Assisted reproduction: a safe, sound future
Terminology

**Assisted reproduction technologies (ARTs)**
The collective name for all artificial approaches used to help women to conceive. They include *in vitro* fertilisation (IVF) and intra-cytoplasmic sperm injection (ICSI).

**Blastocyst**
The hollow ball of cells formed five days after fertilisation from which the embryo and placenta are formed.

**Clinics**
UK infertility clinics licensed by the Human Fertilisation and Embryology Authority to carry out assisted reproduction treatments.

**Cytoplasmic transfer**
Material from a donor egg is transferred into a patient’s egg to overcome problems with embryo survival.

**Efficacy and effectiveness**
Efficacy studies set out to determine whether a new treatment works. Effectiveness trials compare new and existing treatments to find out which is best – often in particular circumstances or patient subgroups. Both assessments are important in informing patient choice.

**Embryo culture**
Growing a newly fertilised egg in the laboratory using conditions and nutrients designed to allow the very early embryo to develop outside the womb before it is transferred to the mother.

**Endometriosis**
Endometrial cells form the inner lining of the womb and are shed during a woman’s period. In endometriosis these cells attach themselves to the outside of the womb and/or ovaries, and in and around the fallopian tubes, causing internal bleeding, pain and reduced fertility.

**Implantation**
The process by which an embryo embeds itself in the womb lining at the start of pregnancy.

**Imprinting**
The selective activation/inactivation of a gene depending on which parent it is inherited from.

**In vitro fertilisation (IVF)**
This assisted reproduction technique mixes collected eggs and sperm in a laboratory to achieve fertilisation outside the body. The embryos produced may then be transferred into a female patient.

**Intra-cytoplasmic sperm injection (ICSI)**
In this assisted reproduction technique, a recognised practitioner injects a single sperm cell directly into a woman’s egg to fertilise it. There are various forms of ICSI, including the extraction of immature sperm directly from the testicle.

**Obstetric**
Relating to the medical specialism of caring for women during and after pregnancy.

**Ovarian hyperstimulation syndrome**
A complication following fertility drug treatment to stimulate the ovaries to produce many eggs. Symptoms range from mild – swollen ovaries, bloating and discomfort – to sickness and breathing difficulties and, much less often, life-threatening fluid build-up.

**Pre-implantation genetic diagnosis**
A screening procedure in which a recognised practitioner removes one or two cells from an embryo to test for specific genetic disorders/characteristics before proceeding with embryo transfer.

**Research Ethics Committee/s**
Review and approval by a Research Ethics Committee (REC) is required, almost without exception, before any medical research in the NHS involving human participants can proceed. RECs are independent of the researchers and their funding and host organisations, and ensure that researchers meet their legal obligations to safeguard the rights, dignity and welfare of all potential participants.

**Singleton**
A child that is carried and born on its own, rather than as one of twins, triplets or multiple offspring.

**Sperm/egg donation**
To circumvent either male or female infertility, sperm or eggs from a fertile third party donor are used to achieve conception.
Background

The first ‘test-tube’ baby, Louise Brown, was born in 1978. Since then, assisted reproduction technologies (ARTs) have helped many couples with fertility problems to have children. Today, more people than ever before are using ART treatment – many commentators believe this reflects the changing social and personal priorities that have increased the age at which couples want to start a family. In 2000/01 there were about 25,000 ART treatment cycles in the UK, each costing between £2,000 and £5,000 per cycle. Most of these were carried out by private clinics.

Today, ART is a rapidly moving and fiercely competitive field. There is a wide and ever-growing range of techniques on offer, with clinics eager to introduce the latest methods and some patients prepared to undergo any treatment that might help them to conceive. But while innovations in ART bring new hope to infertile couples, little research has been done to show whether or not these are superior to conventional procedures, and in particular what the long-term health implications might be for the mother or the resulting child.

Although there is widespread acceptance, based on experience, that current ART procedures are generally safe, the evidence for this, particularly in terms of long-term safety, is relatively weak when compared to other similarly well-established clinical techniques. Too little is known about the basic mechanisms of early human development – whether natural or assisted – about interactions between the mother and her growing baby, or about the overall risks and benefits of ART to draw firm conclusions about whether a new treatment may have any unforeseen adverse consequences.

Fundamental reproductive biology research and thorough evaluation of ART are both vital to providing the information we need. Would-be parents need to know not only which treatments offer them the best prospects of having a healthy child, but also that these are safe and worth what clinics are charging. And with couples willing to go to great lengths to have a child, it is of paramount importance to safeguard the health of these children, from the moment they are conceived until they grow up and want to start families of their own.
The imperatives of families and health professionals and the overriding need to protect public health, can only be met if society as a whole has access to reliable information about the benefits and risks of ART.

Concerned by uncertainties about ART in general and the increasing introduction of new technologies, the HFEA (see box) approached the Medical Research Council (MRC) for advice on the scientific evidence of any potential health risks. The MRC set up an independent working group with a wide remit to look into the whole area of ART research, focussing on possible risks to the embryo and child (see box). In addition to scientific experts and HFEA and Department of Health representatives, the group included ethicists, and spokespeople to advocate consumers’ interests. The Working Group and two specialist subgroups that it set up each held two meetings during 2002/03; this report summarises their work.

The Human Fertilisation and Embryology Authority

The legal responsibility for regulating specified technical and ethically sensitive ART procedures, such as in vitro fertilisation (IVF), in the UK and ensuring their suitability and safety lies with the Human Fertilisation and Embryology Authority (HFEA, www.hfea.gov.uk), which was set up in 1991 following the passing of the Human Fertilisation and Embryology Act 1990. Before a new treatment covered by the Act can be used it must have an HFEA licence, which is not approved until expert review has satisfied the HFEA that the treatment is safe. However, as things stand, there is no legal requirement for clinical testing and/or trials to rigorously assess new treatments before they are introduced.1

Working Group tasks

- Review current knowledge of ARTs and their possible health effects and identify gaps in what is known about the science of human fertilisation and reproductive biology.
- Report back on the priorities for ART research to inform a range of interested parties, from people receiving or considering ART treatment and their families, to scientists and clinicians, legislators, regulators and funders.
- Advise on how to address research needs, taking account of the views and priorities of families and other stakeholders, and the need for quality, value for money and ethical and legal safeguards.

1 The 1990 Act is currently under review, and the law may change relating to some of the issues this report raises.
Working Group findings

The wide-ranging Working Group discussions covered issues including: how best to assess the risks and benefits of existing and new technologies; how to identify research priorities; the merits of retrospective versus prospective studies; whether systematic reviews are needed; the scope for improved data collection and follow-up; the scope for feasibility studies and clinical research; and ethical and social considerations such as consent, consumer consultation, differing cultural and societal values and public attitudes to risk.

Room for improvement

The potential risks of ARTs should be seen in their true perspective. By far the greatest risks to both mother and child arise from the practice of implanting several embryos to increase the chances of having a baby, and the consequences of a possible multiple pregnancy. Women can have side-effects from taking high doses of fertility drugs to stimulate their ovaries, and obstetric complications are more likely before, during and after multiple births. In general, multiple births tend to be less healthy than singletons, in part because they are often born prematurely, and have low birth-weights, reduced survival and increased chances of disability. And as well as placing additional strains on families, there are wider social effects – for example, an increased demand for health service resources. The public purse bears many of the costs that ART incurs after a woman falls pregnant, as it is usually the NHS rather than private clinics that provides pre- and post-natal care and helps her to give birth.

A dramatic global rise in the frequency of twin and triplet births can be largely attributed to the increasing use of ARTs. A recent World Health Organisation (WHO) report (www.who.int/reproductive-health/infertility/l.pdf) highlighted the need to reduce multiple ART births as the highest priority for change in ART practices. Twins and triplets account for over a half of ART babies born in the UK. Before the HFEA was set up, fertility clinics were allowed to transfer as many embryos as they wanted to increase the chances of a successful pregnancy. The HFEA reduced this number to three, and then in 2001 to two – or three in exceptional circumstances. New HFEA guidelines issued in January 2004 limit the number to two without exception in women under 40 and no more than three in women of 40 and older.

However, some recent studies have suggested that even singleton ART pregnancies are more likely than naturally conceived ones to have complications and poorer outcomes for mother and child. Research on existing and new treatments is needed to discover if this is the case, and if so why. Such research could also help to improve ART efficiency and so reduce the need to transfer more than one embryo. For example, the success rate using frozen human embryos has improved little since the technique was introduced in the 1980s. It stands at around 11 per cent per transfer compared to some 50-60 per cent in animals. This suggests that there is scope for research to improve freezing and other embryo-handling techniques. We are also largely ignorant of any long-term effects such techniques might have on the health of the resulting children.

At present the advice and techniques offered to couples vary widely between clinics. Although most patients pay for expensive new ART treatments themselves, it is often not clear whether these will improve their chances of conceiving compared to well-established treatments. For example, some clinics transfer blastocysts at later stages in their development, but there is scant evidence that this actually improves the chances of pregnancy. And because there are no common guidelines on preservation or storage, different clinics use different techniques to freeze sperm and embryos. Possibly even more significant is the fact that there is no regulation of the ingredients that clinics and their suppliers use in embryo-culture media. While there are no known health risks from such media, there has been no
systematic monitoring, evaluation or follow-up of the different media available.

Proper evaluation is crucial to determine the safety of new treatments before they are widely adopted. Recent safety concerns about intra-cytoplasmic sperm injection (ICSI), which accounted for half of all ART treatment cycles in 2001, highlight the need to improve our understanding of the short-, medium-, and long-term risks and benefits of ART. Some researchers from the UK and abroad have warned that artificial sperm selection may allow unintentional fertilisation with abnormal sperm, and so endanger the health of the children conceived. However, studies of ICSI to date have been too small to draw any firm conclusions and there are not enough data to determine how great a risk this might be in the UK.

The priorities for ART research

While there is clearly scope for further research in most areas, the UK lacks a structured framework to support such studies. The first step should be to create an environment that opens up the whole field of ART to high-quality research. There are two primary goals. First, current procedures for follow-up are too limited and there is a clear need in the UK to establish systems for linking ART treatments to health outcomes, in the short-, medium- and long-term. Secondly, new treatments being licensed and introduced into clinical practice in the UK should be systematically evaluated for their effectiveness compared with existing treatments, and for their long-term safety.

An expanded ART evidence base would:

- Benefit the children conceived.
- Help patients with fertility problems and health professionals to make better-informed decisions.
- Advance scientific understanding and ultimately improve ART practices.
- Help to protect public health by providing evidence to the wider scientific community, the HFEA and the public.

To look at how the evidence-base could be improved, the Working Group set up two expert groups to provide more in-depth advice in the key areas of data requirements and follow-up, and the evaluation of new clinical techniques.
Databases to aid clinical evaluation and follow-up

The experts who looked at the issue of databases identified the most effective way to collect ART data, design databases and integrate these with other data sources, so that information about ART procedures can be linked to health outcomes. The main aim was to improve knowledge and understanding of any potential health risks that ART might pose. This would give patients more reliable information on which to base their choices, and provide the best possible advice to couples trying to conceive, to health professionals, and to children born through ART. The group took into account issues of patient consent and risk perception, data protection and feasibility, and gave a high priority to balancing respect for people’s rights and choices against wider public health concerns.

Background

The HFEA database

The HFEA routinely collects data about ART procedures because it is legally obliged to be able to tell people whether they were conceived through ART, and if so, whether donor sperm or eggs were used and whether they are likely to be related to somebody they intend to marry. Early in 2004, these HFEA records were moved to a new £11m database which was set up to collect data from all ART clinics and provide statistics about the use of ART. However, as a regulator the HFEA was not set up to have research functions and the database was not designed to answer research questions posed by existing, new or yet to be developed ARTs. For example, the HFEA data already collected do not record the mother’s reproductive history or the progress of pregnancies, and rely on parents’ own reports of the outcomes and of any abnormalities rather than doctors’ assessments. Designed to meet the legal requirement for maximum security, the new database prevents anyone from identifying patients through their records and seeking their consent to conduct research. Current UK law does not allow these data to be linked to other data sources, such as NHS records, that could be analysed to reveal ART risks or benefits. These are all obstacles to follow-up studies based on comprehensive and reliable data.

Recommendations

A new framework for research

A new monitoring framework should be put in place to collect and collate more comprehensive information than the constraints of the present system allow. There is a need to work closely with the HFEA to avoid unnecessary duplication of data, and with the ART clinics which are best placed to collect ART data, including follow-up information obtained from parents who have given the appropriate consents. Data collection will benefit greatly from the electronic data exchange system that HFEA is rolling out to all ART clinics.

The HFEA does not currently collect information to answer the kind of research questions that follow-up studies would seek to address. As part of this exercise a list of key additional data categories were drawn up for consideration for incorporation into the new HFEA database. The suggestions included: the NHS numbers of patients and their partners and children; data on the laboratory conditions and techniques used to treat embryos in different ART treatments; information about how pregnancies progress; and, crucially, whether a healthy, thriving baby is born.

Given the importance of obtaining information about longer-term outcomes it was recommended that, after
thorough exploration of the ethical implications, consideration should be given to obtaining follow-up data through data linkage to other databases, for example national cancer and death registries, and other NHS medical records.

This framework would generate a comprehensive, high-quality resource which, with appropriate consent, would enable more specific research studies on all aspects of ART to be carried out.

Keeping a lookout

Follow-up systems should be able to provide comprehensive statistical data and support high-quality research to identify potential risks to:

The mother:

- Over-response to drugs to stimulate ovulation, for example ovarian hyperstimulation syndrome, and any evidence of increased ovarian cancer risk.
- Multiple births and obstetric complications.
- Psychological problems.

The child:

- Miscarriage, still birth, or birth complications such as brain damage or consequences of prematurity.
- Birth defects or effects on childhood development that might be linked to invasive techniques such as ICSI, sperm selection and pre-implantation genetic diagnosis. According to some preliminary research these techniques might lead to faulty imprinting, and could have predicted effects including genital malformations and cancer susceptibility.
- Growth abnormalities or other effects in children or adults caused by their embryonic environment. For example, possible biological consequences of embryo freezing or culture conditions used for IVF or blastocyst transfer.
- Adult fertility problems inherited from parents. For example, defective sperm production in men, or endometriosis in some women.
- Possible psychological problems relating to sense of identity. For example, having a non-biological parent in cases of sperm/egg donation.

Future generations:

- The risks are largely unknown. However it is possible that genetic defects may be passed on, and limited studies in humans and animals have hinted at possible intergenerational effects.

Continues overleaf...
Follow-up and consent

Follow-up studies fall into three broad categories, each requiring different degrees of consent.

1. Use of HFEA data alone to produce statistics on pregnancy outcomes and abnormalities.

2. Longer-term follow up requiring confidential, secure linkage to routine health data to produce a database of anonymised information. This would need to be approved by a Research Ethics Committee.

3. Direct contact with families to obtain more detailed information on longer-term health outcomes of children and their mothers. These studies would need scientific peer review and approval by an appropriate Research Ethics Committee.

Patient consent to research is an especially complex area, and it should remain an important consideration in the context of ongoing developments in European Union and UK legislation. Consent should be appropriate to the kind of follow-up study being done and allow for the extent of personal information that different patients are willing to provide. Some people, for example parents who may not want their children to know how they were conceived, might not consent to take part in follow-up studies.

Patient consent forms should be accompanied by clear and appropriate information. They should be simple, flexible enough to allow for future research, and should ideally be based on existing HFEA record-keeping so that clinics only need to use one form. They should give parents the option to agree to be contacted for their permission for follow-up research that involves face-to-face contact with researchers. The HFEA, which is revising its consent forms along NHS lines, could incorporate the necessary changes along with advice from others it has consulted.

Long-term ART effects may appear at any time from early childhood to adulthood. In line with the WHO’s recent recommendation for 20- to 30-year follow-up to monitor male infertility (www.who.int/reproductive-health/infertility/1.pdf), follow-up studies should ideally continue until puberty or beyond, but only after thorough consultation to ensure that this is ethically acceptable. Recognising that making children aware of how they were conceived may be a difficult issue for the family and the child, it is important to think about the practical implications and principles now, before increasing numbers of ART-conceived children reach maturity. Even if follow-up beyond puberty proves not to be feasible, important health concerns still need to be addressed.
Evaluation of clinical procedures

The opportunities were examined to reconfigure the existing regulatory framework to evaluate new technologies as they are introduced, so as to minimise the health risks to children and their parents. The primary aim was to overcome some of the existing constraints and develop a better system of evaluation for ART. The issues considered included: potential obstacles to clinical trials, such as the difficulties of designing randomised controlled trials and funding them in a predominantly commercial arena; how to decide on the priorities for ART trials; and how trials would operate, including in broader national and European contexts. Throughout their deliberations, the subgroup worked on the basis that the mother’s health and well-being are important, but the health of children, who have no choice about how they are conceived, must be the overriding concern in demonstrating whether ART treatments are safe and effective.

Background

Under the current system, independent experts review new ART procedures and advise the HFEA committee that considers licence applications. This committee can stipulate whether or not and how a technique should be used, for example limiting it to a clinical study, and can revoke a licence at any stage if a technique is found to be unsafe. A yearly feedback system – six months for new techniques – enables procedures to be changed in light of emerging findings. Although these decisions are based on all the relevant evidence to hand, this system lacks the strong body of clinical research that underpins many other treatments. Furthermore, the systems for follow-up after treatments have been introduced are too limited. As things stand, too few ART patients are aware of whether or not the treatments they receive are standard practice, and of different treatments’ benefits and risks.

Action is needed to standardise good practice and guidelines, and to accelerate the feedback system to keep pace with new developments. Such a move would be timely. In February 2004 the National Institute for Clinical Excellence (NICE) recommended that infertility treatment cycles on the NHS should be made more routinely available throughout the UK (www.rcog.org.uk/resources/Public/Fertility_full.pdf).

Fortunately, most of the components needed to set up a better evaluation system are already in place. The HFEA can by law require clinical evaluation as a condition of licensing a new treatment and there are well developed precedents; for example, the NICE Interventional Procedures programme and the Health Technology Assessment (HTA) programme that is run by the Department of Health. The culture of inter-clinic collaboration that already exists provides an essential foundation on which to build studies large enough to provide reliable safety, efficacy and effectiveness data. Although other countries, such as Finland, have found that competition and commercial considerations can frustrate national studies, comparing ART techniques across all clinics would have the dual advantages of compensating for variations in how individual clinics carry out a particular technique, and making it possible to detect small but significant differences in outcome that single clinics might miss. Cross-clinic working should be helped by a new NHS memorandum of understanding with the private sector, through the Association of British Insurers and Providers, which places the same data collection and submission expectations on private clinics as on NHS research.
Recommendations

Retrospective vs prospective studies
Designing studies based on the analysis and evaluation of ART data collected in the past is fraught with difficulty. The records are neither comprehensive nor standardised and the scope of patient consent is not always clear. There are also potential biases. Patients’ reports of their pregnancy outcomes may be coloured by their experiences (reporting bias), and the data may not equally represent all ART groups. For example, children conceived through donor insemination whose parents do not want them to know about their origins could be under-represented. For this reason, laying a sound groundwork for future research is likely to be considerably more rewarding than conducting research using existing data.

Demonstrating safety and efficacy
Waiting to assemble enough information on long-term safety and efficacy to conduct exhaustive ART safety assessments would cause unnecessary delay and prevent rapid feedback to patients and their doctors. It would be more productive to focus initially on critical safety issues from conception to six months old, taking a healthy single live birth as the key indicator of a technique’s efficacy. This timeframe would capture miscarriages and the immediate consequences of prematurity, and simultaneously provide data for long-term evaluation. Interim approval based on predictive indicators could be given in advance of full follow-up data on pregnancy outcomes and the child’s health. Such indicators could include normal embryo appearance, good implantation rates, an expected rate of development and full-term delivery. Although randomised-controlled trials are seen as the gold-standard, they are not always practical, so other evaluation methods, for example case-controlled studies or comparative research using animal models, should not be ruled out.

Improving ART evaluation
Regarding evaluation, the Working Group proposed that a new process should be implemented that would enable the HFEA to ensure there was a strong evidence base for licensing new technologies as well as assessing the long-term outcomes of existing ones. The members envisaged independent expert representation in the assessment of all current, new and emerging ART technologies and treatments. The evaluation process would draw on expertise in ART research, epidemiology, statistics, informatics and clinical trials as well as knowledge of existing legal and ethical frameworks. Stakeholder input from clinics, patients, professional bodies and other interested parties, would be a key element (see Overall conclusions and recommendations, opposite).

The HFEA would decide whether or not, and under which conditions, an evaluation should be continued or a new treatment should be licensed and introduced. It would also provide legal and ethical advice having canvassed expert opinion and taken patient and lay views into account. If necessary, the HFEA could issue provisional licences – of limited duration or restricted to a number of uses – to help it decide whether a treatment should be approved, evaluated further, or withdrawn because of inadequate evidence of safety or efficacy.

Patient involvement
Patient-based research should be the touchstone of clinical studies and any new arrangements should be developed within an ethical framework sympathetic to patients’ views and priorities. The process should engage closely with clinics and patients, rather than making participation a condition of getting a licence or of receiving treatment, as is the case in some parts of the world where ART is only provided on condition that the parents allow access and linkage to medical records. These important public-health issues need careful public discussion. Patient involvement in shaping research priorities would greatly help anonymised follow-up through health records and participation in research and clinical trials. A recent MRC-funded survey by the patient interest group Infertility Network UK (www.infertilitynetworkuk.com) – formerly called CHILD – suggested that most people seeking ART treatment would be happy to participate in such studies.
Overall conclusions and recommendations

It is widely acknowledged that improved evaluation of the safety and outcome of ART treatments is needed to give a better idea of any health effects, especially those with implications for the children of treated couples. This will allow society as a whole to weigh the rights of individual parents against its responsibility to safeguard public health, and give would-be parents and their clinicians the information they need to take difficult choices about the safest and most suitable treatments for them and their future children.

Current research into the potential adverse effects of ART in the UK is hampered by strict laws about data release, linkage to NHS information systems, consent and confidentiality, and by a lack of comprehensive, accessible data sources suitable for routine follow-up, further research or clinical evaluation. While there is limited scope for isolated studies, these would be difficult, costly and time-consuming to undertake, and subject to potential bias, particularly if they attempted to investigate what has happened in the past.

To redress these imbalances, the UK’s key priorities should therefore be:

- To establish a monitoring framework for ART. This framework would be based on core data collected by the HFEA, potentially linking standard clinical information on parents’ reproductive histories and detailed records of ART clinic procedures and treatments, to health outcome data (short- to long-term). Record linkage raises ethical issues of information and consent which would need independent review and would inform the processes used to allow routine follow-up of children conceived through ART, and their mothers. This recommendation ties in with ongoing work by the HFEA to enhance its database and introduce electronic data exchange with ART clinics; it would assist the Authority in fulfilling its current legal role and provide a resource for future ART research.
- To develop a new evaluation system configured to deliver robust conclusions about the safety, efficacy and effectiveness of all new ART techniques – including refinements to existing techniques, techniques introduced from abroad, and entirely new procedures – the HFEA should limit the scope of licences for new ARTs while they are under evaluation. Over time, evaluation should be extended to include ART procedures already in use and others, such as cytoplasmic transfer, not currently under the HFEA’s jurisdiction.
**Taking action**

This advice aims to help the HFEA in developing its policy on the implementation and monitoring of new and existing ART procedures, working in partnership with the Department of Health. In conjunction with the scientific report of the Working Group (see References) it will also serve to inform the MRC and the scientific community of some of the research priorities in this important area of public health.

**Ethics and governance framework**

- A balanced ethics and governance framework, based on public consultation and including medical and scientific input, should be developed to regulate core data collection and all follow-up studies using these data.

**Data gathering and follow-up studies**

- Data-holding and coordination processes should be set up, in close collaboration with the HFEA, the NHS and ART clinics, to monitor the immediate and long-term health of all children conceived through ART and their mothers. The aim would be to provide a basic monitoring system for the different ARTs, enable data linkages, support clinics’ work on consent and data-transfer, and assist researchers wishing to use data for separate in-depth studies.

- Clinical data should be collected and linked with NHS medical record systems which provide the most efficient way to monitor and identify potential adverse health effects. The ethical issues around obtaining consent to access such data need to be fully explored and approaches should be discussed with ART patients and clinics to examine what influences people to give or withhold their consent, and their views about the need for and acceptability of research.

- A new approach should be adopted which encourages the use of high-quality clinical trials, or other appropriate methodologies to evaluate ARTs. This coordinated activity would need to involve the HFEA, the NHS, private clinics, the scientific community and research funders such as the MRC.

- The existing National Institute for Clinical Excellence and the Department of Health’s HTA programme are well placed to contribute to additional independent evaluation and monitoring of the safety and outcome of ARTs whenever necessary.

- Study designs should take into account ethical governance and other issues arising when patients pay for their treatment. Other practical issues, such as who pays service support costs in trials that involve both private and public sectors, will also need to be considered.
### Working Group and Subgroups membership

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<th>Name</th>
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<td>Working Group, Subgroup 1 (Professor Steve Smith, Imperial College London, attended instead as Board representative).</td>
</tr>
<tr>
<td>Professor Henry Leese</td>
<td>Department of Biology, York.</td>
<td>Past HFEA member. Embryology and biochemistry.</td>
<td>Working Group.</td>
</tr>
<tr>
<td>Dr Gillian Lockwood</td>
<td>Medical Director of Midland Fertility Services and Chair of the British Fertility Society Ethics Committee.</td>
<td>Clinician with statistical background.</td>
<td>Subgroup 1.</td>
</tr>
<tr>
<td>Professor Neil Marlow</td>
<td>Consultant lecturer in Child Health, Department of Child Health, University of Nottingham.</td>
<td>Prematurity and the maturation of visual attention in infancy, motor skills in low birthweight children, pre and perinatal risk factors for psychosocial development.</td>
<td>Subgroup 1.</td>
</tr>
<tr>
<td>Dr Joan Morris</td>
<td>Department of Environmental and Preventive Medicine, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry.</td>
<td>Consultant statistician, helps run National Down’s Syndrome Cytogenetic Register.</td>
<td>Subgroup 1.</td>
</tr>
<tr>
<td>Professor Eve Roman</td>
<td>Chair of Cancer Epidemiology in the Academic Unit of Epidemiology and Health Services, School of Medicine, University of Leeds.</td>
<td>Epidemiology, especially large scale population-studies. Runs data collection unit for Leukaemia Research Fund.</td>
<td>Subgroup 1.</td>
</tr>
<tr>
<td>Professor André Van Steirteghem</td>
<td>Centre for Reproductive Medicine, Belgium.</td>
<td>Epidemiology; introduced ICSI technique, author of cohort studies on ICSI.</td>
<td>Working Group (overseas member).</td>
</tr>
<tr>
<td>Name</td>
<td>Location</td>
<td>Expertise</td>
<td>Role</td>
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<tr>
<td><strong>Professor Stephen Smith</strong></td>
<td>Principal of the Faculty of Medicine, Imperial College London.</td>
<td>Member of the MRC Physiological Medicine and Infections Research Board. Basic and clinical studies in reproductive health. Gynaecology consultant for IVF clinic.</td>
<td>Working Group, Subgroup 1 (attending for Professor Anne Johnson), Subgroup 2.</td>
</tr>
<tr>
<td><strong>Mr Jonathan Sussex</strong></td>
<td>Member of the MRC Consumer Liaison Group.</td>
<td>Lay representative.</td>
<td>Working Group.</td>
</tr>
<tr>
<td><strong>Dr Jane Thomas</strong></td>
<td>Director/representative of Clinical Effectiveness Support Unit, Royal College of Obstetricians and Gynaecologists. National Collaborating Centre for Women’s and Children’s Health.</td>
<td>Coordinating development of NICE clinical guidelines on fertility. Member NICE antenatal subgroup advising the UK National Screening Committee on antenatal screening programmes, etc.</td>
<td>Subgroup 1, Subgroup 2 (Dr Moira Mugglestone attended first meeting on Dr Thomas’s behalf).</td>
</tr>
<tr>
<td><strong>Professor Simon Thompson</strong></td>
<td>Director, MRC Biostatistics Unit, Cambridge.</td>
<td>Population statistics.</td>
<td>Working Group, Subgroup 2 (Dr Ian White attended first meeting on Professor Thompson’s behalf).</td>
</tr>
<tr>
<td><strong>Dr Steve Troup</strong></td>
<td>Liverpool Women’s Hospital.</td>
<td>Clinical embryology.</td>
<td>Subgroup 1.</td>
</tr>
<tr>
<td><strong>Mr Edward Webb</strong></td>
<td>Department of Health observer.</td>
<td>Policy on assisted conception.</td>
<td>Subgroup 2 (Ms Kim Hayes attended first meeting on Mr Webb’s behalf).</td>
</tr>
<tr>
<td><strong>Ms Sarah Willett</strong></td>
<td>National Institute for Clinical Excellence (NICE).</td>
<td>NICE Interventional Procedures programme.</td>
<td>Subgroup 2.</td>
</tr>
<tr>
<td><strong>Miss Elizabeth Woodeson</strong></td>
<td>Department of Health observer.</td>
<td>Policy on assisted conception.</td>
<td>Working Group, Subgroup 1 (Mr Ted Webb attended the second meeting on Miss Woodeson’s behalf).</td>
</tr>
</tbody>
</table>

**HFEA representatives**

- Mr Ian Hammond
  Senior Regulatory Adviser (joined Dr O’Toole at 2nd meeting of main Working Group)

- Dr Chris O’Toole
  Head of Research Regulation (primary HFEA contact for Working Group)

- Mr David Tellis
  Director of Information Management (contact for new HFEA database)

**MRC Head Office representatives**

- Mr Mark Baines
  Administrative support

- Ms Suzanne Green
  Administrative support

- Mrs Elizabeth Mitchell
  MRC Consumer Liaison Group coordinator

- Dr Catherine Moody
  Scientific secretary to the Working Group and Subgroups

- Dr Joe McNamara
  Physiological Systems and Clinical Sciences Board Programme Manager

- Dr David Neil
  Scientific writer/Publications officer
References

- **Current Practices and Controversies in Assisted Reproduction**
  [www.who.int/reproductive-health/infertility/1.pdf](www.who.int/reproductive-health/infertility/1.pdf)

- **Fertility: assessment and treatment for people with fertility problems**
  National Collaborating Centre for Women’s and Children’s Health. Commissioned by the National Institute for Clinical Excellence.
  [www.rcog.org.uk/resources/Public/Fertility_full.pdf](www.rcog.org.uk/resources/Public/Fertility_full.pdf)

Further information

- Human Fertilisation and Embryology Authority: [www.hfea.gov.uk](www.hfea.gov.uk)
- Infertility Network UK: [www.infertilitynetworkuk.com](www.infertilitynetworkuk.com)
- A scientific report on Assisted Reproduction Working Group discussions is available at: [www.mrc.ac.uk](www.mrc.ac.uk)

Acknowledgements

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