.

Are there many twins born after other forms of fertility treatment, too?

3.3 The number of twins born after other forms of fertility treatments (for example IUI) is harder to assess, because information about them is not collected centrally (because it lies outside the HFEA's remit). However, international studies have estimated that around 25 out of every 100 twins born each year (25 percent) are the outcome of treatment with ovulation drugs or IUI⁵. This means that, overall, around half the twins in the UK (around 50 out of every 100) are born to mothers who had some kind of fertility treatment.



³ Latest published HFEA register data: 23.6% multiple births rate after IVF.

⁴ HFEA register data.

⁵ Derom et al in Multiple Pregnancy eds Isaac Blickstein and Louis G Keith 2005.

Why are there so many twins after IVF?

3.4 The high twin rate after IVF is caused by the number of embryos that are transferred during IVF. If two embryos are transferred, and both implant in the woman's womb, then she will be pregnant with (non-identical) twins. The risk of an embryo splitting, which then leads to identical twins being born, is also higher after IVF, for reasons that are not well understood. This means that where one embryo is transferred, twins can be born, and where two embryos are transferred, triplets might be born in the end. Currently, the majority of IVF triplets are born to women who only had two embryos transferred.

What is the problem with the high rate of twins after IVF?

3.5 The most important concern the HFEA has about the high number of twins is that many more twins than singletons are unwell when they are born, and some (albeit a minority) suffer from health and developmental problems for many years. This makes multiple pregnancy and birth the most serious risk to IVF children's health and wellbeing.

Box 3: Risk – a difficult concept

Much of the work of the Expert Group, and much medical literature generally, is based on the concept of risk. But it is not always easy to relate risk estimates to an individual case or to include them in the decisions you are making about your own treatment.

Risk estimates can also be problematic when the actual numbers are small. For example, a woman's risk of death during pregnancy and childbirth is doubled when she is pregnant with twins. However, the background risk of maternal death is so small in the UK (around four in 100,000), that even for mothers of twins the risk is still very low. This can make it more difficult to weigh up risks when you are making decisions about your own treatment.

Because the very extreme outcomes (like permanent disability or even death) are still relatively rare, even amongst twins, it might seem that doctors and the HFEA exaggerate the risks. But the main reason why doctors take these risks so seriously is that they are avoidable. If only one embryo was transferred to those women most at risk of conceiving twins, these bad outcomes would be reduced. It is the avoidability of these risks that makes them a moral issue.

Less extreme outcomes are far more frequent: hospitalisation at the start of life, hospital stays of more than four weeks, breathing difficulties, feeding problems and so on, affect many more twins than singletons (see below for details).

Some fertility patients point out that the risk they worry about most is the risk of not getting pregnant at all. This is a risk that epidemiologists (public health experts) might not find very problematic at all, because not getting pregnant is not a dangerous state of health. But clearly, when making decisions about single or two embryo transfer, all these concerns need to be brought into balance. It would be very easy to reduce the number of twins dramatically by only ever allowing one embryo to be transferred during IVF. But this would reduce many women's chances to get pregnant so much that it would be difficult to accept. This is why **no-one suggests blanket bans on two embryo transfers**. The arguments made by the Expert Group (and also the way other health systems have introduced single embryo transfer) is to focus on those women who are most at risk of having twins (these are the same women who have the highest chance of getting pregnant with IVF).

4. What are the health risks for twins?

4.1 All the major risks of morbidity and mortality (ill health or death) are significantly increased for twins compared with singletons. These risks are mostly due to twins being born prematurely and with a low birth weight. Whereas the average gestation for a singleton IVF baby is around 40 weeks, twins are born on average much earlier (35.8 weeks)⁶, with many being born before 35 weeks, at a time when they are likely to require intensive medical care. The statistics are even worse for triplets: more than 90 percent are born before 37 weeks, and many are born at such young ages that they will survive only with serious health problems⁷. Here are some of the risks:

- At least half of all twins (50 percent) are born prematurely (before 37 weeks) and at low birth weight
- Between 40 and 60 out of every 100 IVF twins (40 to 60 percent) are transferred to neonatal intensive care units when they are born (this compares to around 20 percent of singleton IVF babies)⁸
- Eight percent of twins require assisted ventilation, and six percent suffer from respiratory distress syndrome (this compares to 1.5 percent and 0.8 percent for singletons respectively)⁹
- A small minority of twin babies will be so severely affected that they will have ongoing health and developmental problems for many years to come (for example cerebral palsy, which affects around eight out of every 1000 twins, compared to only two out of every 1000 singleton babies)¹⁰

Are IVF twins and naturally conceived twins similarly affected by these risks?

4.2 IVF twins tend to be non-identical twins, because they come from two separate eggs. So some of the specific problems that identical twins have (particularly if they share a placenta) are less frequent in IVF twins. But the bulk of the health problems for twins stem from being born too early and too small. This equally affects IVF and naturally conceived twins.

4.3 Some studies focus on the outcomes for IVF twins in particular¹¹. For example, a UK study published recently investigated the impact fertility treatments with their high multiple birth rates have on perinatal mortality (the risk of death in the first year of life). It estimates that in 2001 alone, had all the IVF babies born in the UK been singletons, 73 deaths of babies could have been avoided¹². The equivalent figure for 2003 is 126 avoidable deaths of IVF twins¹³.

The HFEA believes that this represents a significant and unacceptable risk to IVF children.

⁶ HFEA register data.

⁷ Details on IVF babies' gestational ages can be found in the Expert Group Report.

⁸ Ombelet et al *Human Reproduction* 2006; 21: 1025 – 1032.

⁹ *ibid.*

¹⁰ Topp et al *Acta Obstetrics and Gynecology Scandinavia* 2004; 83: 548 – 553.

¹¹ See for example Pinborg et al. *Human Reproduction* 2003; 18: 1234 – 1243. Also Kjellberg et al. *Human Reproduction* 2005; 21: 210 – 216.

¹² Oakley L and Doyle P *BJOG* 2006; 113: 738 – 741.

¹³ Personal correspondence with the authors.

5. What are the health risks for mothers of twins?

5.1 Multiple pregnancy and birth carries significant risks for mothers too.

- Around 20 percent (20 out of every 100) women pregnant with twins suffer from pregnancy induced hypertension,¹⁴ compared to around one to five percent of women pregnant with a singleton
- The risk of pre-eclampsia increases almost three fold for twin pregnancies and is nine times higher for women pregnant with triplets. The background risk of pre-eclampsia for women pregnant with a singleton baby is between two and ten percent (between two and ten out of every 100)¹⁵
- The incidence of gestational diabetes is two to three times higher than in singleton pregnancies. For women with a singleton pregnancy the risk of gestational diabetes is around four percent (around four out of every 100)¹⁶

5.2 These complications do not usually mean that the woman will suffer permanent or long-term damage to her health. But they will require women to stop work, and in more serious cases will mean that the woman has to stay in hospital for the last weeks of her pregnancy and that the birth might have to be induced early, in order to protect the child.

But what about the risks of IVF?

5.3 Some IVF patients point out that they are undergoing stressful and painful IVF, which is in itself not risk free, and that the risks of pregnancy, let alone multiple pregnancy, are remote and easier to tolerate. Some risks of IVF are well documented, for example ovarian hyper stimulation syndrome (OHSS). Other risks have been discussed extensively, for example the possibility of an increased risk of ovarian cancer for IVF patients in later life, but a connection between IVF and cancer has never been proven. Were pregnancy rates to drop if only one embryo is transferred in the first fresh cycle, some women would have to undergo an additional treatment cycle in order to conceive. We are aware that undergoing an additional IVF cycle can be a stressful and even traumatic experience for women and their partners and we agree that it is important not to lose sight of the often difficult reality of IVF treatment. However, we want to make sure that the stress of pregnancy and birth complications, prematurity and hospitalisation aren't added to the stress of IVF where this is avoidable.



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¹⁴ Santema et al Eur J Obstet Gynecol Reprod Biol 1995; 58: 9.

¹⁵ Duckit et al BMJ 2005; 330:565.

¹⁶ Carlin et al and Neilson. in: Multiple Pregnancy Kilby et al (eds) RCOG 2006.

6. What are the consequences for families of twins?

6.1 The Expert Group also reviewed the evidence on what life is like for parents and siblings of twins. In the UK, no free help is routinely available to parents of small twins or even triplets. Some mothers and families with twins experience severe parenting stress, increased maternal depression, a reduced ability to work outside the home and an increased rate of divorce have all been reported for mothers of twins¹⁷.

6.2 It has also been suggested by a number of studies that parents who have twins after fertility treatments find looking after them even more stressful than parents of naturally conceived twins¹⁸. It is not clear why these differences occur, but one possible explanation is that people's often lengthy and difficult experience of infertility and its treatment impacts on their experience of raising children¹⁹. Importantly, more parents of IVF twins will be first time parents, and first time parents find it on the whole much harder to cope than parents of twins who already have had a child before²⁰.

6.3 Some fertility patients argue that it seems insensitive or even cruel to tell them that, although they want to have a family so much, if they did end up with twins some of them would find it hard to cope. But research shows that parents of singleton babies have a better chance of enjoying their family life and of feeling confident about their parenting role than parents of young twins who might end up feeling exhausted or even depressed.



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¹⁷ Ostfeld, BM et al. *Twin Research* 2000; 3: 234 – 241; Glazebrook, C et al. *Fertility and Sterility* 2004; 81: 505 – 511; Groothuis, J et al *Pediatrics* 1982; 70: 769 – 773; Bryan, E. *BJOG* 2003; 110: 24 - 28.

¹⁸ Cook R et al. *Human Reproduction* 1998; 13: 3244 – 3246. These findings were confirmed by a recent larger study. See: Olivennes F. et al. *Fertility and Sterility* 2005;84: 725 – 733.

¹⁹ Ellison, M and Hall J. *Fertility and Sterility* 2003; 80: 405 – 414.

²⁰ Colpin, H et al. *Human Reproduction* 1999; 14: 3133 – 3137.

7. Problems in neonatal and children's services

7.1 Some of the media reporting around twin births after IVF focuses on the increased needs of IVF twins for expensive neonatal hospital care. The Expert Group did discuss the evidence for pressures on NHS children services, but it strongly felt that arguments about money should not determine IVF best practice.

7.2 In particular, the Group was keen to avoid the impression that IVF patients are being blamed for 'using up NHS resources'. The whole point of the NHS is that care is given when it is needed without asking questions about *why* a person is in need of medical care. But it is also reasonable to ask whether it is necessary in the first place for the children themselves to be born too ill to be taken home immediately.

7.3 The extent of the problem is clear:

- Because they are born too early, 40 to 60 percent of twins are admitted to neonatal intensive care when they are born and more than ten percent spend more than four weeks there. This is almost ten times more than singleton babies²¹.
- The NHS cost of neonatal care for twins is 16 times higher than the cost of looking after singletons, and the cost of neonatal care for triplets is 109 times higher²².

- One UK study points out that if just the money spent on IVF triplets in the first year of their lives was saved, that money could buy almost 2000 extra cycles of IVF for the NHS²³. Even more savings could be redirected into providing IVF cycles on the NHS if single embryo transfer was introduced for a sub - group of patients.

7.4 Providers and parent-users of neonatal services describe a situation that is already under severe strain. It is especially difficult to find two cots in the same clinic for twins and also to find a bed for the mother. It is not unknown to have the mother in one hospital and each of the twins in two other hospitals²⁴.

7.5 To some fertility patients it seems that arguments like the ones above are simply about cost cutting, which seems particularly unfair since most IVF patients have to pay for their fertility treatment themselves. But the point of these arguments is that the health problems of twins, which make them so much more dependent on NHS care, are *avoidable*. If fertility doctors only transferred one embryo during IVF, IVF children would have virtually the same chances as naturally conceived children of being born as full-term and normal birthweight singletons. No-one argues that children in need of care shouldn't get it. But the Expert Group argues that there is no good reason for so many IVF children needing intensive medical care in the first place.



²¹ See studies on health risks for twins above.

²² Ledger, WL. BJOG 2006; 113: 21 – 25.

²³ *ibid.*

²⁴ See for example Neonatal Perinatal Epidemiology Unit (2005).

Part 3: Single embryo transfer – methods, problems, international experience

8. Putting back only one embryo during IVF

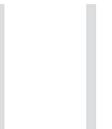
8.1 The above sections argued that it would be better for IVF children, mothers, their families and NHS services if more children born after IVF were singletons rather than twins or even triplets. Because the reason for the high multiple rate after IVF is the transfer of two embryos, the only way the multiple pregnancy rate can be brought down further is by transferring only one embryo to those patients at most risk of conceiving twins²⁵.

8.2 Where single embryo transfers are already used in medical practice, a 'normal' IVF treatment would be as follows:
The woman is given hormones in order to produce more than one egg in one month. When the eggs are mature, they are retrieved (from the ovaries, with a long needle that is inserted into the vagina). The eggs are mixed with sperm, and those that fertilise are monitored for two or three days. The embryo that is most likely to implant (this is judged by embryologists) is then used for transfer back to the woman's womb.

All the other embryos that are judged to have an acceptable potential to implant at a later stage are placed in a freezer. If the initial cycle fails, i.e. the woman does not get pregnant, the frozen embryos are thawed and used one after the other, until the woman either gets pregnant, or all the embryos have been used up. In the latter case, the treatment could start again as outlined above.

8.3 When considering the transfer of only one embryo, it is important to balance the wish to reduce the risk of multiple pregnancy with the desire to maintain current pregnancy rates. In the countries where the proportion of twin births has been successfully reduced, not *all* women have only one embryo transferred. Two embryo transfers are still offered to those women who have lower chances of success. If all fertility patients, regardless of their own circumstances, could only ever have one embryo transferred, this would damage their chances of getting pregnant. Therefore, **the HFEA is not proposing a blanket ban on two embryo transfer.**

²⁵ The literature also discusses selective abortion (fetal reduction), where one fetus is killed in order to produce a singleton pregnancy, as a way of bringing down the multiple rate, but for IVF twin pregnancies this is considered only as a last resort, because it is a medically risky and morally and psychologically difficult procedure.



9. How did other countries introduce the change?

9.1 A number of countries have introduced policies that make the majority of IVF cycles single embryo transfer cycles: Belgium, Sweden, Finland, the Netherlands, and to a lesser extent Denmark and Norway.

9.2 Initially, a number of randomised controlled studies on single embryo transfer were conducted in clinics across Northern Europe. These trials showed a clear reduction of the twin rate, but also produced a **lower pregnancy rate** for the first fresh cycle of IVF where only one embryo was transferred. However, once a frozen/thawed follow-on cycle was included in the pregnancy rate based on one egg collection (cumulative pregnancy rates), pregnancy rates were equivalent for single and two embryo transfer cycles, with much lower twin and complication rates after single embryo transfer cycles²⁶. The trial data convinced many doctors internationally, that single embryo transfer was a promising strategy for increasing the proportion of singleton births, but that the freezing of spare embryos (cryopreservation) and their subsequent use in a follow-on cycle had an important role to play in maintaining success rates.

9.3 Only patients who were considered most likely to conceive were included in the initial trials. There were some variations in the inclusion criteria, but on the whole the women were young (often no older than 35 years), had at least one good quality embryo and were undergoing their first or second IVF cycle.

It is likely that any policy adopted by either the HFEA or clinicians in the UK in the future will also limit the use of single embryos to patients with good chances of conceiving.

9.4 When single embryo transfer policies were adopted nationally in the countries in question, **success rates did not actually drop**, even based on the first fresh cycle of IVF. Overall, the twin rate dropped significantly, without impacting on women's chances of conceiving. So the picture that emerged from the initial trials was not fully confirmed once the new policies were rolled out. The graph (box 4) represents the Swedish experience with the introduction of single embryo transfer (SET).

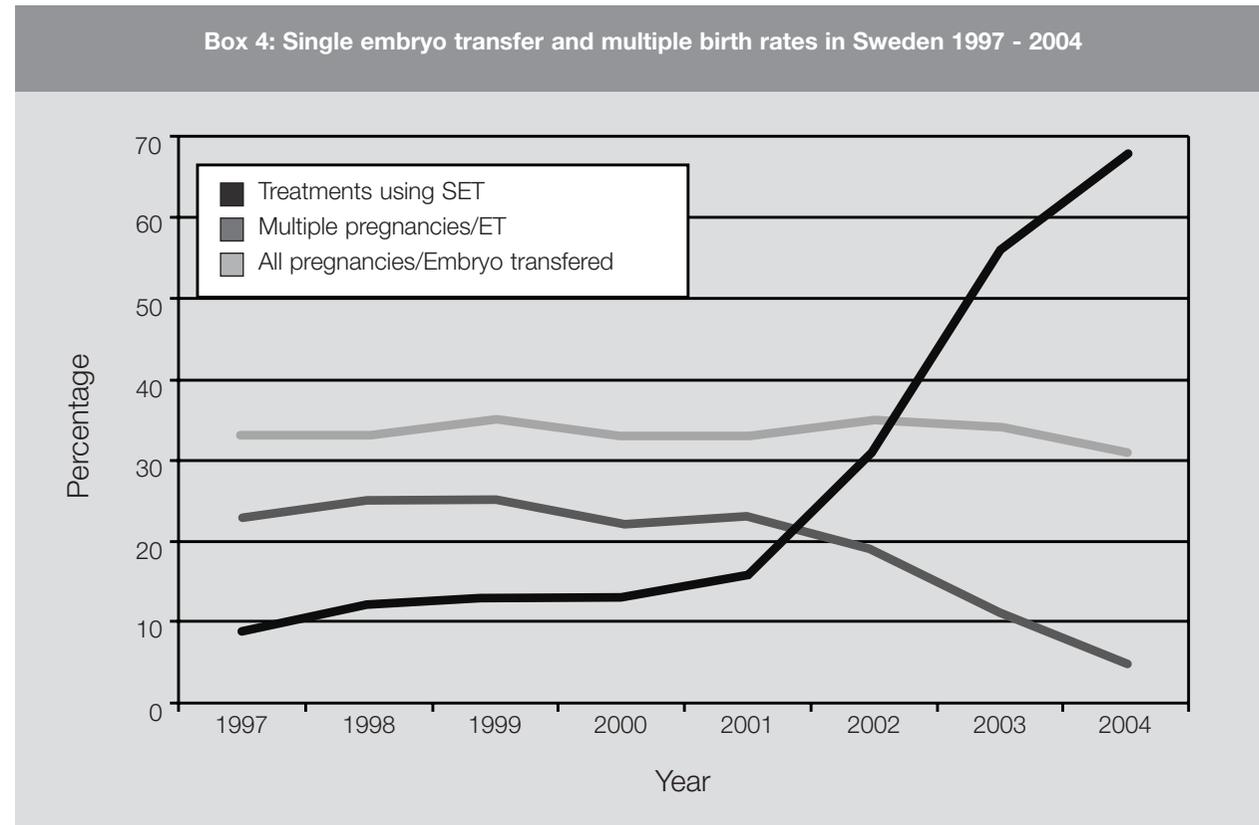
9.5 The graph shows a clear link between the single embryo transfer rate and the multiple pregnancy rate:

- When 30 percent of IVF is done with single embryo transfer cycles, the twin birth rate is around 20 percent
- When 50 percent of IVF is done with single embryo transfer cycles, the twin birth rate is around ten percent
- When 70 percent of IVF is done as single embryo transfer cycles, the twin birth rate is around five percent

9.6 In Sweden, the overall pregnancy rate remained virtually the same over the years, while single embryo transfers were increasing. Thus women's chances of conceiving were not harmed. The **discrepancy** between the published trial data and the actual international experience is not easily explained, but it might have to do with patient selection for trials (this means that they are not diverse enough to represent the whole population of patients in an entire country).

It might also be the case that had practice not changed in these countries, success rates would have actually gone up slightly, and with the introduction of single embryo transfer they stayed the same. This would mean that the increase in single embryo transfers prevented a slight rise in pregnancy rates that would have otherwise occurred.

²⁶ The published literature on the single embryo transfer trials conducted internationally is discussed in much more detail in the Expert Group Report 'One child at a time'. See www.hfea.gov.uk/multiplebirths



10. What effect would single embryo transfers for those patients with the best overall prognosis to conceive have?

10.1 The HFEA thinks that **one cannot predict with certainty whether IVF pregnancy rates in the UK will drop slightly if more single embryo transfers were used** (as the trial data suggests) or not (as the international data collected on whole countries suggests). The HFEA is convinced that **even if pregnancy rates did fall slightly, the cumulative pregnancy rate will remain the same for single and two embryo transfer cycles**. Cumulative pregnancy rates look at whether a woman achieved a pregnancy once all the good quality embryos (including frozen ones) created after one egg collection have been used for embryo transfers. So statistics based on cumulative pregnancy rates treat all the transfers following one egg collection (and freezing) as one treatment attempt.

10.2 However, there might also be differences between the UK sector and fertility services in other countries that make it more difficult to apply the Scandinavian experience to the UK. The following factors need to be taken into account by the HFEA:

- The failure to fully implement the National Institute of Health and Clinical Excellence (NICE) guideline on fertility treatments, which obliged English and Welsh Primary Care Trusts (PCTs) to offer three full cycles of IVF (including frozen/thawed follow-on cycles) to all women aged under 40
- The subsequent fact that many IVF patients find it difficult or impossible to access NHS funded treatment which might make them resistant to even the slightest possible drop in success

rates, particularly if they do not have access to NHS funded cryopreservation and frozen/thawed follow-on cycles

- The fact that most IVF (around three quarters) is offered in the private sector, with clinics competing for patients who are focussing on maximising their chances of success in one fresh cycle
- The publication of headline 'success rate' figures by the HFEA, which might make it harder for clinics to start using more single embryo transfers, if they fear that this will position them lower down any IVF 'league table'

10.3 The Expert Group advised the HFEA that in their view, the overall lack of NHS funded IVF treatment is the biggest obstacle to the unproblematic introduction of single embryo transfers in the UK²⁷. However, none of the relevant issues, from NICE guidelines to PCT commissioning of fertility services, is within the regulatory remit of the HFEA (because the legislative basis of the HFEA's regulation, the HFEA Act, does not extend the HFEA's powers into these areas).

10.4 We are aware that any change would be more acceptable for patients and clinicians if patients could rely on the NICE-prescribed three full cycles of NHS funded IVF, but there is nothing the HFEA can easily do to change the situation²⁸. We are working with other organisations with responsibility for these questions, like NHS commissioners, the Department of Health and NICE itself.

But essentially, the HFEA has to decide what to do about multiple births, without being able to also make decisions about access to NHS funded treatment. This puts the HFEA in a difficult position: We believe that there are strong public health arguments for an increased use of single embryo transfers, because fewer IVF children will be born vulnerable and in need of intensive care. We are particularly convinced that the inclusion of frozen/thawed follow-on cycles and the cost of freezing in the NHS provision of 'a full cycle of treatment' would make the situation fairer and more acceptable to many patients. But the HFEA might have to make decisions about changes to its guidance without being able to resolve the difficult funding situation.

10.5 One issue that is clearly within the HFEA's control is how the HFEA collects and publishes the outcome data for all the IVF cycles that are performed in the UK. The Expert Group stated that the publication of a single headline figure based on individual embryo transfers, rather than taking all the embryo transfers following one egg collection together, was a potential obstacle to the introduction of single embryo transfer in the UK. The Expert Group recommended that the HFEA should investigate ways of accumulating pregnancy data following one egg collection, and should also consider new methods of data presentation that could give a more rounded picture of a clinic's performance, including whether a clinic is responsible for the birth of many sets of multiples.

The HFEA is taking these recommendations forward by doing a detailed analysis of its outcome reporting with a view to identifying possible improvements.

10.6 The HFEA is aware that the UK fertility sector is different from the countries that have so far successfully introduced single embryo transfer. However, we are convinced that lessons still can be learned from the international experience:

- Internationally, single embryo transfer policies were introduced without damaging women's chances of conceiving
- The proportion of singleton births after IVF was massively increased in Northern European countries, with fewer IVF children needing special care at the start of their lives
- It is easier to introduce this change when patients have easy and equitable access to publicly funded IVF
- Frozen/thawed follow-on cycles are essential to maximise women's chances of a successful pregnancy with single embryo transfers
- Applying single embryo transfer successfully means identifying those women at highest risk of conceiving twins. They are the same women who have the best chances of getting pregnant after IVF in the first place

²⁷The situation is somewhat better for fertility patients in Scotland, where patients meeting the eligibility criteria can receive two or three fully funded IVF cycles. In Northern Ireland only one cycle was made available. The Expert Group Report discusses in much detail the situation in England, which is marked by inconsistencies, but an overall shortage of NHS provision.

²⁸The HFEA conducted research with its patient advisory panel Fertility Views in 2005, which confirmed this point. For more detail see <http://www.whiteloopdev.co.uk/>

Box 5: Predicted outcome and single embryo transfer

You might be a patient who wonders whether the transfer of only one embryo would be appropriate in your own case. **Whether the transfer of only one embryo is the right treatment for you depends on your prognosis for getting pregnant at all after IVF.** It is not always easy to predict a woman's chances of conceiving after IVF, but a number of factors have been identified as relevant:

- The woman's age (the older a woman is, the lower her chances are of conceiving after IVF)
- Her obstetric and gynaecological history (what causes her fertility problem, has she been pregnant, maybe with IVF, before)
- The number of previous failed IVF attempts (a high number of previous failed IVF attempts relates to a lower chance of conceiving)
- The woman's ovarian response (how do the woman's ovaries respond to the hormone stimulation, and how many eggs does she produce)
- The number and quality of embryos that are created (the more good quality embryos there are, the higher a woman's chances are of conceiving)
- The availability of good quality embryos on day five or six of culture (the Expert Group believed that where there is more than one good embryo on day five and six, the case for only transferring one was overwhelming)

The patients with the best predicted outcome need to have only one embryo transferred during IVF in order to increase the number of singleton babies born after IVF without damaging overall pregnancy rates.

Based on the above evidence that making 50 percent of all IVF cycles single embryo transfer cycles will lead to less than ten percent of twin pregnancies, the 50 percent of patients who have the best chances of conceiving should be given only one embryo during IVF. Just focussing on age (which is one of the determining factors), there are some figures that can help to make decisions:

- 47.5 percent of all treatment cycles in the UK in 2003/04 were offered to women under 35 (up to their 35th birthday)
- 56.5 percent of all treatment cycles were offered to women under 36 (up to their 36th birthday)

So if the HFEA or a clinic were to set criteria for which women should only have one embryo transferred, and it wanted to cover around 50 percent of all treatment cycles, it could opt for an age limit of around 35 years. But age is not the only criterion that needs to be considered. For example, the number of previous failed IVF attempts needs to be taken into account when successfully targeting single embryo transfer to the right patients. This is because the reasons that prevented successful treatment in the first two or three cycles of IVF are thought to also reduce the risk of twin birth in further cycles (the woman's embryos seem less likely to implant). This means that single embryo transfers are normally restricted to the first one or two IVF cycles a woman has.

So if you are an older IVF patient, or you have already had two or three previous failed IVF attempts, it is unlikely that you would be restricted to single embryo transfer, even if policies in the UK did change.

Part 4: Reducing multiple births after IVF – options for HFEA regulation

11. Single embryo transfer – who should decide?

11.1 The Expert Group advised the HFEA that it should aim to at least halve the twin birth rate after IVF, and should try to bring it to below ten percent. This is still a much higher twin rate than would occur naturally. But based on the international experience, it has been shown possible to achieve this reduction without harming IVF patients' chances of conceiving in the first place. The HFEA has been convinced that a twin birth rate of no more than ten percent presents a reasonable compromise between achieving better health outcomes for IVF children and patients' chances of conception. The following options for regulation are aimed at achieving that reduction.

11.2 Based on the international experience discussed above, a reduction of the twin birth rate to below ten percent can be achieved if at least 50 percent of IVF cycles involve the transfer of only one embryo. This means that the 50 percent of IVF patients with the best prognosis and therefore the highest risk of conceiving twins should only

be offered one embryo for transfer during IVF. They will be younger patients (for example, no older than 35 years), with at least one good quality embryo, who have not had more than one or two previous failed attempts at IVF.

11.3 The crucial question for the HFEA as the regulator of fertility services in the UK is: **Who should make the decision about whether only one or two embryos should be transferred to a woman during IVF?**

- Should the clinician and patient decide entirely by themselves?
- Should they be guided by voluntary professional guidelines?
- Should they follow a maximum twin rate they are not allowed to exceed?
- Or should the HFEA make a policy decision about who should only have one embryo transferred, and this policy is then applied by clinics to all patients?

The remainder of this document discusses the various approaches.

²⁹Clinicians always have discretion about how they apply HFEA guidance, particularly in exceptional circumstances, and this is taken into account by Authority Licence Committees.

³⁰As yet unpublished and unverified HFEA data shows that the incidence of triplets has been more than halved since the strict two embryo policy was introduced in 2003.

Box 6: Current HFEA guidance on embryo transfer

Section 8.17 – 8.22, 6th edition Code of Practice

The early years of IVF (before the HFEA was set up in 1991) were characterised by overall low pregnancy rates but a high proportion of very high order births (triplets, quadruplets and even more). The HFEA has always considered the transfer of unlimited numbers of embryos as unsafe and introduced a maximum of three embryos from its very first Code of Practice in 1991 onwards. This effectively stopped very high order births.

Because the number of triplet births continued to rise (with IVF pregnancy rates rising generally), this guidance was gradually tightened between 2001 and 2004. Currently, a maximum of two embryos is permitted for women under 40, or those receiving donor eggs (which come from young women). For women over 40 a maximum of three embryos is allowed.

Initially, HFEA guidance allowed clinicians more discretion in how they applied this guidance, but this 'softer' approach failed to change the sector's practices. Consequently, the HFEA decided to make the two embryo rule for women under 40 mandatory²⁹. This approach has proven successful: The number of triplet births has finally dropped without affecting overall IVF success rates³⁰. But the number of twins born after IVF continues to rise.

12. Options for HFEA regulation

12.1 The Expert Group identified a number of options for regulation that the HFEA might wish to take up. Initially, the Group also included ‘doing nothing’ as an option for consideration. However, after the discussion of the available evidence on the inherent risks of twin pregnancy and birth, the Group decided that doing nothing was no longer a justifiable approach for the HFEA to take. As a minimum, the HFEA should engage with practitioners, patients and the wider fertility sector through education and joint working, trying to convince the sector of the need for change. The HFEA agrees with this analysis. The table (box 7) contains the remaining options.



Box 7: Regulatory options	
Policy option	Possible impact
Option 1: HFEA to work with clinics, patients and professional bodies to increase awareness of risks of multiple births and to encourage increased use of single embryo transfer	<ul style="list-style-type: none"> ● Might lead to change over time, if the case for change is found convincing by clinicians and patients ● Could also encourage the professional bodies (those organisations that represent fertility professionals) to develop (non-binding) guidelines for the clinical use of single embryo transfer
Option 2: Set a maximum twin rate of no more than 10 percent that each clinic must not exceed – this could be phased in over a number of years	<ul style="list-style-type: none"> ● Would leave the decision making about individual patients to clinicians, while at the same time influencing their overall judgement in favour of doing more (around 50 percent) single embryo transfer cycles
Option 3: Develop Code of Practice guidance that defines in which cases only one embryo should be replaced, based on for example age, number of previous treatment cycles, medical history and possibly embryo quality	<ul style="list-style-type: none"> ● Would reliably reduce the proportion of twins born after IVF ● Clinicians would have to follow guidance, similar to current two embryo transfer policy
Option 4: A combination of options 2 and 3 above, i.e. clinics could initially be given an overall maximum twin birth rate. If they fail to achieve it, they have single embryo transfer criteria imposed on them by the HFEA	<ul style="list-style-type: none"> ● Might motivate clinicians to exercise their clinical discretion responsibly in order to avoid the imposition of more rigid HFEA guidance

Discussion

- 12.2 Broadly speaking, the above options range from the very flexible, where the HFEA refrains from regulatory action (option 1), to the very restrictive, where the HFEA takes full responsibility for selecting patients for single embryo transfer (option 3). There are advantages and disadvantages with these two general approaches to regulating the fertility sector.
- 12.3 A very flexible approach (option 1) allows clinicians to do what they consider best for each of their individual patients, without being bound by policy, guidance or targets. However, a very flexible approach might not lead to an effective reduction of the twin rate after IVF. The previous experience with the move from three to two embryo transfer showed that professional guidance on its own (which is not binding), and also HFEA guidance which allowed clinicians more flexibility, failed to reduce effectively the number of triplet pregnancies. Some clinicians failed to take the problem of triplet births seriously. The problems of self-funding patients and league tables discussed above may also work as obstacles to change.
- 12.4 A more restrictive approach (option 3), on the other hand, can lead to more consistent and effective change of clinical practice, but it might make it more difficult for doctors to take into account the individual circumstances of any given patient. This could disadvantage patients who are for example young, but have a poor prognosis for other reasons. There is a particular problem with embryo quality in this approach. Embryo quality is important for selecting the right patients for single embryo transfer, but it is a difficult criterion for the HFEA to use for guidance, because it is not judged consistently across the UK fertility sector.
- 12.5 There are also differences in how these different approaches could be enforced. If the HFEA set some simple and consistent criteria regarding which patients should have only one embryo transferred (option 3), this would be easy to follow for clinics and easy to check for HFEA inspection teams. If more discretion is left to clinicians (for example option 2), it might be harder for clinicians to see whether they are doing enough to reduce the incidence of twin pregnancies. It would also be harder for the HFEA to enforce its policy, if clinics do not seem to achieve the required change. A maximum twin rate could be backed up with either professional or HFEA guidance on how the reduction could be achieved (this would in effect be a combination of option 2 and 3).
- 12.6 Setting a maximum twin rate for clinics (option 2) would be a departure from current HFEA guidance – it would constitute a novel approach to regulating clinics, which would require careful consideration of the possible impacts a ‘target’ might have on clinical practice. A maximum twin rate could also be phased in over a number of years. This would make the transition less abrupt, but would possibly

- also prolong controversy and uncertainty.
- 12.7 These are the options for regulation the Expert Group identified for the HFEA. Their possible impact on regulating the sector is discussed in more detail in Annex A (regulatory impact assessment). Please give us your views in the enclosed questionnaire.



Part 6: Annexes

Annex A: Partial regulatory impact assessment (RIA)

This RIA considers which impact upon centres, patients and other parties the options discussed in this consultation document are likely to have. Financial impacts, which are the core of most RIAs are not the sole focus of this RIA, although they are included. It also discusses the wider practical, regulatory, enforcement and clinical implications of the various options for reducing the incidence of multiple births after IVF.

Title of the proposal

Reducing the incidence of multiple births after IVF – options for regulation

Purpose and intended effect

i) Objectives

The aim of this policy review is to consider whether the HFEA should change its guidance to centres on the number of embryos that can be transferred during IVF in order to reduce the number of twin pregnancies and to increase the proportion of singleton pregnancies after IVF and related treatments. To this end, the views of the relevant stakeholders and the wider public are sought.

If new guidance is considered necessary, it aims to strike the right balance between achieving public health improvements (by reducing the proportion of IVF twins that are vulnerable due to prematurity and low birth weight) and protecting clinical and patient autonomy (by making treatment choices that take account of patients' diverse circumstances and preferences).

ii) Background

Since its first edition, the HFEA Code of Practice limited to three the number of embryos available for transfer during IVF. The number has been reduced from three to two (for women under 40) over recent years. This has effectively reduced the number of triplet and higher order births, but the proportion of twin pregnancies after IVF remains high, with one in four IVF pregnancies leading to the birth of twins.

Internationally, a number of health care systems and fertility sectors have moved to single embryo transfer as the norm for fertility patients with a good prognosis to conceive. This achieved a reduction in twin pregnancies, with their inherent risks for babies and mothers, without reducing women's overall chances of conceiving through IVF. This review aims to investigate whether the UK sector should follow this international example, and if so, which role HFEA guidance or standards should play.

iii) Rationale for government (HFEA) intervention

This consultation aims to investigate whether HFEA intervention is indeed necessary or best placed to introduce the desired change in clinical practice. The Expert Group set up by the HFEA in order to identify regulatory options considered action by the HFEA essential for making progress because of the way the UK fertility sector is organised. They argue that progress is less likely to happen without HFEA intervention because of obstacles to change: most patients fund their own treatments and clinics compete for mostly private patients, often on the basis of 'league tables' based on pregnancy rates after one fresh cycle of IVF.

Consultation

i) Within Government

Views from the Department of Health and the National Patient Safety Agency will be sought during the consultation process.

ii) Stakeholders

- Patient groups and individual patients (previous, current and prospective)
- Groups representing families of twins and users of neonatal services
- Clinicians, embryologists, nurses, other practitioners working in fertility services
- Professional bodies (ACE, BFS, RCOG, RCPCH, RCN, BICA, RCM)
- NHS commissioners and public health professionals

Equity and fairness

Single embryo transfer is only proposed for a sub-group of patients. So ultimately, not all patients will be treated the same. However, equity and fairness would only be affected if the differential approach to embryo transfer was not based upon evidence and therefore imposed an unreasonable level of restriction upon some patients. Were the HFEA to impose single embryo transfer criteria through its guidance, the desire to improve public health outcomes would have to be carefully balanced with the need to protect patient and clinical autonomy. For further details, see the Equality Impact Assessment attached as Annex C.

Small businesses impact test

Small businesses are defined as having fewer than 50 employees. Most private fertility clinics will fall into this category. Where the options outlined in this document increase the regulatory burden for clinics (for example if they have to work up their own patient selection criteria for single embryo transfers and monitor outcomes in terms of twin pregnancies, this has to be justified on public health grounds. Since private fertility clinics are providers of health care, it is not unreasonable that some regulatory burden is imposed in order to significantly improve the health outcomes for IVF children and their mothers. We do not believe that any of the options contained in this document have an unjustifiable impact on small business.

Competition assessment

It is not anticipated that any of the options presented in the document will significantly affect competition between licensed centres in the private sector. If clinics are obliged to reduce their twin rate, and some manage to do so better than others without damaging women's chances of conceiving, it might give them a competitive advantage over other clinics; this would enhance public health through positive competition.

Enforcement and sanctions

Compliance with guidance or standards contained within the HFEA's Code of Practice is achieved through the HFEA's licensing and inspection system. Non compliance with guidance in the Code of Practice may or, in some

circumstances must, be taken into account by a licence committee when it is considering whether to issue, renew, vary or revoke a licence.

Monitoring and review

Monitoring of the impact of guidance contained within the HFEA's Code of Practice is achieved through the HFEA's own licensing and inspection process and reviewed in the light of emerging evidence. All guidance is reviewed prior to publication of each edition of the Code of Practice.

Options: Benefits and costs

Options for regulation were identified by the Expert Group, and discussed and reviewed by the HFEA's Regulation Committee and the Authority itself. They are now being consulted upon. The following section considers the costs and benefits of each of the policy options outlined in this consultation paper. If responsibility or costs are transferred to other parties outside assisted conception units (such as the NHS, but also patients), this is considered a 'transfer'.

Option 1:

HFEA to work with clinics, patients and professional bodies to **increase awareness** of risks of multiple births and to encourage increased use of single embryo transfers

Benefits	Costs	Transfer
<ul style="list-style-type: none"> ● Might strengthen self-reliance and best practice in the sector ● Wouldn't lead to resentment by clinicians or patients, since pace of change would correspond to clinicians' and patients' willingness to co-operate ● Wouldn't necessarily increase administrative burden (but if professional bodies and clinicians decide to tackle the problem, they would clearly have to handle some data collection and so on) 	<ul style="list-style-type: none"> ● Not all clinicians might comply ● Clinicians who change their practice might see a drop in the fresh cycle birth rate compared to those who continue transferring two embryos ● Patients might seek out clinicians who perform fewer single embryo transfers to maximise their chances to conceive in one fresh cycle ● Incentives remain in place that prevent change ● Didn't work when the move from 3 to 2 embryo transfer was introduced by professional guidelines only 	<ul style="list-style-type: none"> ● Possibly over time there will be a slight reduction of neonatal and paediatric transfer costs to the NHS, but change might only happen slowly ● Professional bodies would have to shoulder some responsibility for developing guidance and for disseminating best practice through training

Option 2:

Set a maximum twin rate of no more than ten percent that each clinic must not exceed, which could be phased in over a number of years

Benefits	Costs	Transfer
<ul style="list-style-type: none"> ● Clinicians can work out their own selection criteria, taking account of individual patients' needs ● Patients can assume that they get 'tailored' treatment ● Targets can be phased in over a prescribed time ● Policy can be adjusted to new developments in practice - it won't get out of date ● Monitoring by results rather than by input 	<ul style="list-style-type: none"> ● Would require clinics' commitment, capacity and resources to develop and monitor appropriate criteria ● Might reduce birth rates, at least in the first fresh cycle ● Possible difficulty of enforcing and penalising inappropriate practice; HFEA might need to review how to ensure compliance ● Will create time lag before targets can be policed ● Might lead to target driven practice which might not correspond with clinical priorities (i.e. patients might be refused or might be offered treatment choices that are target driven). For example if a clinic reaches its maximum rate half way through the year and then cannot offer two embryo transfers anymore 	<ul style="list-style-type: none"> ● If patients require an additional embryo transfer because the first fresh single embryo transfer cycle fails, they will be burdened with additional costs unless the NHS picks up the bill ● In order to maintain patients' chances of success, NHS would have to include frozen embryo transfer cycles into its IVF commissioning ● Might increase costs of NHS provision of IVF if more cycles are purchased, but these costs would be compensated by significant anticipated savings in neonatal and paediatric care if more IVF babies were born as full-term, normal birth weight singletons

Option 3:

Develop Code of Practice guidance that defines in which cases only one embryo should be replaced, based on for example age, number of previous treatment cycles, medical history and possibly embryo quality

Benefits	Costs	Transfer
<ul style="list-style-type: none"> ● Clarity ● Enforceability (perhaps apart from embryo quality) ● Certainty about reduction of multiple pregnancy rates over a short timeframe ● Guidance allows some degree of flexibility for clinicians, but it is limited ● Level playing field for clinics 	<ul style="list-style-type: none"> ● Possible resentment from clinicians and patients since it would reduce flexibility and clinical discretion ● Might reduce success rates, particularly for patients with a poorer prognosis to conceive, if the guidance criteria were not sufficiently flexible ● Evidence base is not equally strong for all the criteria that would need to be included in the guideline, for example embryo quality is not judged uniformly, which would make it difficult to enforce ● Clinics or patients might challenge guidance through the courts 	<ul style="list-style-type: none"> ● If further treatment cycles are needed, many patients would not have access to (further) NHS funding; costs for many patients would therefore increase ● In order to maintain patients' chances of success, NHS would have to include frozen embryo transfer cycles into its IVF commissioning ● This might increase the cost of NHS IVF purchasing, but NHS might make significant saving on neonatal and paediatric care costs if the proportion of singleton births after IVF is increased

Option 4:

A **combination** of options 2 and 3 above, i.e. clinics could initially be given an overall maximum twin birth rate. If they fail to achieve it, they have single embryo transfer criteria imposed on them by the HFEA

Benefits	Costs	Transfer
<ul style="list-style-type: none"> Might motivate clinicians to use their clinical freedom in a way that corresponds to public health needs in order to protect their autonomy (and possibly success rates) from regulatory intervention 	<ul style="list-style-type: none"> New regulatory approach for the HFEA; would require careful and potentially resource-intensive co-ordination of new guidance with licence committee imposed licence conditions Not always easy to decide whether failure to meet target is simply to do with the (real) unpredictability of treatment outcomes or whether clinics simply fail to make an effort Possible time-lag before twin rates are finally reduced Might lead to long-drawn out arguments between HFEA and individual clinics, disadvantaging those clinics that simply complied in the first instance 	<ul style="list-style-type: none"> If further treatment cycles are needed, many patients would not have access to (further) NHS funding; costs for many patients would therefore increase In order to maintain patients' chances of success, NHS would have to include frozen embryo transfer cycles into its IVF commissioning This might increase the cost of NHS IVF purchasing, but NHS might make significant saving on neonatal and paediatric care costs if the proportion of singleton births after IVF is increased

Annex B: Equality Impact Screening

Reducing the incidence of multiple births after IVF – options for regulation

Screening Procedure:

The options for regulation have been screened in relation to the seven equality categories:

- Age
- Disability
- Ethnicity
- Faith
- Gender
- Human rights
- Sexual orientation

Evidence of higher or lower participation by different groups

Where the use of fertility services differs between these various groups, this is partly based on medical evidence (age, gender, disability), partly due to financial restrictions (which lie outside the remit of this screening), partly due to personal choice (for example faith based or other objections to the use of fertility services). Regulatory constraints which are not based on medical evidence but which would limit the use of fertility services by any of these groups are not proposed.

Indication that particular options create problems for specific groups

It is hoped that where a particular proposal might create a problem which is specific to any of the above groups that this will be highlighted during the consultation process. In light of the responses to the consultation we will assess whether particular groups are specifically affected by any of the proposals contained in this document.

Evidence of different needs, experiences, issues and priorities in relation to particular options

It is necessary that any policy proposal that is ultimately adopted takes account of the different needs, experiences, issues and priorities of various groups – this is why regulatory intervention needs to carefully balance the desire to improve public health outcomes with the need to protect clinical and patient autonomy.

In light of the points above, it has been decided that a full equality impact assessment is unnecessary at this stage for the following reasons:

- There is no evidence that any of the proposed options would impose regulatory constraints on any of the above groups that are not based on medical evidence
- Inequalities of access to fertility services are largely due to financial restrictions which lie outside of the remit of this screening process
- The decision not to carry out a full equality impact assessment will be reviewed in light of the responses to the consultation

Annex C: The independent expert group on multiple births after IVF

The independent expert group on multiple births after IVF was set up in October 2005. Professor Peter Braude, from the Royal College of Obstetricians and Gynaecologists chaired the group. Its members were:

Mr Sam Abdalla – Clinical Director Lister Hospital

Professor David Barlow – Former Chair of the NICE fertility guideline development group

Professor Siladitya Bhattacharya - Head, Department of Obstetrics and Gynaecology, University of Aberdeen

Kate Brian – Journalist and patient representative

Clare Brown – Chief Executive, Infertility Network UK

Jane Denton – Director, Multiple Births Foundation

Dr Alun Elias-Jones – Consultant paediatrician and neonatologist, Leicester Royal Infirmary

Dr Jan Gerris – Fertility specialist, Middelheim Hospital, Antwerp, Belgium

Dr Patricia Hamilton – President, Royal College of Paediatrics and Child Health

Helen Kendrew – Specialist fertility nurse, British Fertility Society

Professor Bill Ledger – Fertility specialist, University of Sheffield

Professor Brian Lieberman – Fertility specialist, St Mary's Hospital Manchester

Dr Dave Morroll – Consultant embryologist and Chair of Association of Clinical Embryologists

Dr Karl Nygren – Chairman of the EIM (European IVF monitoring) consortium of ESHRE

Dr Claire O'Donnell – Public health specialist, Cheshire and Merseyside Specialised Services Commissioning Team

The Expert Group met six times and discussed the following issues:

- Outcome data for twin and higher order births
- Data on the impact of multiple births on children's and neonatal services
- The international experience of moving towards elective single embryo transfer (eSET) policies
- Patient perspectives on eSET
- Information about the commissioning and funding of IVF by the NHS
- Ways of presenting ART outcome data that might encourage the use of eSET
- Possible policies for the reduction of multiple pregnancies

The agendas and minutes of the Expert Group meetings can be found on the HFEA website at www.hfea.gov.uk/multiplebirths

This is also where you can find the Group's final report 'One child at a time' that was presented to the HFEA in October 2006.

Glossary of terms

ACE

Association of Clinical Embryologists. It is the professional body of and for embryologists in the UK, set up to promote high standards of practice in clinical embryology and to support the professional interests of embryologists working in the UK.
www.embryologists.org.uk

Anaemia

A condition characterised by too few red blood cells in the bloodstream, resulting in insufficient oxygen supply to tissues and organs.

Antenatal (prenatal) care

Care provided between conception and birth.

ART

Assisted Reproductive Technologies.

BFS

British Fertility Society. A national multidisciplinary organisation representing professionals practising in the field of reproductive medicine.
www.britishtfertilitysociety.org.uk

BICA

British Infertility Counselling Association. A professional organisation for fertility counsellors and counselling in the UK. It seeks to promote the highest standards of counselling for those considering or undergoing fertility investigations and treatment.
www.bica.net

Blastocyst

An embryo that has developed for five to six days after fertilisation.

Blastocyst transfer

This is performed when the embryos are cultivated for 4-5 days to approximately 64-cell stage at embryo transfer.

Cerebral palsy

A condition where parts of the brain are damaged, usually through lack of oxygen, often during the process of birth or when a premature baby cannot breathe properly, which affects the person's control over muscle movements. It is not progressive (i.e. it doesn't get worse as time goes by) and it does not necessarily affect a person's cognitive development or intelligence.

Chorionicity

Refers to the connection between the fetus and the placenta in twin pregnancies. Monochorionic twins share a placenta. Dichorionic twins each have their own placenta and gestational sac.

Code of Practice

A Code issued by the HFEA containing guidance and rules for fertility and research centres. The Code can be found on the HFEA website.
www.hfea.gov.uk

Cohort (observational) study

Study of a group of people with shared characteristics, normally after a health care intervention you wish to evaluate.

Cryopreservation

Preserving substances at very low temperatures in vapour-phase or liquid nitrogen at -196 degrees centigrade. E.g.: frozen sperm, embryos, eggs, testicular tissue and ovarian tissue.

Culturing *in vitro*

Developing outside the body (i.e. in the laboratory).

Cumulative or fresh/frozen pregnancy rates

Pregnancy rates that are added up after all the eggs collected during the initial stimulated cycle have been used up, including those that were initially frozen.

DET

Double Embryo Transfer. Transferring two embryos at the same time to a woman undergoing IVF.

Dichorionic twins

Twins that each have their own placenta and gestational sac.

Dizygotic twins (non-identical twins)

Dizygotic twins form when two separate eggs are fertilised by separate sperm (two zygotes). These twins are no more alike than any other brothers or sisters.

Egg collection

Procedure by which eggs are collected from the woman's ovaries by using an ultrasound guided needle, or by using a laparoscope (an instrument used for looking into the abdomen) and a needle. Also known as egg retrieval.

Embryo grading systems

Systems used to rate embryos so that only the embryos with the highest chance of implantation are chosen for transfer or freezing.

Embryologist

Scientist who handles human embryos outside the woman's bodies: fertilising the eggs, culturing them *in vitro*, selecting the best ones for transfer, and freezing additional ones.

Embryo morphology

The configuration of the embryo, used to judge the quality of the embryo (its potential to implant or survive freezing).

Embryo score

See embryo grading.

eSET

Elective Single Embryo Transfer. The principal way in which multiple births after IVF can be reduced, by only transferring one embryo at a time to the woman's womb.

ESHRE

European Society for Human Reproduction and Embryology. The main aim of ESHRE is to promote interest in, and understanding of, reproductive biology and medicine.
www.eshre.com

EU Tissue Directive

The EU Tissues and Cells Directive sets standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissue and cells intended for human application. It was adopted by the European Parliament on 7th April 2004.

Fertility Friends

Fertility Friends is an online meeting place for couples in the UK since 2002. Its aim is to help people through the difficult process of assisted conception by sharing thoughts, experiences and knowledge with others.
www.fertilityfriends.co.uk

Fetal reduction

Also called multi-fetal pregnancy reduction or selective abortion, where one or more of the fetuses is aborted in order to achieve a singleton or lower order multiple birth.

Fetus

Middle stage of development between the embryonic stage and the birth of the baby, when all main recognisable features are shown, i.e. from the end of the second month of pregnancy.

Fresh cycle

An IVF cycle using fresh (not previously frozen) embryos for transfer.

Glossary of terms

Frozen or thawed cycle

An IVF cycle using embryos that were frozen after creation and then thawed for transfer.

Gestational age

Fetal age of a newborn, calculated from the number of completed weeks since the first day of the mother's last menstrual period to the date of birth. The normal gestation is 40 weeks.

Gestational diabetes

A glucose intolerance which occurs in pregnancy, usually noticed between the 24th and 28th weeks of pregnancy. In most cases the blood glucose level returns to normal after delivery. Although the symptoms of this form of diabetes are mild and non-serious for the mother, elevated blood glucose in the mother has been associated with an increased risk of fetal and newborn death. Risk factors for gestational diabetes include maternal age over 25, family history of diabetes, obesity, birth weight over 9 lb in a previous delivery and multiple pregnancy.

Gestational weight

The weight of a newborn at gestational age.

Haemorrhage

Bleeding.

HFE Act

The Human Fertilisation and Embryology Act 1990.

HFEA

Human Fertilisation and Embryology Authority. The HFEA's primary remit is to license and monitor UK clinics that offer IVF (in vitro fertilisation) and DI (donor insemination) treatments, and all UK-based research with human embryos. It also regulates the storage of eggs, sperm and embryos.
www.hfea.gov.uk

HFEA register

A confidential register of information about donors, patients and treatments provided by HFEA licensed treatment centres. It was set up in 1991 and it contains information concerning children conceived from licensed treatments from that date onwards.

HFEA's patient panel

A group of previous or current IVF patients who help the HFEA with its policy development by giving their views and commenting on proposals. Anyone undergoing or considering fertility treatments can join it.
www.hfea.gov.uk

Higher order pregnancies

A pregnancy with three or more fetuses. These pregnancies can arise from one, two or more fertilized eggs implanted in the uterus and developing into babies.

Hypertension

Persistently high arterial blood pressure. Hypertension may have no known cause or be associated with other primary diseases or conditions and is one of the most common risks of pregnancy.

Iatrogenic multiple births

Medically induced multiple births.

ICSI

Intra-Cytoplasmic Sperm Injection. Process in which a single sperm is inserted directly into the egg, thus bypassing all natural barriers a sperm has to encounter. This technique is usually used when there is a low sperm count or reduced sperm motility.

Implantation

The embedding of a fertilised egg in the uterus/womb.

IUI

Intrauterine Insemination. Injection of sperm into the uterus of a woman.

IVF

In Vitro Fertilisation. The mixing of human eggs and sperm in a laboratory to achieve fertilisation outside the body.

Licence Committee

An HFEA committee that ensures compliance of licensed centres with HFEA guidance.

MFPR

Multifetal Pregnancy Reduction. See: fetal reduction.

Miscarriage

The loss of a pregnancy before the fetus is 24 weeks old.

Monochorionic twins

Twins sharing a gestational sac and placenta. This bears higher risks for the fetuses during pregnancy and birth. It can only occur in identical twins because they develop out of the same egg, part of which develops to form the placenta.

Monozygotic twins

Twins who are derived from a single egg (zygote). Monozygotic twins form when one fertilised ovum separates into two identical zygotes.

Morbidity

A state of disease.

Mortality

Death. The risk of mortality refers to the number of patients who die after a medical intervention or event.

Neonatal intensive care

Intensive care for newborn babies.

NICE

National Institute for Health and Clinical Excellence. A special health authority which was set up by statutory instrument in 1999 to make resource allocation decisions in the NHS more explicit and transparent, and to address the problem of the 'postcode lottery'.
www.nice.org.uk

NICE guidelines

Guidelines issued by the National Institute for Health and Clinical Excellence.

Obstetric care

The care of women during pregnancy, childbirth, and the period during which they recover from childbirth.

Operative delivery

Expulsion or extraction of the child and the after-birth involving surgery.

Ovary

The female reproductive organ producing oocytes (eggs).

Ovarian sensitivity

The number of eggs retrieved in relation to the total number of FSH units (see above) administered.

Ovarian stimulation

Stimulation of the ovaries with drugs in order to retrieve multiple eggs.

Glossary of terms

Oxygen dependence

Describes patients who are not strong enough to breathe sufficiently themselves and are therefore dependent on the artificial input of oxygen.

Paediatric services

Medical services relating to the care and medical treatment of children.

PCT

Primary Care Trust. Regional NHS bodies that are responsible for commissioning (ordering and buying) NHS services locally.

Perinatal care

The care and management for newborn babies, up to seven days after the day of delivery.

Perinatal death

Stillbirths and deaths up to 7 days post-partum.

Placenta

The organ in the womb that provides the fetus with nutrition and oxygen during the pregnancy.

Pre-eclampsia

A disorder that occurs during pregnancy and the postpartum period and affects both the mother and the unborn baby. Affecting at least 5-8% of all pregnancies, it is a rapidly progressive condition characterized by high blood pressure and the presence of protein in the urine. Pre-eclampsia and other hypertensive disorders of pregnancy are a leading global cause of maternal and infant illness and death.

Prematurity

The current World Health Organisation definition of prematurity is a baby born before 37 weeks of gestation, counting from the first day of the last menstrual period.

Pre-term labour

Labour prior to 37 weeks of gestational age.

Randomisation

The process by which patients in a clinical trial are randomly assigned to different treatments. Randomisation minimises the differences among groups by equally distributing people with particular characteristics among all the trial arms. It is considered the best way to assess the efficacy of a given medical treatment.

Randomised controlled trial (RCT)

In a RCT, the research participants are randomly allocated, usually by computer, to either the control or the active arm of the study. Those in the active arm are given the new treatment, while those in the control group are given either an inert placebo or the current best available treatment. Researchers will be interested in whether more of the patients in the active arm are showing signs of improvement than in the control group. RCTs are considered to be the 'gold standard' in medical research.

RCOG

Royal College of Obstetricians and Gynaecologists. The RCOG is dedicated to the encouragement of the study and the advancement of the science and practice of obstetrics and gynaecology. www.rcog.org.uk

RCPCH

Royal College of Paediatrics and Child Health. The main objects of the College are to advance the art and science of paediatrics, improve standards of medical care to children, and to educate and examine doctors in paediatrics. Additionally, the College has a function in providing information to the public on the healthcare of children. www.rcpch.ac.uk

Selective abortion (multifetal pregnancy reduction)

Abortion in order to achieve a singleton or a lower order multiple birth.

Significance

A statistical concept which means that although differences in outcomes might have been measured, they were not clear enough to be certain that they were not simply due to chance. The smaller a study sample is, the less confident you can be that findings are significant in this sense of the word.

Single embryo transfer (SET)

The transfer of only one embryo into the woman's womb during a cycle of IVF.

Singleton pregnancy

A pregnancy with only one fetus.

Spontaneous multiple pregnancy

Pregnancy with two or more fetuses after natural conception.

Thromboembolism

Obstruction of a blood vessel by a blood clot carried by the blood stream.

Twin-to-twin transfusion syndrome

Syndrome caused by the fact that fetuses share the placenta unequally, which leads to imbalanced circulation between the placenta and the fetuses.

Uterus

A small, hollow, muscular organ found in the female pelvis that carries the fertilised ovum through the nine months of pregnancy, enlarging to accommodate the fetus as it grows.



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