Human Fertilisation & Embryology Authority

Authority meeting - agenda

16 September 2015

Etc Venues, 51-53 Hatton Garden, London EC1N 8HN

Agenda item		Time
1.	Welcome, apologies and declaration of interests	10:40am
2.	Minutes of 8 July 2015 **HFEA (16/09/2015) 762**	10.45am
3.	Chair's report (verbal)	10:50am
4.	Chief Executive's report (verbal)	11:00am
5.	Committee chairs' updates (verbal)	11:10am
6.	Strategic performance report **HFEA (16/09/2015) 763** For information	11:20am
7.	Regulating mitochondrial donation **HFEA (16/09/2015) 764** For decision	11:35am
	Lunch	**12:20pm**
8.	Business plan 2016/17: outline objectives **HFEA (16/09/2015) 765** For decision	1:00pm
9.	Information for Quality: update **HFEA (16/09/2015) 766** For information	1:20pm
10.	Compliance activities 2014/15: a review **HFEA (16/09/2015) 767** For information and decision	1:50pm
11.	Compliance activities 2014/15: analysis of risk **HFEA (16/09/2015) 768** For information	2:05pm

12.	Compliance activities 2014/15: analysis of inspection findings **HFEA (16/09/2015) 769** For information	2:30pm
13.	Compliance activities 2014/15: clinical governance learning **HFEA (16/09/2015) 770** For information	2:45pm
14.	Compliance and enforcement policy **HFEA (16/09/2015) 771** For decision	3:00pm
15.	Any other business	3:15pm

Authority paper

Strategic delivery	Setting standards ☑	Increasing and informing choice ☑	Demonstrating efficiency, economy and value ☑
Paper title	Minutes of Authority meeting 8 July 2015		
Agenda item	**2**		
Paper number			
Meeting date	16 September 2015		
Author	Charlotte Keen, Information and Access Policy Manager		
For information or decision?	Decision		
Recommendation	Members are asked to confirm the minutes as a true and accurate record of the meeting		

Minutes of the Authority meeting on 8 July 2015 held at ETC Venues, Hatton Garden, 51-53 Hatton Garden, London, EC1N 8HN

Members
There were 10 members at the meeting, 7 lay members and 3 professional members.

Members present
Sally Cheshire (Chair)
Dr Susan Price
Professor David Archard
Dr Andy Greenfield
Anthony Rutherford
Dr Alan Thornhill
Bishop Lee Rayfield
Kate Brian
Margaret Gilmore
Anita Bharucha

Apologies
Yacoub Khalaf
Rebekah Dundas

Observers
Ted Webb (DH)
Steve Pugh (DH)

Staff in attendance
Peter Thompson
Nick Jones
Juliet Tizzard
Sue Gallone
Catherine Drennan
Paula Robinson
Suzanne Hodgson
Rosa Wotton
Joanne McAlpine
Charlotte Keen

1. Welcome, apologies and declaration of interests

1.1. The Chair opened the meeting by welcoming Authority members and members of the public to the fourth meeting of 2015. As with previous meetings, it was being audio-recorded and the recording would be made available on the HFEA website to enable interested members of the public who were not able to attend the meeting to listen to the HFEA's deliberations. This was part of the HFEA's drive to increase transparency about how the Authority goes about its business.

1.1. Apologies were received from Yacoub Khalaf and Rebekah Dundas.

1.2. Declarations of interest were made by:

- Anthony Rutherford (Consultant in Reproductive Medicine and Gynaecological Surgery at a licensed centre)
- Kate Brian (Regional organiser for London and the South East for Infertility Network UK)

2. Minutes of Authority meeting held on 13 May 2015

2.1. Members agreed the minutes of the meeting held on 13 May subject to minor amendments. The Chair agreed to sign the minutes as amended.

3. Chair's report

3.1. The Chair informed members that, since the last Authority meeting, she had attended a range of events with organisations in the IVF sector and the wider health and care system.

3.2. On 27 May the Chair, together with the Chief Executive, had their annual accountability meeting with Felicity Harvey, Director General of Public Health and the HFEA's senior sponsor, and her team at the Department of Health. The meeting was to review the HFEA's performance over the 2014/15 business year and to identify key priorities for 2015/16. The meeting went well. The Department was pleased with the work the HFEA was doing and would continue to give the support required in order for the HFEA to achieve its objectives.

3.3. The Chair and the Chief Executive, together with members of the Senior Management Team and the Chief Inspector, continued with their programme of visits to clinics outside of the regular inspection schedule in order to hear from clinics what they felt they did well and where they thought improvement was needed. These visits would then enable the HFEA, as the regulator, to consider how to help improve the quality of care across the sector.

3.4. On 29 May, the Chair and the Chief Executive visited the Leeds Centre for Reproductive Medicine, where Anthony Rutherford, Authority member, is a senior clinician. The Chair advised members that on the same day she gave a talk on delivering outstanding practice and patient care at the Northern Fertility Nurses Conference in Leeds.

3.5. On 22 June, the Chair and Chief Executive visited the Lister Fertility Clinic, where Sam Abdalla, a former Authority member, was currently the Person Responsible. On 1 July, the Chair and the Chief Executive visited the Assisted Conception Unit at Guy's Hospital, the largest preimplantation genetic diagnosis (PGD) unit in the country, led by Authority member, Yacoub Khalaf.

3.6. The Chair expressed her thanks to the Person Responsible and all of the staff at each clinic for their warm welcome and for taking the time to explain their work.

3.7. Finally, on 23 June, the Chair informed members that she had chaired the HFEA Remuneration Committee, with two Authority members in attendance, to confirm the pay remit and proposed rewards for staff based on 2014/15 performance.

4. Chief Executive's report

4.1. The Chief Executive advised members that on 10 June he attended the Audit and Governance Committee (AGC) as part of the end-year accounts and annual report sign-off process. The HFEA Annual Report was subsequently laid before the Houses of Parliament and published on the HFEA website. The report was different to previous years in that it had been stripped down to the essential statutory requirements. In the past, the Executive had set the report in a wider context with an introduction from the Chair and the Chief Executive, but it was now felt that such commentary could be more effectively delivered through other avenues.

4.2. On 17 June, the Chief Executive attended the National Information Board's (NIB) Leadership Summit meeting. The NIB was an initiative led by the Department of Health involving all of the health sector's arm's length bodies (ALBs) to make significant changes to the way in which information was used within the health and care system. The HFEA's role was limited given its specialist remit although it was appropriate that it was involved.

4.3. Last week, the Chief Executive advised members the Government had announced to Parliament that the HFEA would be subject to a triennial review, together with several other health ALBs. It had long since been Government policy that all public bodies should be subject to a periodic review. The review would look at the functions of the organisation and whether those functions were carried out in the most efficient way possible.

4.4. The HFEA had, of course, already been reviewed twice very recently and the Chief Executive emphasised that the terms of reference of the triennial review would not reopen the fundamental decisions that were reached in either the McCracken review in 2013 or the 2012 review conducted by the Government. The Chief Executive reminded members that the McCracken review had explicitly looked at whether or not the HFEA should merge with the Human Tissue Authority (HTA), and concluded that it should not. The 2012 review had looked at whether the responsibilities of the HFEA should transfer to the Care Quality Commission (CQC) or the Health Research Authority (HRA), and had also concluded that they should not.

4.5. The Chief Executive emphasised that all public bodies should be subject to scrutiny and the Executive would approach the review in an open and constructive spirit. The review process should take no more than six months. A call for evidence had been issued on the Department of Health's website and had been publicised in Clinic Focus. The Chief Executive welcomed two members of the review team from the Department of Health who were observing the meeting.

4.6. Press Coverage: the Chief Executive summarised press coverage since the last Authority meeting, details of which had been circulated to members.

4.7. A court case involving the HFEA had recently concluded in the High Court. The case involved a couple who wished to export their deceased daughter's eggs to the USA for possible future use. The HFEA's Statutory Approvals Committee (SAC) had considered the application on three separate occasions in response to evidence that was brought by the couple, but on each occasion SAC were of the view that there were sufficient issues with the daughter's consent, such that the

law meant they should deny granting an export licence. The couple then decided to go to the High Court for a judicial review, and following a detailed judgement, a judge ruled that, on all three counts, the decision of SAC was correct. At the same time, the judge denied the couple permission to seek leave to appeal and the claimants had now appealed directly to the Court of Appeal asking it to overturn the judge's decision. The Court of Appeal would now decide whether to grant leave to appeal.

4.8. Although the case had been widely reported both in the UK and across the world, the HFEA felt it was inappropriate to comment further, given the distressing nature of the case, other than a prepared statement, and had turned down a number of interview requests on the grounds that neither the HFEA nor, more importantly, the couple, would benefit from extended coverage of the case.

4.9. The Chief Executive advised members that Kate Brian, an Authority member, had recently completed a documentary for Radio 4 on the birth of the national sperm bank and its first few months of life. It was an insightful piece that painted a mostly positive picture of events, without ignoring the difficulties and complexities that came with such a project. The Chief Executive advised members that the programme was still available on BBC iPlayer.

5. Committee chairs' updates

5.1. The Chair of the Statutory Approvals Committee (SAC) reported that the committee had met on 28 May and 25 June. There had been five PGD applications in May to consider. Three were approved as submitted, one was approved on an individual basis and the other was approved in respect of a number of types but not all of the types contained in the application. In June there had been three PGD applications and one request for Special Directions; the minutes of these decisions had not yet been published.

5.2. In the absence of the Chair of AGC, the Director of Finance and Resources advised members that the committee had met on 8 July and, aside from the usual standing items, had received reports on:

- The HFEA People Strategy and HR Risks, from the Chief Executive
- An IfQ update from the Director of Compliance and Information
- The strategic risk register from the Head of Business Planning
- The audit completion report from the National Audit Office
- A progress report and the annual assurance statement from DH Internal Audit
- Information assurance from the Director of Finance and Resources
- The annual report and accounts, including the governance statement, from the Head of Finance.

5.3. The Deputy Chair of the Scientific and Clinical Advances Advisory Committee (SCAAC) advised members that the committee had met on 10 June and welcomed three new members: Sheena Lewis, Professor of Reproductive Medicine at Queen's University, Belfast; Jane Blower, an embryologist at Leicester Fertility Centre; and Professor Gudrun Moore, a specialist in molecular medicine at Great Ormond Street hospital.

5.4. The committee received an update on alternative methods for deriving embryonic stem cells and embryonic-like stem cells, an update to the guidance on

preimplantation genetic screening (PGS) in the HFEA's Code of Practice, and a novel process application. SCAAC also received a presentation on freeze-all cycles from Dr Abha Maheshwari, consultant of Reproductive Medicine at Aberdeen Fertility Centre, and a presentation on reproductive immunology from the HFEA's Scientific and Clinical Policy Manager.

5.5. The Director of Strategy and Corporate Affairs advised members that the Executive Licensing Panel (ELP) had met four times and considered four renewal applications, three of which were approved and one adjourned; five interim inspections, all of which were approved; and twelve variations, all of which were approved except for two variations of research project objectives which had been referred to the Licence Committee. ELP also considered one treatment and storage initial licence application, two voluntary revocations and one Special Directions to enable continued licensed activity, all of which were granted.

6. Strategic performance report

6.1. The Chair introduced this item, advising that the strategic performance report was a general summary of both the HFEA's performance measures, the success towards implementation of the strategy, the HFEA's programmes and their development, and generally the wider performance of the Authority.

6.2. The Director of Finance and Resources advised members that the strategic performance report included the management accounts as at the end of April 2015. The management accounts for the end of June were just being finalised. The trend of treatment fees being less than expected had continued, with a shortfall of about £73,000 on treatment fee income for the first quarter. There was currently no cause for concern as there had been similar savings on expenditure on salaries in particular, and legal expenses had been less than anticipated.

6.3. Quarter end discussions would shortly be taking place with each of the budget holders to consider forecast expenditure and that, together with the work the finance team were carrying out on projecting treatment fee income, should provide a clearer picture.

6.4. Looking further ahead, the Director of Finance and Resources advised members that consideration needed to be given to the costs incurred following the office move next financial year, and the potential impact on fees.

6.5. The Department of Health had awarded the HFEA a small amount of capital funding in order to refresh the IT equipment in advance of the office move. The Department had also provided cover for capital expenditure from reserves on the IfQ programme and also the support programme for donor-conceived people and donors. Discussions were still taking place with the Department of Health in relation to the extent of the cover required.

6.6. The Director of Strategy and Corporate Affairs reported on work being undertaken in her Directorate and performance against some of the objectives in the strategy.

6.7. The Director of Strategy and Corporate Affairs reminded members of the three areas of ambition within the HFEA strategy and the topics under each:

- **Setting standards**
    - Improving the quality of care.
    - Improving the lifelong experience of donor conception.
- **Increasing and informing choice**

  - Using HFEA data to improve outcomes.
  - Ensuring patients have access to high quality information.
- **Efficiency, economy and value**
  - Ensuring the HFEA remains demonstrably good value.

6.8. In improving the quality of care, the Director of Strategy and Corporate Affairs advised members that the main area of work had been implementing a system for regulating mitochondrial donation, which was a cross-cutting piece of work across all Directorates in the organisation.

6.9. In the area of improving the lifelong experience of donor conception, the Director of Strategy and Corporate Affairs updated members on the piloting of a new counselling and support service for donors and donor-conceived people. The service which is being run under contract by PAC-UK, had been launched on 1 June 2015 and had already received referrals.

6.10. In the area of using HFEA data to improve outcomes, the Director of Strategy and Corporate Affairs advised members that there was an agenda item later in the meeting about the sector's performance around multiple births, which was a good example of how the HFEA could use data it collected from clinics to help them improve their practice.

6.11. There had been a cluster of activity around ensuring patients had access to high quality information, including:

- rewriting information for the HFEA website and changing the tone of voice
- publishing information on new or untested treatments
- preparing for the new website and Choose a Fertility Clinic (CaFC).

6.12. In the area of ensuring the HFEA remains demonstrably good value, the Director of Strategy and Corporate Affairs advised members of the change in the way the HFEA communicated by saving money on design and using lower cost social media for communications in order to improve efficiency.

6.13. The Director of Strategy and Corporate Affairs provided members with an overview of the HFEA's brand refresh, which included a revised logo, designs for our publications and corporate templates and a new house style for written communications. The aim of the work was to make our external communications clearer, more engaging and more cost effective.

6.14. The Director of Strategy and Corporate Affairs updated members on work on mitochondrial donation which included an online survey during June, asking focused questions about licensing, inspection and follow-up. This had provided high quality helpful responses. There had also been a workshop in June which looked at:

- staff competence and inspection
- screening and eligibility of donors (age, family limit and haplotype matching, diseases and genetic conditions)
- follow-up of children born
- information for patients and donors
- the case by case approval process.

6.15. During the summer the Executive would be analysing the survey and workshop feedback, and drawing together recommendations for the September Authority meeting. From mid-September, the Executive would:

- implement the Authority's decisions
- let the clinics know what the requirements would be
- launch the application system on 29 October.

6.16. The Director of Compliance and Information advised members that the programme of activity in 2014/15 relating to inspections and information audits had been completed within the timeframe. The two red areas highlighted in the report related to a slight increase in the time taken to submit reports back to clinics after they had been inspected, although this demonstrated a proportionate and quality-focused approach, investing extra time where necessary in order to get the report right. The second area related to the very small number of tissue-typing applications. Given the infrequency of such applications, clinics did not always immediately submit the relevant information to enable the HFEA to process the application quickly and make a swift decision.

6.17. Following a discussion, members noted the presentation and the latest strategic performance report.

7. Strategic risk register

7.1. The Head of Business Planning presented this item in a revised format in order to provide members with an overview of the risks as a complete set, showing the relative risk tolerances and residual risk scores. Five of the twelve risks were currently high and deemed above tolerance.

- Legal challenge: a relatively high risk tolerance of 12 was set for this particular risk due to the inevitability of some degree of resource diversion owing to the nature of the HFEA's work. The residual risk was currently higher than tolerance at 15.
- IfQ – improved information access: the residual risk of 12 was higher than tolerance (set at a medium level of 8) due to approval process delays at the first stage of the programme, and the risk to the quality of the final product that could be delivered if there were any further approval delays encountered.
- Data – incorrect data being released: although good controls were in place for dealing with PQs and other externally generated requests, volumes could not be controlled and the HFEA had been subjected to extremely high volumes in the first half of the year. The residual risk of 12 was therefore higher than the tolerance threshold of 8. It was not yet possible to tell if further high volumes would occur during the mitochondria project and in the course of the subsequent start-up of applications processing.
- Financial viability – income and expenditure: the residual risk of 12 was above tolerance (set at 9), although 2014/15 overspend was able to be met from reserves.
- Capability – knowledge and capability: the residual risk of 9 was above the current tolerance level of 6. Staff turnover could lead to fluctuations in overall capability, although the period of highest turnover appeared to be ending.

7.2. The Head of Business Planning also provided a brief overview of the remaining high level risks, that were currently within or at tolerance. In particular, the regulatory model risk had recently decreased in its residual risk score and was well below tolerance, following the completion of recent recruitment and the implementation of a new, more resilient, staffing model.

7.3. Following a discussion, members noted the latest version of the risk register and agreed that the new way of presenting the risks was clear and informative.

8. Multiple births annual update

8.1. The Researcher in Epidemiology and Statistics reminded members that in 2009 the HFEA, together with professional bodies and stakeholder groups, introduced a multiple births policy with the aim to reduce the multiple birth rates by promoting elective single embryo transfer (eSET). Central to that policy was the introduction of a series of targets, starting in 2009 with the maximum multiple birth rate of 24% for clinics, with the intention to reduce this in steps over a series of years to 10%, which was the current target.

8.2. In 2011, the HFEA published a multiple births data report, based on the 18 months of data available at the time. This had showed an initial growth in eSET, a growth in blastocyst transfers and a corresponding decline in multiple pregnancy rates in that short period of time. Since then the Executive had provided annual updates to Authority members, and also provided updates to the Multiple Births Stakeholder Group. Verified data was now available to the middle of 2014. The latest report with this data would be available on the website during the week of 13 July 2015.

8.3. **Shift to eSET:** in 2008, the majority of women under 35 had a double embryo transfer, but by 2013, eSET had increased significantly and double embryo transfer had decreased. There had clearly been a shift away from double embryo transfer towards eSET.

8.4. 86% of women under the age of 38 were now receiving eSET, with two thirds on their first cycle and another 17% on their second cycle. Whilst eSET had grown dramatically, the patient profile had remained fairly steady. About 40% of IVF treatment cycles were funded by the NHS and the remaining 60% funded by the patients themselves. Looking at fresh eSET cycles, that proportion was reversed with 61% NHS funded.

8.5. **Shift to blastocyst transfers:** the Researcher in Epidemiology and Statistics explained that blastocysts were embryos which had been cultured for a longer period (five to six days) in the laboratory. Previously most embryo transfers would be carried out at cleavage stage, which was at two to three days in the laboratory. There had been a significant growth since 2011 in frozen embryo transfers carried out at the blastocyst stage. It was noted that more women were able to freeze embryos and consequently more frozen embryo transfers were taking place, with a 10% growth in frozen embryo transfers between 2012 and 2013.

8.6. **Fresh blastocyst transfers:** the shift to eSET in relation to fresh blastocyst transfers was even more significant. In 2008, the majority were double embryo transfers and in 2013, eSET was over 50%. This was a really important change because, whilst the data showed early on that blastocyst transfers were associated with a better pregnancy rate, they were also associated with very high multiple pregnancies.

8.7. **Pregnancy and multiple pregnancy rates:** the pregnancy rate had stayed fairly steady from 2008 but had recently started to increase and was now up to about 34 to 35%. The multiple pregnancy rate had steadily declined and currently stood at around 16%.

8.8. The Researcher in Epidemiology and Statistics provided members with a summary of a comparison of pregnancy rates for the number of embryos transferred and the stage at which it was carried out. The important thing to bear in mind was the multiple pregnancy rate. For eSET, the multiple pregnancy rate was under 2% at both cleavage and blastocyst stage, whereas for double blastocyst transfer the multiple pregnancy rate was over 40% and about 33% for cleavage stage. There was therefore a lot of risk associated with a double blastocyst transfer but very little gain in terms of a higher pregnancy rate.

8.9. **Cumulative rate, first fresh cycles started 2013:** the data in the HFEA register now allowed the Executive to track women through the whole of their treatment. The data showed that the pregnancy rate was slightly higher for eSET, but with a multiple pregnancy rate of around just 2%, compared to 32% following a double embryo transfer.

8.10. The Researcher in Epidemiology and Statistics provided members with a summary of the conclusions of the findings in the updated report.

- Findings showed that the strategies pursued by clinics, in line with HFEA policy, had been a clear success with the multiple pregnancy rate after IVF dropping from one in four to one in six and continuing to decline, while the pregnancy rate was increasing.
- There had been a swift cultural change in IVF which had tangible health benefits for patients and their babies.
- Younger women on their first cycle who had an eSET had a higher pregnancy rate than those that had a fresh double embryo transfer.
- When this was followed by a subsequent single frozen embryo transfer, the pregnancy rate was higher still, but the multiple rate remained very low.
- Routinely collected data had successfully influenced change and improved outcomes.

8.11. The Researcher in Epidemiology and Statistics advised members that this had been a joint effort and expressed her thanks to the professional bodies, clinicians and scientists, patient groups and patients involved in making this policy a success.

8.12. Following a discussion, members noted the information given in the multiple births report.

9. Opening the register (OTR) update

9.1. The Donor Information Manager presented this item and reminded members that the HFEA strategy put patients (including donors and donor-conceived people) and the quality of care they received at the centre of its work. The OTR service was therefore fundamental in the achievement of the following strategy objectives and recent developments and improvements in this area of work contributed further to this aim.

- **Our vision: high quality care for everyone affected by assisted reproduction. This encompassed:**

  - support for patients, donors and donor-conceived people
  - excellent service and information from the HFEA.

- **What we will do:**
  - We will improve the lifelong experience for donors, donor-conceived people, patients using donor conception and their wider families.
- **How we will work:**
  - We will make the quality of care experienced by patients, donors and donor-conceived people our central priority and the primary consideration in our decision making.

9.2. The Donor Information Manager provided a summary of OTR applications received over the last five years. There had been a 20% increase during 2014, with parents and donors being the main groups applying. Since processes for dealing with such applications had developed and become more rigorous over time, they inevitably now took longer to process. Between January and June 2015, the OTR team had dealt with and responded to 136 applications.

9.3. In addition, the Donor Information Manager advised members that 79 donor-conceived individuals had joined the Donor Sibling Link (DSL), the HFEA's voluntary contact register, since its launch in 2010. Under this scheme, registrants agreed to the HFEA sharing their name and contact details with any of their donor-conceived genetic siblings who had also joined. The number registering was still small, with 11 per year in 2011 and 2012, but increasing to 21 per year in 2013 and 2014, but registration was likely to grow significantly in the coming years.

9.4. The HFEA had also received 149 applications from anonymous donors (those who donated after 1991 but before 1 April 2005) to remove their anonymity. Over the last three years, there had been a slight increase in re-registering although numbers were disappointingly low with only 12 applying in 2014.

9.5. In 2013, the HFEA received its first application for identifying information from an adult donor-conceived individual with an identifiable donor. In total, six applications of this nature had been received; two each year so far, and earlier this year the HFEA had its first DSL match. In each of these cases the HFEA offered and coordinated (where requested) support and intermediary assistance to the donor-conceived individuals and donors concerned.

9.6. The Donor Information Manager advised members that there had been significant progress and policy developments in OTR request handling over the last three years, which were set out in more detail in the paper. These included:

- a steer on key operational issues from the Authority in June 2012
- development of a redaction framework for OTR staff
- website content created in 2013 to enable past applicants to check if their donor had re-registered as identifiable
- development of a guidance pack for clinics to improve the sharing, quality and disclosure of donor information.

9.7. The Donor Information Manager provided members with an overview of the HFEA's pilot support and intermediary service, which was identified as a high priority by a group of key stakeholders in June 2013. In July 2013, the Authority approved recommendations to work with stakeholders to scope out models for a

three year pilot and explore, at the same time, what specialist support should be provided for other people affected by donation.

9.8. Since then, the HFEA had worked closely with stakeholders to develop a service which provided both of these recommendations. As mentioned earlier in the meeting, a contract was subsequently awarded to PAC-UK, an adoption support agency with relevant expertise and suitably qualified staff. The HFEA had delivered two days of training to PAC-UK in May 2015 and created a suite of leaflets to complement, or act as an alternative to, the service. The service was then launched as a pilot on 1 June 2015.

9.9. As part of the OTR process, applicants were supplied with a link to an online confidential feedback questionnaire. The Donor Information Manager provided members with a summary of those survey responses.

- The majority of respondents discovered they could apply for information from the HFEA register through the HFEA website, with others finding out through sources such as their clinic.
- Only a quarter of respondents said they had spoken to someone at the HFEA before applying, although 100% of those rated this experience as helpful or very helpful.
- Expectations among respondents varied in terms of the amount of information they received. 58% considered it adequate, 26% did not have any expectations, 16% expected to receive more information and 2% expected to receive less information.

9.10. The survey also gave respondents the opportunity to add any further comments they had on the information they had received or the process itself, and the majority stated that they had found the process straightforward, efficient and speedy, and were grateful for both the existence of the OTR service and the high level of service received.

9.11. Following a discussion, members noted:

- the significant policy and process developments over the last three years to the OTR service, which were in line with delivering the HFEA 2014-2017 strategy
- the trend showing increases in the number of applications
- the positive feedback received about the OTR service provided by the HFEA.

10. Information for quality: update and data dictionary

10.1. The Director of Compliance and Information explained that the IfQ programme was a comprehensive review of the information that the HFEA held, the systems that governed the submission of data, the uses to which it was put and the way in which the information was published.

10.2. The Director of Compliance and Information explained that IfQ was a critical component of the HFEA's strategy and encompassed:

- the redesign of the HFEA's website and Choose a Fertility Clinic (CaFC)
- the redesign of the 'Clinic Portal' and combining it with data submission functionality that was currently provided via the HFEA's separate Electronic Data Interchange (EDI) system
- a revised dataset and data dictionary approved by the Standardisation Committee for Care Information (SCCI)

- a revised Register, to include the migration of historical data contained within the existing Register
- redesign of the HFEA's supporting IT infrastructure.

10.3. The Director of Compliance and Information advised members that, given the importance of the programme to the Authority's strategy, updates on progress were provided to each meeting of the Authority and approval for direction and actions sought. This update, in particular, introduced the concept of an overriding vision of the work in three main parts, addressed progress in technical services and considered consequences for organisational change.

10.4. **The website:** the Director of Compliance and Information advised members that the HFEA website represented the organisation's personality, style and tone and would embody the HFEA's refreshed brand, with links to HFEA social media channels. The website would be updated on a regular basis, with less text and more interactive elements.

10.5. The website also encompassed the work on CaFC, although the Director of Strategy and Corporate Affairs would discuss this area in more detail at item 11 on the agenda.

10.6. **The clinic portal:** the clinic portal would be the key window to the HFEA for clinics. There would be a seamless transition from a password protected website to the portal, which would provide useful information about requirements placed on licensed clinics and their key staff. It would make the risk tool accessible together with other useful publications. The portal would also enable clinics to access information about their own performance.

10.7. A key component of the clinic portal was the way in which clinics submitted data to the HFEA. The new clinic portal would provide an easier and more pleasant way for clinics to submit their data and users would be able to adapt the system around their work rather than their processes being determined by the HFEA system. It would also prevent simple errors by having a real-time verification facility.

10.8. **HFEA internal systems:** an IT strategy would be implemented which supported all the IfQ developments and provided economic and efficient hosting and storage arrangements, utilising the benefits of the 'cloud' as appropriate. The IT strategy would provide business continuity and security, with desktop services meeting high service standards, and would be based on simplicity and 'agile' development principles. Once the development phase of IfQ was complete, where contracts with suppliers were in place to allow for minor improvements, there would be a move to a more evolutionary approach where business leads within the organisation would understand from their knowledge of user feedback what improvements to systems were needed and would bid for resource accordingly using a business case approach.

10.9. The Director of Compliance and Information provided a summary of the procurement process.

- The Authority had agreed the budget for 2015-16 of £1.134m.
- The procurement process had been conducted by the Crown Commercial Service with two preferred suppliers selected.
- Progression from each phase – Alpha, Beta, and Live - was dependent on performance requirements being met, with the Chief Executive approving

progress to each phase on the basis of a recommendation from the IfQ Programme Board.

- In addition the Board would recommend approval to stages of expenditure within these phases and expenditure would be signed off by both the Director of Compliance and Information and the Director of Finance.
- All approvals would be reported to the Audit and Governance Committee.
- A substantial contingency of around 20% of budget was also protected, which was considered both prudent and best practice.
- Approval from the Department of Health and the Government Digital Service was necessary to progress from Alpha to Beta with the development of a public service digital interface having to meet necessary standards.

10.10. The Director of Compliance and Information reminded members that the Gateway Review which had been highlighted at the previous Authority meeting, had advised of the need to have increasing regard to the consequences of the programme for the HFEA's ways of working, and in turn the implications on teams. There was also the expectation of substantial external impact, with the benefit of a significant technological investment felt by a range of stakeholders.

10.11. The period between July and November would be intensive and focused on research, development and testing, with a group of internal and external users involved in that process. There would be increased stakeholder engagement, with a stakeholder group meeting taking place on 29 July.

10.12. In terms of ways of working, agile development encouraged seeing change as evolutionary and ever-present. Consequently, continued engagement with staff was ongoing since different ways of working would inevitably necessitate changes to some roles within the organisation.

10.13. Following a discussion, members:

- approved the vision for change which would guide all of the work
- noted the progress as regards procurement of third party suppliers in line with corporate and Government approval process, and associated costs
- noted that progression from the alpha stage was dependent on external approval (with an update report provided to members at that point)
- noted the arrangements informing organisational change resulting from the realisation of the IfQ Programme.

11. Choose a fertility clinic (CaFC)

11.1. The Director of Strategy and Corporate Affairs reminded members that, at their meeting in January 2015, members had agreed that the quality of a clinic should be measured in a multi-dimensional way, through patient feedback, inspection findings and success rates. Members asked the Executive to consider the details in more depth and the presentation and paper sought to update members on progress.

11.2. The Director of Strategy and Corporate Affairs showed members how CaFC was currently presented. The general assessment was that the design had become outdated and did not succeed in highlighting the more important feature of a page. There was no overall sense of the quality of a clinic, information was buried and hard to find and patients found that success rate information, while

statistically correct, was confusing to the extent that some patients preferred the simpler presentation on clinic websites.

11.3. The Director of Strategy and Corporate Affairs reminded members that, having taken on board most of the recommendations from the IfQ Advisory group presented to them in January, members agreed that they wanted CaFC to offer:

- a better balance between statistical and non-statistical information
- easier comparison between clinics
- non-statistical information that included inspection findings, patient reviews and the availability of donated eggs, sperm or embryos
- a patient review feature which should not consist of free-text feedback
- information about the availability of donated eggs, sperm or embryos consisting of types of donors available, the source and waiting times for treatment
- top-line statistical information consisting of births per embryo transferred, followed by the cumulative success rate.

11.4. Since then, the Executive had set up two work streams, one on statistical information and one on non-statistical information, to take this work forward. The two groups had subsequently drafted a comprehensive set of recommendations which had recently been approved by the IfQ programme board.

11.5. In relation to statistical information, the Executive recommended that:

- cumulative success rates per egg collection should be shown over a two year period
- data ranges needed to balance statistical reliability with ease of understanding, potentially increasing sample sizes by:
    - reducing age stratification from 6 to 2 - under 38, and 38 and over
    - using a measure which contained more types of cycles.

11.6. The Director of Strategy and Corporate Affairs advised members that further consideration was required in relation to the presentation of data ranges, possibly in a much more graphical, visual way than the current numerical way. Ultimately, options would need to be tested out on users to find the best solution. The important issue was to try and present fair, comparable data in such a way that it was statistically reliable but also understandable to users.

11.7. The Director of Strategy and Corporate Affairs advised members that, when inspectors carried out an IVF clinic inspection, they split the areas of focus into four areas:

- the protection of the patient, and children born following treatment
- the experience of patients
- the protection of gametes and embryos
- how the centre looked after important information.

11.8. Inspectors did not consider it appropriate to have an overall inspection score for a clinic, although they did anticipate being able to give an inspection score in each of the four areas of practice. Inspectors had been asked to consider how they could reduce the areas to three, without changing the format of the current inspection reports, in order to summarise inspection findings using a traffic light system to show clinics' levels of compliance with regulatory requirements.

11.9. In relation to patient feedback, the Executive recommended the following approach, although further consideration was required following user testing:

- asking five short questions to derive five ratings
- a 1-5 rating shown for each area, plus an averaged overall rating
- showing the number of reviews
- providing a link to the inspection questionnaire.

11.10. The Director of Strategy and Corporate Affairs advised members that for waiting times for donor conception treatment, the Executive recommended that CaFC should show how available egg, sperm and embryo donors were in a particular clinic, together with four general time periods. Again, this proposal would need to be tested out on users.

11.11. The newly formed stakeholder group would be meeting at the end of July and every month during the autumn period in order to help further refine the proposals in relation to CaFC. The Executive would then give members an update on progress in the autumn.

11.12. In discussion, some members expressed concern over the suggested reduction in the age bands from six down to two. A member also pointed out that such statistics were historical data in relation to a clinic's performance and as such should not be presented as a predictive tool. It was agreed that this issue was best resolved through testing with users. More generally, members noted the progress made on the CaFC review and gave their endorsement to the proposals and direction of travel, including the commitment to testing out the concepts in order to work out how the Executive could improve the proposals.

12. Any other business

12.1. The Chair confirmed that the next meeting would be held on 16 September 2015 at ETC Venues, Hatton Garden, 51-53 Hatton Garden, London, EC1N 8HN.

I confirm this to be a true and accurate record of the meeting.

Chair _____

Date

Strategic performance report

Strategic delivery:	☐ Setting standards	☐ Increasing and informing choice	☒ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	6		
Paper number	HFEA (16/09/2015) 763		
Meeting date	16 September 2015		
Author	Paula Robinson, Head of Business Planning		
Output:			
For information or decision?	For information		
Recommendation	The Authority is asked to note and comment on the latest strategic performance report.		
Resource implications	In budget		
Implementation date	Ongoing – strategic period 2014-2017		
Communication(s)	CMG reviews performance in advance of each Authority meeting, and their comments are incorporated into this Authority paper. The Department of Health reviews our performance at each DH Update meeting (based on the CMG paper). The Authority receives this summary paper at each meeting, enhanced by additional reporting from Directors. Authority's views are fed back to the subsequent CMG performance meeting.		
Organisational risk	☐ Low	☒ Medium	☐ High
Annexes	Annex 1: Strategic performance scorecard		

1. Introduction

1.1 The attached paper summarises the main performance indicators up to the end of June 2015, following discussion by the Corporate Management Group (CMG) at its August performance meeting. Overall performance is good, with very few performance measures in the red, and good progress towards our strategic aims.

2. Recommendation

2.1 The Authority is asked to note the latest Strategic Performance Report.

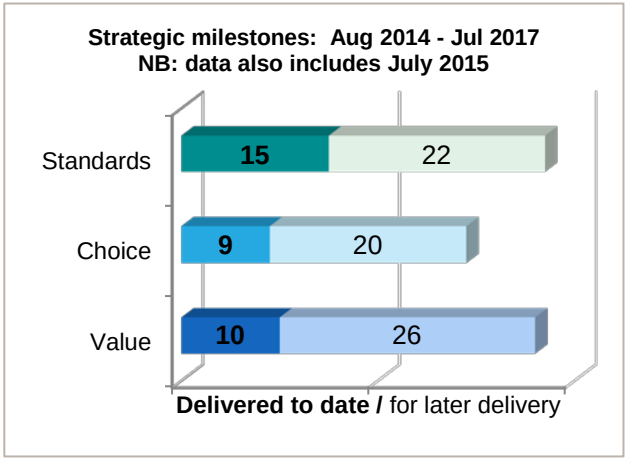
Annex 1: Strategic performance scorecard

1. Summary section

Dashboard – June data

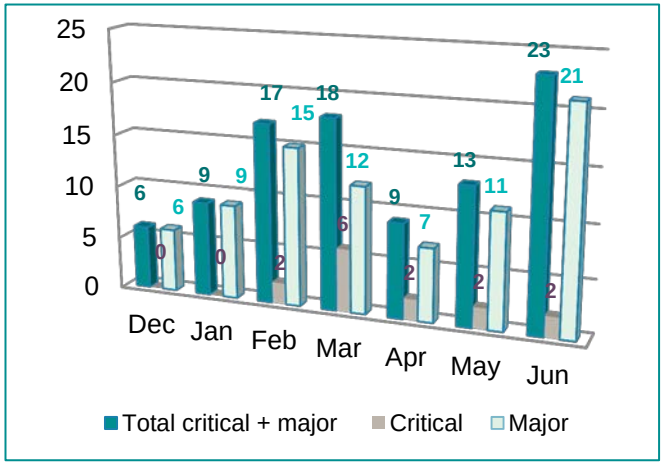
Strategic delivery totaliser

(see overleaf for more detail)



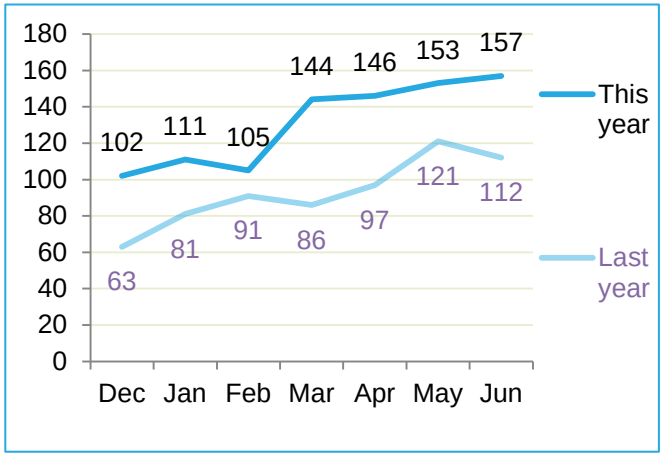
Setting standards:

critical and major recommendations on inspection

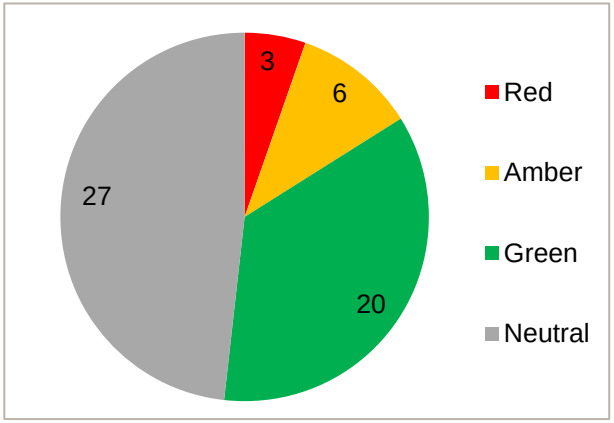


Increasing and informing choice:

public enquiries received (email)

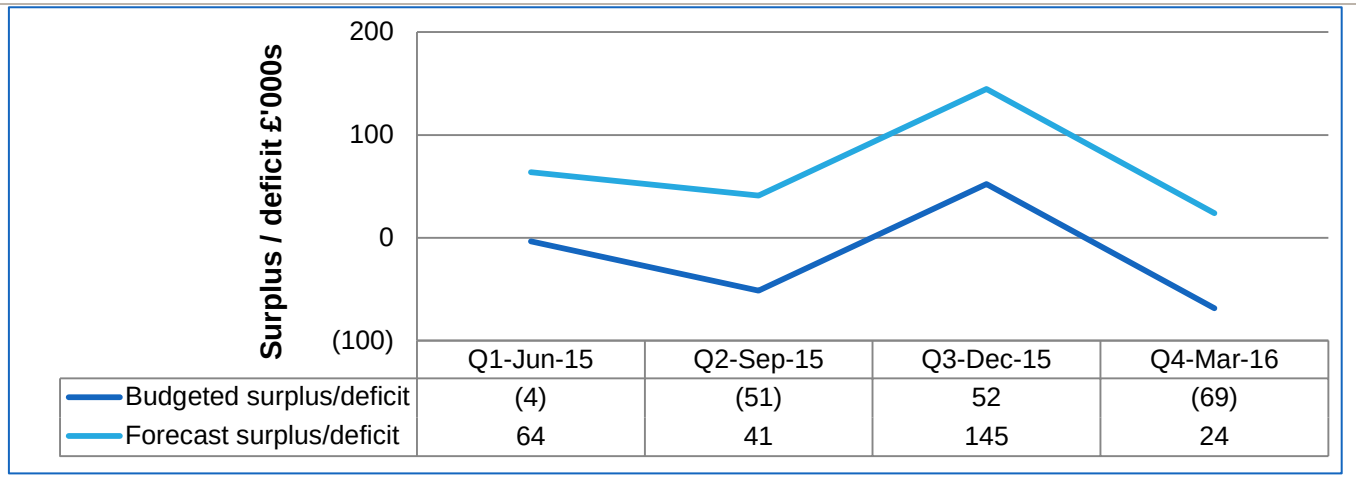


Overall performance - all indicators:



(See RAG status section for detail.)

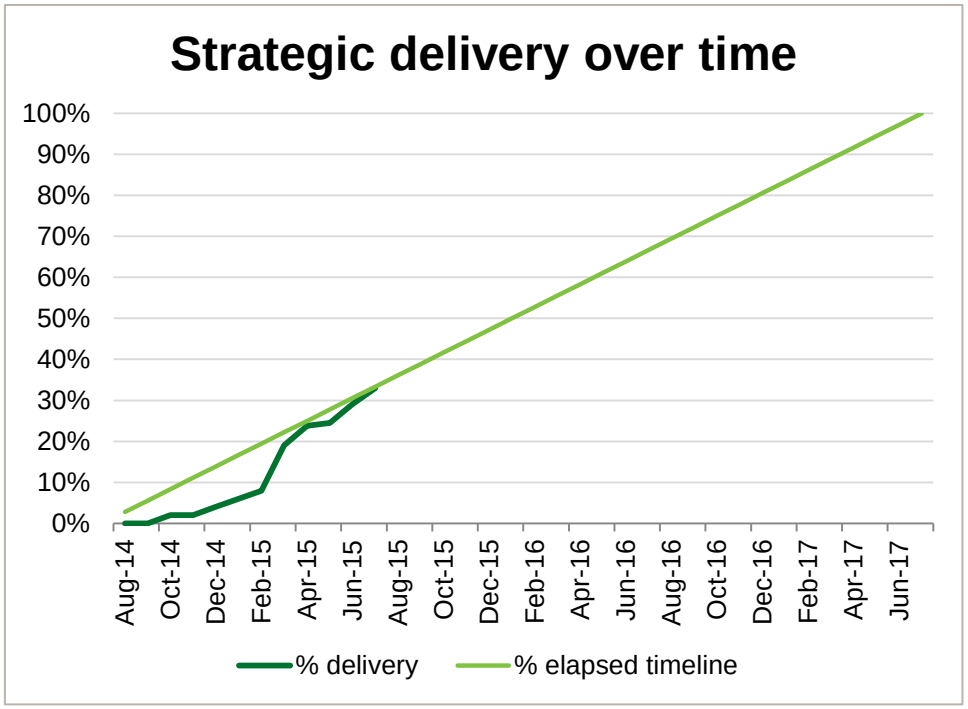
Efficiency, economy and value: Budget status: cumulative surplus/deficit

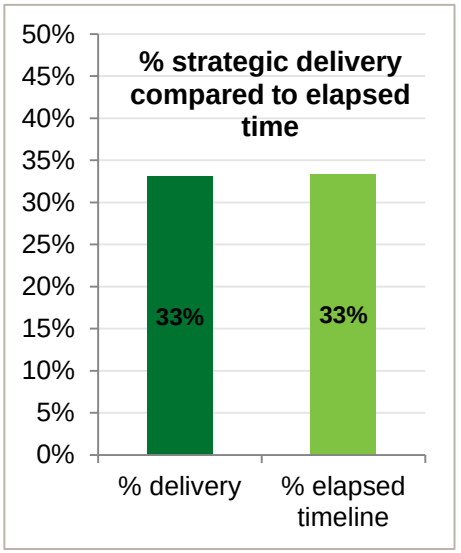


	Q1-Jun-15	Q2-Sep-15	Q3-Dec-15	Q4-Mar-16
Budgeted surplus/deficit	(4)	(51)	52	(69)
Forecast surplus/deficit	64	41	145	24

Dashboard - Commentary

Strategic delivery (to end of July) – summary:





We are broadly on track, with one third of items completed at one third of the way through the three year strategic period. The calendar of deliverables needs to be reviewed as soon as the detailed plan for Information for Quality (IfQ) programme delivery is available. There is a separate agenda item to update the Authority on progress with IfQ.

Strategic delivery in June and July

Setting standards

June saw the start-up of our counselling support service pilot, which will improve the availability of counselling support for donor-conceived people wishing to access information held on the HFEA Register. The start-up was delayed by two months, owing to initial difficulties in identifying a supplier who could deliver the contract within our budget. The success of the three year pilot will be gauged at annual intervals.

We held a well attended Licensed Centres Panel meeting, engaging with the sector on a range of topics. We also attended the annual ESHRE conference, so as to engage with the wider scientific community on current issues, to inform our policy work. During ESHRE we held a horizon scanning meeting to assist our future planning.

We continued to fulfil our role as an EU competent authority, participating in a competent authorities meeting in June.

Increasing and informing choice

The work to redevelop the website is behind schedule as a result of earlier approval delays, but is now going well. We have made good progress following the procurement of the suppliers Reading Room. The project board is established and meeting regularly to progress the work, and further user research is under way.

In July we published our report ‘Improving outcomes for fertility patients: multiple births 2015’, looking at elective single embryo transfer (eSET) and multiple birth figures.

Efficiency, economy and value

There has been a great deal of planning, sequencing and technical preparation work for the IfQ projects to improve the clinic portal and our information systems. The first ‘agile sprint’ of work began with our contractors in July, following the successful completion of tendering. As part of the IfQ programme, we will need to prepare an organisational blueprint setting out the way we will need to work in order to fully realise the benefits of the programme once it is delivered. This work has been rescheduled for the autumn as a result of the earlier approval delays.

Our annual report and accounts were successfully completed and laid in Parliament at the end of June, in keeping with statutory requirements.

Red/amber/green status of performance indicators

The red key performance indicators (KPIs) shown in the ‘overall status - performance indicators’ pie chart on the dashboard are as follows:

Total number of outstanding errors in the system taking into account the eight weeks centres are given to resolve.

This rose by 13% in June, compared to a target of reducing this by 5% or more each month.

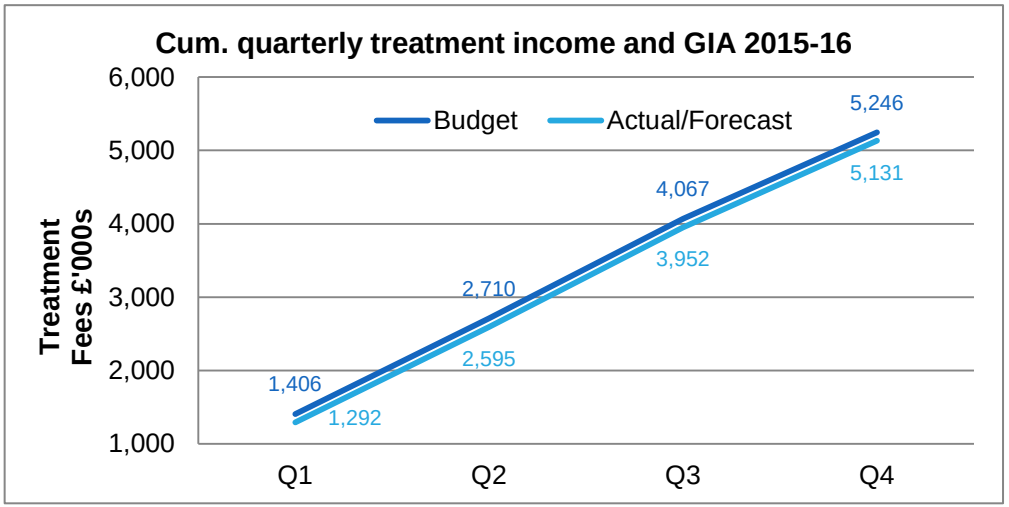
This is likely to be because we are focusing our staff resources on improving the quality of our data for the future, through IfQ. This means that at present we are not able to do as much proactive work with clinics on resolving errors in the data they submit. The effort we are investing in IfQ is critical to improving the situation – it will pay off in the long run, by greatly reducing both the error rate and the effort involved for clinics in submitting the data. Meanwhile, we are managing the situation by following up with the clinics who have the most errors, and CMG will continue to monitor the situation closely each month.

The average number of working days between a licensing committee date and minutes being finalised.

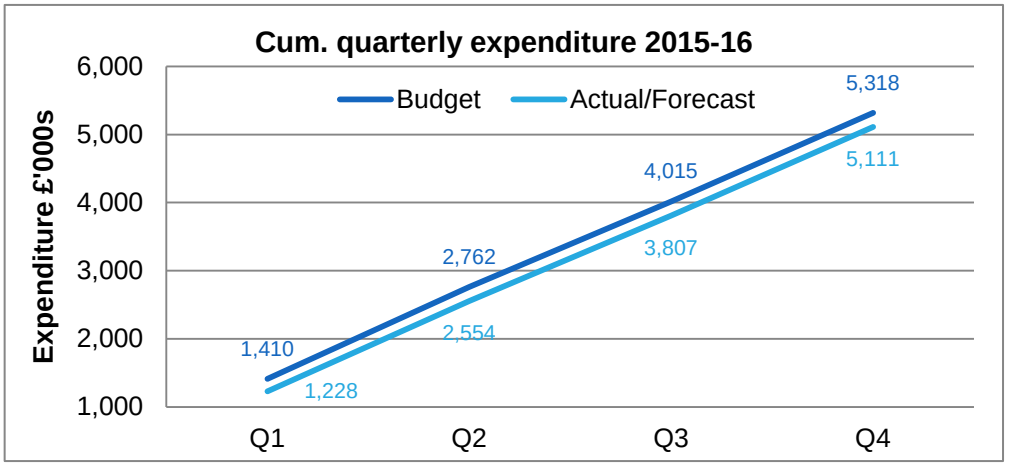
The KPI aim is for 100% of licensing minutes to be finalised within 10 working days. One set of Statutory Approval Committee (SAC) minutes fell just outside this KPI, resulting in a performance score of 78% in June. Another, narrower, version of this indicator focusing solely on PGD decision times was missed for the same reason.

Budget status

The dashboard shows the overall surplus/deficit position. The budget (planned) compared to actual figures are close together because we are only a few months into the financial year and are yet to re-forecast. The graphs below show how the surplus or deficit has arisen.



This graph shows our budgeted (planned) licence fee income and grant-in-aid (GIA) compared to what is actually happening. The first quarter of the year has shown that we have not reached budget (a shortfall of £114k). This was due to the GIA drawdown being short £40k and a drop in treatment fees. The GIA will be drawn down in Q2 instead. The remaining eight months we are expecting to achieve our budget (hence the closeness of the lines in the graph). However another review at the end of quarter two may show significant changes with new information.



This graph is the second component that makes up the surplus/deficit. This excludes costs relating to IfQ, since this is being funded from reserves and accounted for separately.

We are currently spending budget but against reduced income and our year end forecast is showing an under spend of £207k. Again this may change after our detailed review in October.

Quality and safety of care

As agreed previously, the following items are most meaningful when reported on an annual basis. The following items will be presented to the Authority each year in September (and these items therefore appear on the agenda for today's meeting):

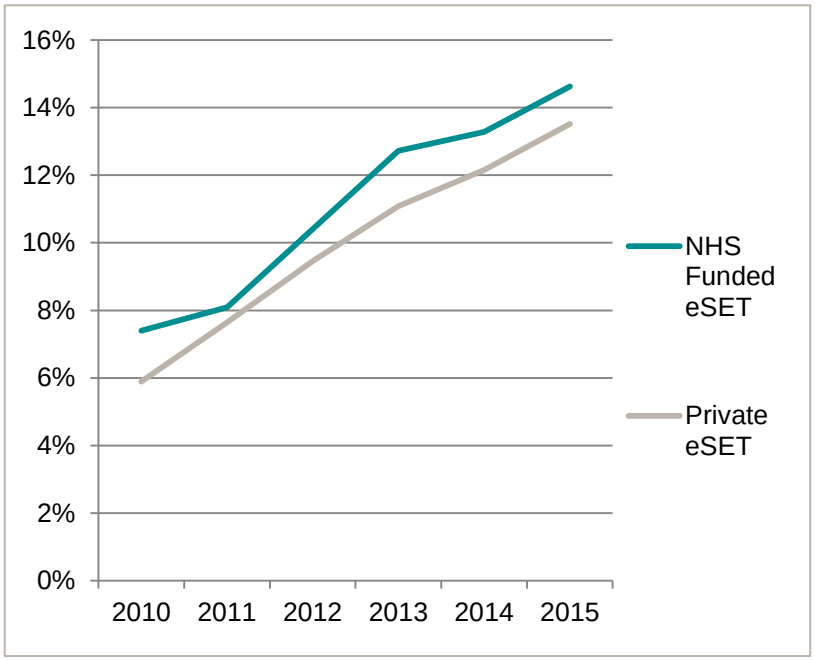
- number of risk tool alerts (and themes)
- common non-compliances (by type)
- incidents report (and themes).

The following figures and graphs were run on 13 August 2015.

ESET split by private/NHS:

Funding	Year					
	2010	2011	2012	2013	2014	2015
NHS Funded:						
Recorded as eSET	4293	4903	6263	7868	8437	5542
	7%	8%	10%	13%	13%	15%
Not recorded as eSET	19284	19493	17868	17719	17824	10120
	33%	32%	30%	29%	28%	27%
Private:						
Recorded as eSET	3422	4630	5696	6854	7718	5122
	6%	8%	9%	11%	12%	14%
Not recorded as eSET	31018	31545	30400	29388	29536	17104
	53%	52%	50%	48%	47%	45%

Graph: eSet % trends NHS/private:

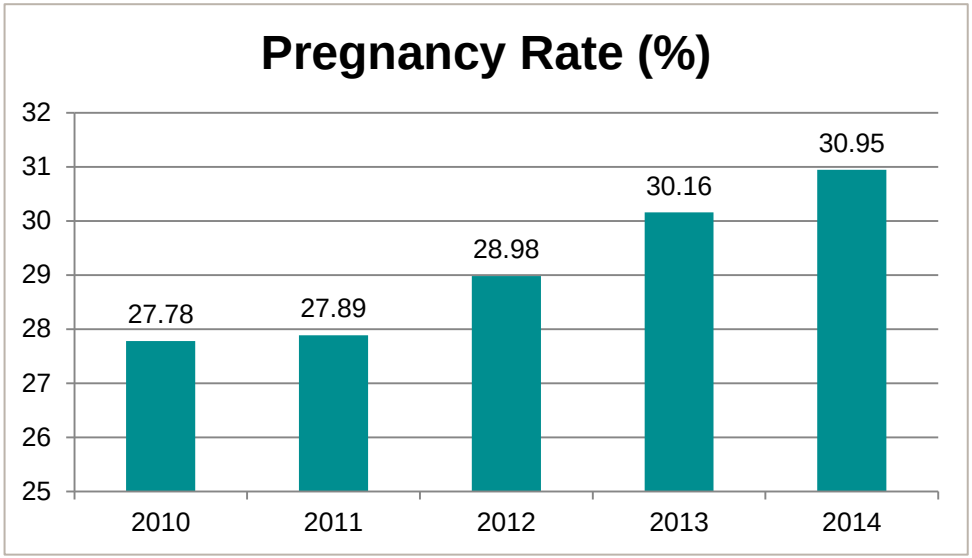


Explanatory text: Looking at all IVF treatment forms; counting those records that the clinics recorded as eSET.

Unfiltered success rates as % - pregnancies (rather than outcomes, since this provides a better real-time picture):

Years	All cycles	Pregnancies	Pregnancy rate
2010	58017	16117	27.78
2011	60571	16895	27.89
2012	60227	17453	28.98
2013	61829	18646	30.16
2014	63515	19658	30.95

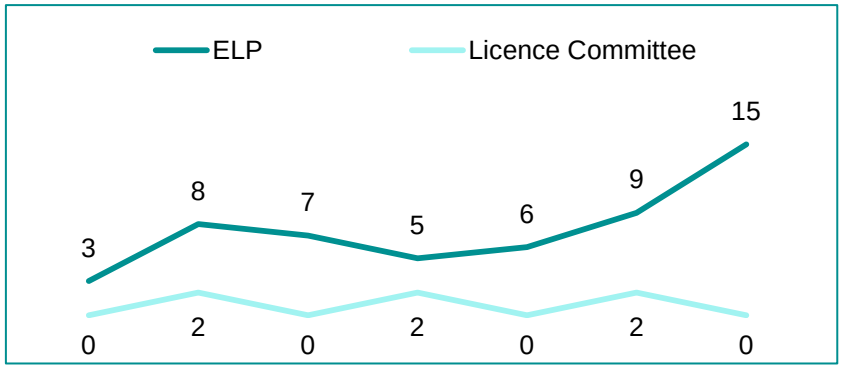
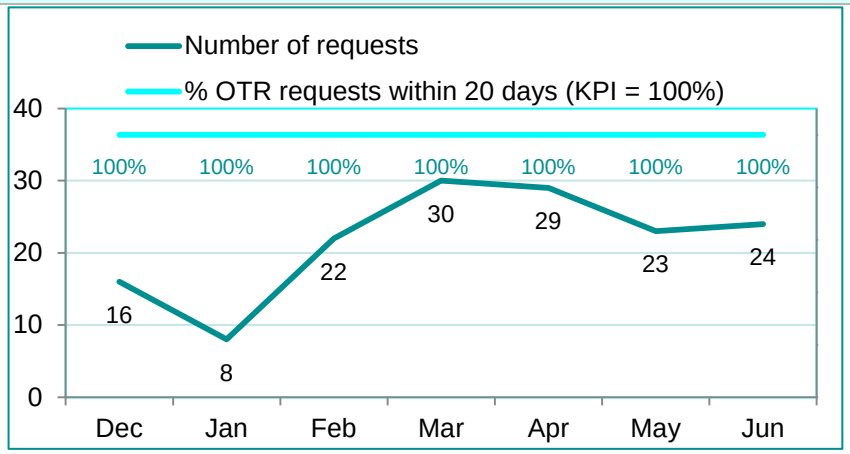
Graph showing the pregnancy rate over recent years:



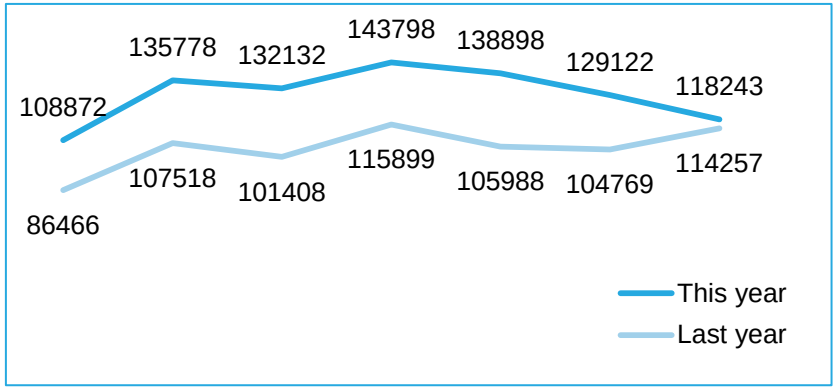
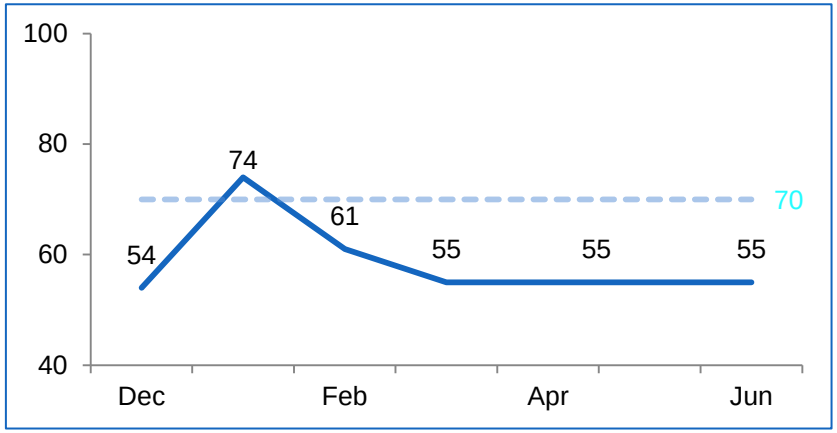
Explanatory text: Looking at all IVF treatment forms, and providing a count of pregnancies - as recorded on the early outcome form.

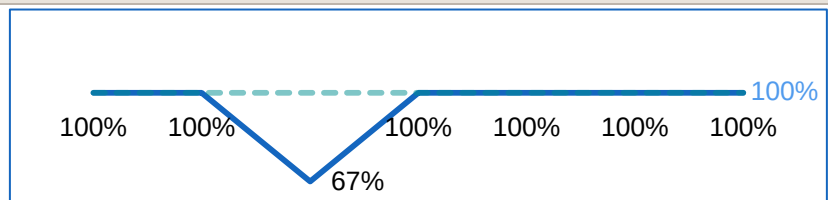
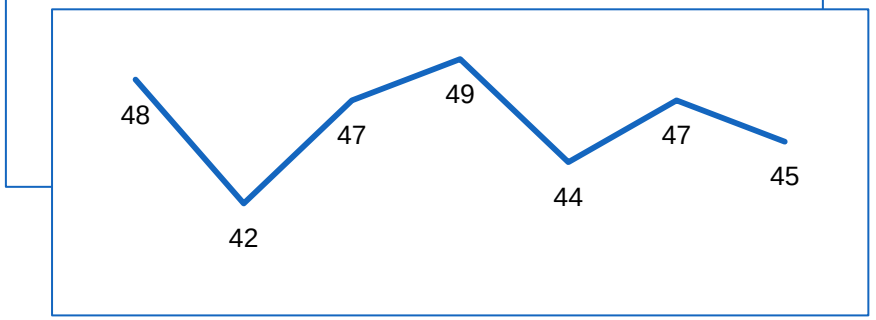
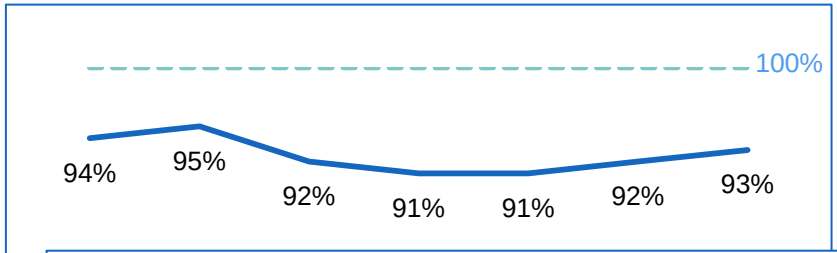
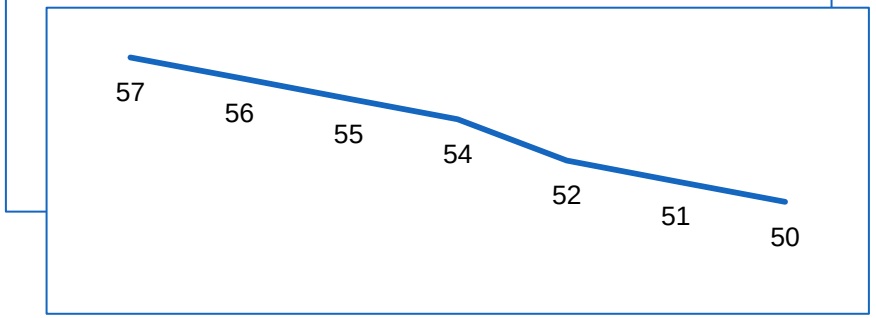
2. Indicator section

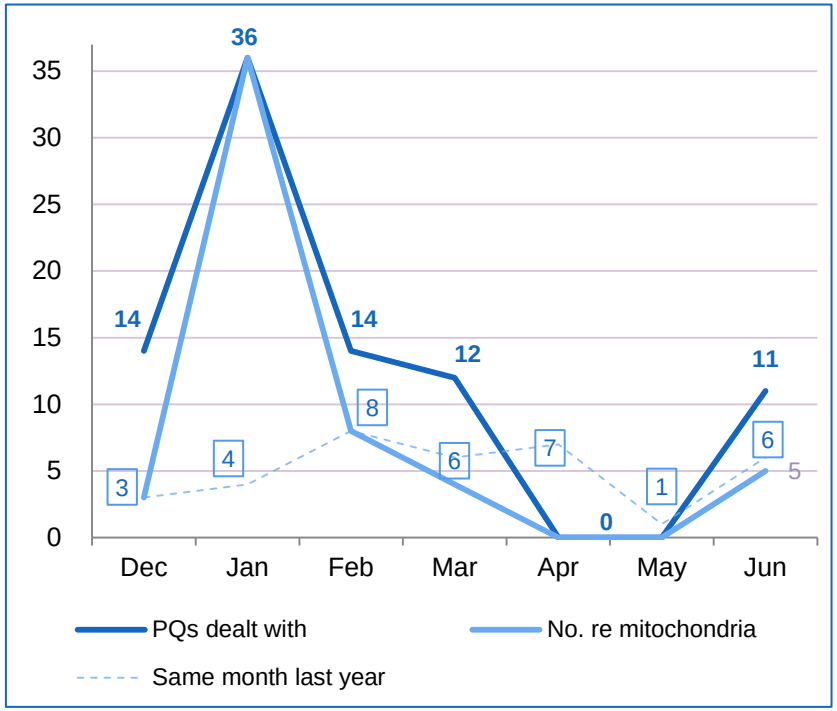
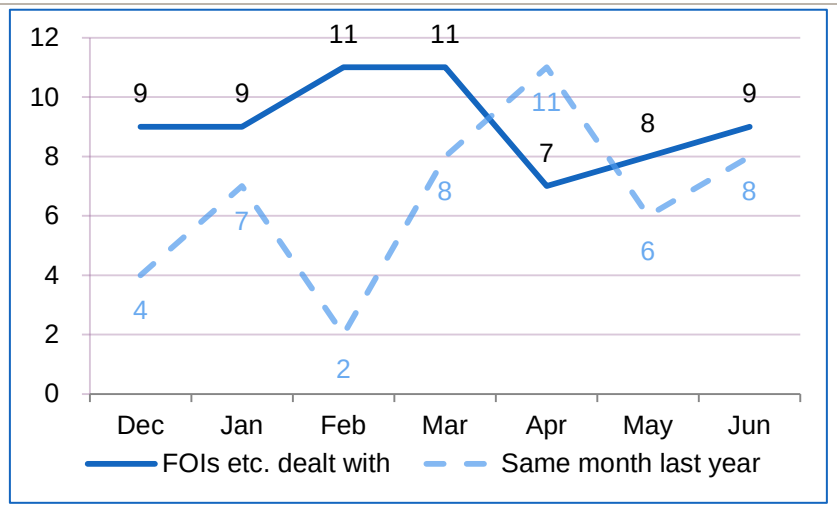
Key performance and volume indicators – June data:

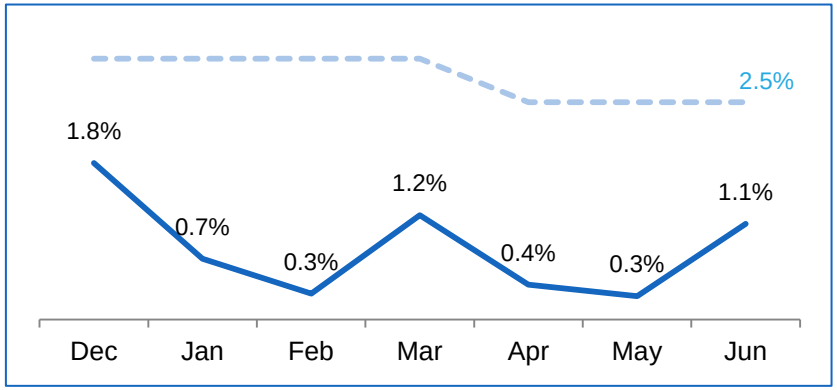
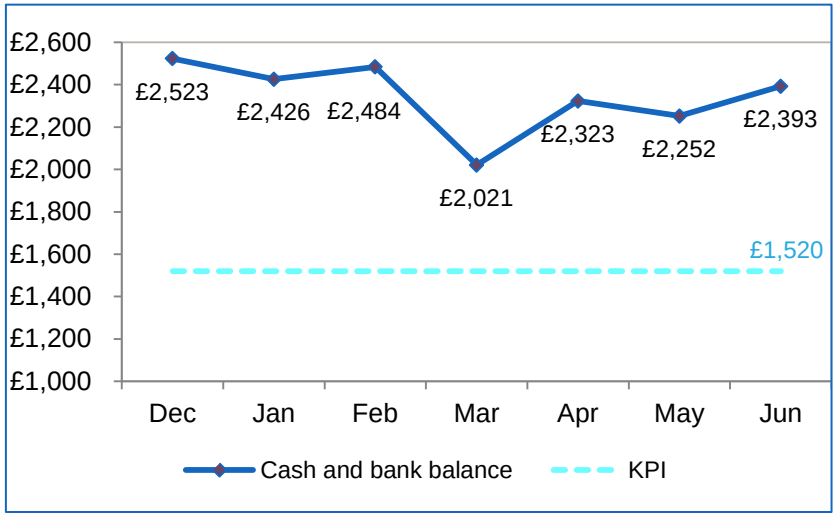
Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Setting standards: improving the quality and safety of care through our regulatory activities.					
Licensing decisions made: - **By ELP** - **By Licence Committee**	15 0	⇩		No KPI – tracked for workload monitoring purposes	Volume indicator (no KPI target).
Setting standards: improving the lifelong experience for donors, donor-conceived people, patients using donor conception, and their wider families.					
Percentage of Opening the Register requests responded to within 20 working days	100% (24)	★		Maintain at 100%	KPI: 100% of complete OTR requests to be responded to within 20 working days (excluding counselling time)

[1] Blue dashed line in graphs = KPI target level. This line may be invisible when performance and target are identical (eg, 100%).
[2] Direction in which we are trying to drive performance. (Are we aiming to exceed, equal, or stay beneath this particular KPI target?)

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Increasing and informing choice: using the data in the Register of Treatments to improve outcomes and research.					
			See graphs focused on quality of outcomes – after dashboard page.		
Increasing and informing choice: ensuring that patients have access to high quality meaningful information.					
Number of visits to the HFEA website (cw previous year)	118,243 114,257	⇩		No KPI – tracked for general monitoring purposes.	Volume indicator showing general website traffic compared to the same period in previous year. Measured on the basis of 'unique visitors'.
Efficiency, economy and value: ensuring the HFEA remains demonstrably good value for the public, the sector and Government.					
Average number of working days taken for the whole licensing process, from the day of inspection to the decision being communicated to the centre.	55 working days	★		Maintain at 70wd or less	KPI: Less than or equal to 70 working days.

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Monthly percentage of PGD applications processed within three months (66 working days).	100%	★		Reach and maintain 100% ↑	KPI: 100% processed (i.e. considered by LC/ELP) within three months (66 working days) of receipt of completed application.
Average number of working days taken.	45	★			
Annualised (rolling year) percentage of PGD applications processed within three months (66 working days)	93%	⇧		Reach and maintain 100% ↑	KPI: As above. (Annualised score). Performance has reached target, but the annualised figure is still being adversely affected by complex multi-type applications received during the rolling year, which take longer to process.
Average number of working days taken.	50	★			

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Number of requests for contributions to Parliamentary questions	Total = 11	⇧		No KPI – tracked for general monitoring purposes.	Volume indicator. The number received in January 2015 was nine times that received in January 2014.
Number of Freedom of Information (FOI), Environmental Information Regulations (EIR) requests and Data Protection Act (DPA) requests	9	⇧		No KPI – tracked for general monitoring purposes.	Volume indicator.

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Staff sickness absence rate (%) per month.	1.1%	★		 Maintain 2.5% or less	KPI: Absence rate of ≤ 2.5%. Public sector sickness absence rate average is eight days lost per person per year (3.0%).
Cash and bank balance	£2,393k	⇧		 Reduce	KPI: To move closer to minimum £1,520k cash reserves (figure agreed with DH).

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes

Management accounts:

Income & Expenditure Account — Jun-2015

Accounting Period
Cost Centre Name
Department Name

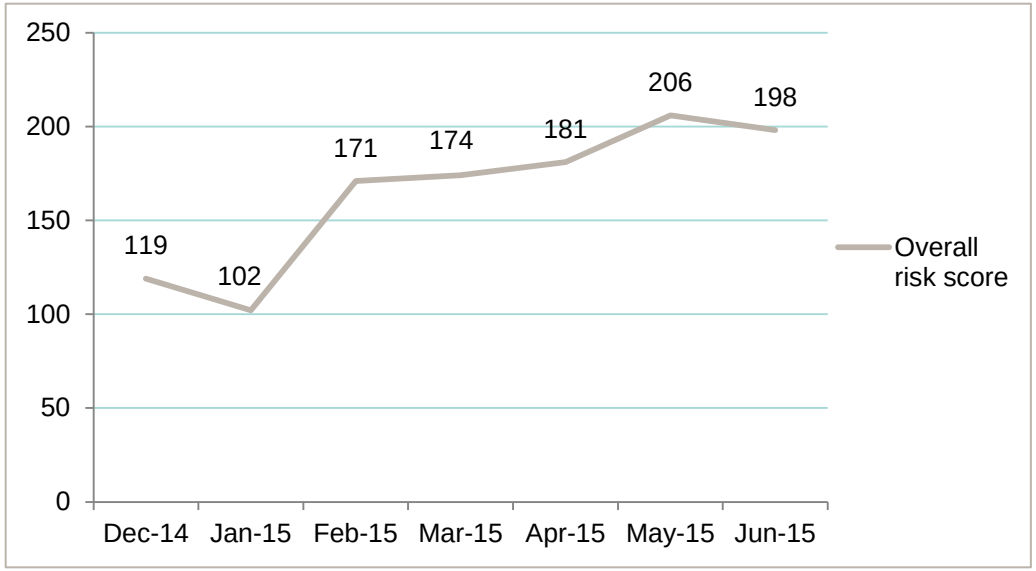
	Year to Date			Full Year		
	Actual YTD £	Budget YTD £	Variance YTD £	Forecast £	Budget £	Variance £
Income						
Grant-in-aid	240	280	-40	1,120	1,120	-
Licence Fees	1,052	1,125	-73	4,047	4,120	-73
Other Income	51	2	50	57	6	51
Total Income	1,343	1,406	-63	5,223	5,246	-22
Revenue costs - Charged to Expenditure						
Salaries (excluding Authority)	649	677	27	2,717	2,744	-27
Shared Services	22	23	0	91	91	-0
Employer's NI Contributions	48	61	13	234	247	-13
Employer's Pension Contribution	135	143	8	571	579	-8
Authority salaries inc. NI Contributions	37	36	-0	146	146	0
Temporary Staff costs	-	-	-	-	-	-
Other Staff costs	70	70	-1	271	258	13
Authority/Committee costs	27	35	8	160	166	-6
Other Compliance costs	15	9	-6	55	39	16
Other Strategy costs	26	57	31	175	175	-
Facilities costs incl non-cash	86	93	7	348	355	-7
IT costs costs	28	26	-2	104	106	-1
Legal costs	79	164	85	310	340	-30
Professional Fees	29	17	-12	78	68	10
Total Revenue costs	1,251	1,410	159	5,260	5,314	-54
Total Surplus/(Deficit) before Capital & Project costs	92	-3	-222	-37	-69	32
IFQ & Other Project costs - Reserves funded	69	86	17	1,155	1,155	-
Other Capital costs	-	-	-	100	100	-
TOTAL NET ACTIVITY	23	-89	-239	-1,292	-1,323	32

Indicator	Performance	RAG	Recent trend[1]	Aim[2]	Notes
Commentary:	Summarised management accounts June 2015 – commentary Treatment fee income up to end of June is approximately 6% less than expected. Grant-in-aid drawn down is 14% less than budgeted. These negative variances are reduced slightly by the interest received on late payment of treatment fees. The shortfall of GIA will be corrected in September's drawdown. Year to date revenue costs are 11% below budget as of 30 June 2015. In this first quarter a detailed review of the remaining nine months expenditure has been undertaken with all directorates. At this point in time we are forecasting under spends in the following areas: staff costs (£48k), facilities costs (£7k), Authority and Committee costs (£6k) and legal costs (£30k) – we received costs from a legal case that has been credited to the legal budget. There are expected over spends totalling £39k. £13k relates to staff travel due to increased inspections and more home workers costs. Within Compliance there is an over spend of £8k which relates to assessment of PGD applications costs which are currently being reviewed. Professional fees are more than expected due to Corporation Tax (£10k) that will need to be paid on interest received from an old debt.					

IfQ indicators:

<table>
<tr><th>Frequency / trigger point</th><th>Metric</th><th>Purpose</th><th>Latest status:</th></tr>
<tr><td>At programme set-up / major reorganisation / new tranche</td><td>MSP health check overall score achieved / maximum score as a %</td><td>Is the programme set up to deliver?</td><td>June: Annual health check will be done after agile sprint zero.</td></tr>
<tr><td>Monthly</td><td>Timescales: burndown chart showing remaining estimate of work.</td><td>Is there scope creep/over-run?</td><td>June: Measure to follow once agile sprints commence and plans are in place to measure against.</td></tr>
<tr><td>Monthly</td><td>Cost: earned value (% complete * estimated spend at completion)</td><td>Is the spend in line with milestone delivery?</td><td>There are four things we can attribute value to: websites and CaFC; Clinic Portal; Register and internal systems; defined dataset, discovery, stakeholder engagement etc. Currently, 25% of the value of the 1.8M programme cost at completion has been attributed to each project.
<table>
<tr><th colspan="7">Earned value</th></tr>
<tr><th>Project</th><th>Jan-15</th><th>Feb-15</th><th>Mar-15</th><th>Apr-15</th><th>May-15</th><th>Jun-15</th></tr>
<tr><td>Websites and CaFC</td><td>1.00%</td><td>1.00%</td><td>1.00%</td><td>1.00%</td><td>10.00%</td><td>10.00%</td></tr>
<tr><td>Clinic Portal</td><td>1.00%</td><td>1.00%</td><td>1.00%</td><td>1.00%</td><td>10.00%</td><td>10.00%</td></tr>
<tr><td>Register and internal systems</td><td>1.00%</td><td>1.00%</td><td>1.00%</td><td>2.00%</td><td>5.00%</td><td>6.00%</td></tr>
<tr><td>Discovery</td><td>98.00%</td><td>98.00%</td><td>100.00%</td><td>100.00%</td><td>100.00%</td><td>100.00%</td></tr>
<tr><td>IfQ Total earned value</td><td>25.25%</td><td>25.25%</td><td>25.75%</td><td>26.00%</td><td>31.25%</td><td>31.50%</td></tr>
<tr><td>% of spend to date</td><td>27%</td><td>28%</td><td>29%</td><td>30%</td><td>31%</td><td>31%</td></tr>
</table>
</td></tr>
</table>

IfQ indicators:

Frequency / trigger point	Metric	Purpose	Latest status:
Monthly	Quality: category A requirements dropped or postponed during this period	Are key requirements being lost from the programme which could trigger a change in the business case?	**June:** To be worked up now that suppliers are in place. This will be reported from July data onwards.
Monthly	Stakeholder engagement: combined stakeholder engagement score	Are we keeping stakeholders with us? Is it getting better or worse?	**June:** A method for capturing this will need to be built into stakeholder plans for the programme – might need to report quarterly. Consideration will be built in the communications programme.
Monthly	Risks: sum of risk scores (L x I)	Is overall risk getting worse or better (could identify death by a thousand cuts)?	

IfQ indicators:

Frequency / trigger point	Metric	Purpose	Latest status:
Monthly	Software: burndown chart	Shows new items added and estimated delivery of the product backlog (or items marked for delivery)	**June:** To be worked up once the product backlog is in place (during the early period of delivery, following full approval and completion of tendering). Reporting will start from August data.
Quarterly	Benefits: value (£) of tangible benefits planned to the delivered by the programme	Is the value of the benefits increasing or decreasing – could trigger a review of the business case?	**June:** No figure available at this stage - to be worked up post-approval and completion of both tendering and then Sprint Zero. Reporting is expected to be able to commence from September onwards.

Regulating mitochondrial donation

Strategic delivery:	☒ Setting standards	☐ Increasing and informing choice	☒ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	7		
Paper number	HFEA (16/09/2015) 764		
Meeting date	16 September 2015		
Author	Joanne Anton, Policy Manager		
Output:			
For information or decision?	For decision		
Recommendation	Agree recommendations for the regulation of mitochondrial donation.		
Resource implications	Staff resource implications (across the Executive)		
Implementation date	29 October 2015		
Communication(s)	Clinic Focus and Code of Practice update, 29 October 2015		
Organisational risk	☐ Low	☐ Medium	☒ High
Annexes	Annex 1: Regulating mitochondrial donation: stakeholder feedback report Annex 2: Summary of Standing Orders changes Annex 3: Draft mitochondrial donation Code of Practice guidance note Annex 4: Draft general directions: • 0001 - Gamete and Embryo donation • 0005 - Collecting and recording information for the HFEA • 0007 - Consent • 0008 - Information to be submitted to the HFEA as part of the licensing process • 0012 - Retention of records		

Annex 5: Draft forms and guidance (to note), including the:

- Licence variation form
- Mitochondrial donation follow-up information sheet
- Patient application form
- Clinical expert review form
- Decision trees for the Statutory Approvals Committee
- Mitochondrial donation: explanatory note for Statutory Approvals Committee
- Consent forms

1. Introduction

1.1. In February 2015 Parliament approved The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 ('the Regulations') to permit the use of maternal spindle transfer (MST) and pronuclear transfer (PNT) to avoid serious mitochondrial disease. The regulations will come into force on 29 October 2015.

1.2. In May 2015 the Authority approved draft proposals for licensing mitochondrial donation and key areas to seek focused stakeholder feedback. Since then, the Executive has continued to work with members to develop and refine these proposals and to take into account expert views from key stakeholders and legal advice. A summary of stakeholder feedback is provided at annex one.

1.3. Mitochondrial donation to avoid serious mitochondrial disease has not been offered at any clinic in the world before. The statutory provisions governing this new treatment are set out in the Regulations and prescribe the steps UK clinics must take before they can offer this new treatment.

1.4. As with any new treatment it is important that it is judged to be safe and effective before it is made available. The HFEA expert panel has considered the safety and efficacy of MST and PNT in three reports and it has recommended a number of tests which it believes should be completed before the treatment is offered. There is no statutory requirement that these tests must be met before MST or PNT is offered in treatment but in passing the Regulations, Parliament expected this to happen before the HFEA could consider licensing the first clinic.

1.5. Accordingly, once these tests have been carried out, we will convene the expert panel to consider the results, and their report will be presented to the Authority. If the panel is satisfied and the Authority accepts their recommendations, we will amend the list of authorised processes that clinics are permitted to use. This will trigger the licensing process and enable clinics to apply to be licensed to offer the treatment. In order to grant a licence, the Authority must be satisfied that the clinic has the relevant skills and competence to carry out the treatments safely and effectively, and if licensed, they will need to seek approval for each patient they propose to treat.

1.6. This paper sets out the three broad stages under the new proposed system that a clinic wishing to offer mitochondrial donation must follow:

1. How to seek approval to carry out mitochondrial donation
2. How to run a good quality service, and
3. What to do after treatment.

1.7. The Authority is asked to approve the final proposals for regulating mitochondrial donation (and the attached documents set out in annexes two to four) for implementation on 29 October 2015. The draft forms and supporting guidance incorporating the new requirements are attached at annex five. These forms are to note only – they do not require formal Authority approval.

2. How to seek approval to carry out mitochondrial donation

2.1. Before any HFEA-licensed clinic can undertake mitochondrial donation for treatment purposes it must follow a two-stage process:

1. it will need to apply to vary its licence to include specific permission to carry out MST and/or PNT. Such applications will be considered by the Licence Committee. If the application is approved, the clinic will be licensed and will not need to repeat this step (unless they wish to seek approval to change their embryologists, see paragraph 2.5 below).
2. it will then need to apply for approval to treat a specific patient. Such applications will be considered by the Statutory Approvals Committee (SAC). This step must be completed for each individual patient.

2.2. These proposals require changes to the Authority's Standing Orders which are highlighted (at annex two).

Licence variation process

2.3. A clinic must first submit a completed licence variation application form and the necessary supporting evidence, to their HFEA Inspector. The Inspectorate will then assess the competence of the clinic and suitability of its premises and processes. We will use the same inspection methodology to assess a mitochondrial donation application as we do to assess an application to vary a licence for other reasons. We will carry out a detailed assessment against all relevant standards, including the new Code of Practice guidance. The Inspectorate will carry out an additional onsite inspection focused on the licence variation which will not affect the clinic's normal inspection cycle. Once a variation has been granted, the Inspectorate will continue to monitor the clinic as part of the usual compliance cycle.

2.4. Today the Authority is asked to approve General Directions 0008 which sets out the necessary evidence needed to support a licence variation (at annex four). These directions require the clinic's Person Responsible (PR) to submit the following evidence:

- suitable validation of their clinic's equipment and processes
- their process for monitoring children born following mitochondrial donation, where patients have consented to follow-up - covering what links the clinic has with research groups or mitochondrial disease specialists, what follow-up will involve (eg, the method and frequency of contact) and what information the clinic will provide to their patients about follow-up
- competency of the clinic staff and suitability of its premises and processes with specific reference to PNT and/or MST - all staff either directly involved in mitochondrial donation techniques, or staff involved with patients receiving such treatment, must be suitably qualified, trained and assessed as competent for the tasks they perform
- competency of the clinic's MST/PNT embryologist(s), including:
  - their specific experience of carrying out MST or PNT in treatment, training or research on human eggs or embryos (eg, embryo survival

rates, blastocyst development, and rate of carryover of mutant mitochondria, in line with key performance indicators) references to support their experience and knowledge, and

- any other information that may demonstrate competence (such as their experience of performing micro-manipulation on human or animal (eg, mice) eggs or embryos).

2.5. A PR wishing to make any changes to their list of authorised embryologists will need to apply to vary the clinic's licence and will be required to submit the relevant competency information for each proposed embryologist for consideration by a Licence Committee.

Developing the proposal for assessing embryologist competency

2.6. The proposed approach of assessing the competence of MST/PNT embryologists goes further than our usual approach to assessing staff competency and beyond the criteria set out in the Regulations. In developing this rigorous approach we have taken account of the views of Authority members and stakeholders in particular from the scientific community, who have all acknowledged that the competence of the individual performing the techniques has a direct bearing on the rate of carry-over of mutant mitochondria. The ability of the embryologist to create embryos following MST or PNT with a low rate of carryover of mutant mitochondria will directly affect whether or not the child is born free from mitochondrial disease – which is the primary purpose of the Regulations and of course the primary reason for patients seeking this new treatment.

2.7. Stakeholders have emphasised the novel nature of the techniques and difficulty of performing the techniques such that a low carry over rate is consistently achieved. In order for the Authority to maintain public confidence in the regulation of new techniques such as this and provide patients with assurance, it is considered crucial that only those embryologists who have been able to demonstrate that they have the requisite skills and experience should be permitted to conduct the two techniques. The two techniques that only the authorised embryologists can do are those defined in Regulations 4 and 7.

2.8. Therefore, for the time being, it is proposed that not only should the PR be required to demonstrate that their MST/PNT embryologists have experience of performing the techniques on human gametes and embryos, but the PR must also demonstrate that the individual can perform the techniques in line with a pre-determined set of performance indicators: embryo survival rates, blastocyst development, and rate of carryover of mutant mitochondria. These performance indicators will be determined by the Authority, taking into account the advice of an expert panel following consideration of the latest research (when it meets to assess the outcomes of the final safety and efficacy tests, as outlined in 1.4-1.5 above). These performance indicators will be added to General Directions 0008 once agreed by the Authority (see recommendation at 2.10).

Recommendation

2.9. The Authority is asked to approve the proposed approach for varying a clinic's licence to perform mitochondrial donation set out at paragraphs 2.3-2.8 above, including the information that clinics need to submit as set out in General Directions 0008 (at annex four) and the consequential changes to Standing Orders (at annex two).

2.10. Members are also asked to note the delegation of later amendments to General Directions 0008, to include performance indicators for MST/PNT embryologists, to a sub-set of Authority members.

Mitochondrial donation licence conditions

2.11. Before the HFEA can issue a licence specifically permitting the clinic to carry out mitochondrial donation the clinic must acknowledge the licence conditions in the usual manner. The new licence conditions specific to mitochondrial donation must be agreed by the Authority today. The proposed conditions relevant to mitochondrial donation are outlined below. It is worth noting that the existing conditions (T1 to T123) are considered sufficiently comprehensive and we therefore need only introduce a small number of new conditions specific to mitochondrial donation. Crucially, we have not sought to impose conditions which merely restate what is contained in the Regulations.

2.12. The new conditions are as follows:

T124 a. No clinic may carry out either the process of pronuclear transfer* (PNT) or maternal spindle transfer* (MST) or part of either process, unless express provision has been made on the clinic's licence permitting it to undertake either or both processes.

b. Neither PNT nor MST may be carried out under third party, satellite or transport agreements.

c. No clinic may provide treatment using gametes or embryos which have been created using PNT or MST unless express provision has been made on the clinic's licence permitting the clinic to undertake either or both processes.

*Wherever reference is made in this licence to PNT or MST or the process of PNT or MST, that is the process defined in Regulation 4 or Regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

T125. PNT and MST must only be carried out on premises of clinics licensed to undertake mitochondrial donation ('MD'). These processes must not be carried out on the premises of a clinic that is operating under a third party, satellite or transport agreement with a clinic that holds a licence to undertake MD.

T126 Donors of gametes for use in PNT and or MST must be screened for pathogenic mitochondrial DNA mutations and an assessment of the risk of transmission of inherited conditions known to be present in the maternal line must be carried out, after consent is obtained. Complete

information on the associated risk and on the measures undertaken for its mitigation must be clearly communicated and explained to the recipient.

T127 a. No alterations may be made to the nuclear or mitochondrial DNA of an egg created by means of the application of MST;

b. No alterations may be made to the nuclear or mitochondrial DNA of an embryo created by means of the application of PNT and no cell may be added to an embryo created by means of the application of PNT other than by the division of the embryo's own cells.

T128. In the case of treatment involving mitochondrial donation the clinic must ensure that it only carries out the process of PNT or MST for a particular, named patient once the Authority has issued a determination that:

- there is a particular risk that any egg extracted from the ovaries of the named woman or any embryo created by the fertilisation of an egg extracted from the ovaries of the named woman may have mitochondrial abnormalities cause by mitochondrial DNA and
- there is a significant risk that a person with those abnormalities will have or develop a serious mitochondrial disease.

T129 Only those embryologists assessed as competent by the Authority to undertake PNT, MST or both, and named on the front of this licence, are permitted to undertake those processes or any part thereof.

Recommendation

2.13. The Authority is asked to approve the new Licence Conditions at paragraph 2.12 of this paper.

Individual patient approval process

2.14. Before a clinic licensed to do MST and/or PNT is permitted to carry out the treatment for a specific patient, it will need to apply to the HFEA for approval. These applications will be considered by the Statutory Approvals Committee (SAC). If granted, approval can only be given for the treatment to be applied for the particular patient, in the circumstances described in the Regulations. Two decision trees for SAC reflecting the regulations have been developed to aid its decision making (at annex five).

2.15. Step one of the approval is the assessment of whether there is a 'particular risk' of the egg or embryo having a mitochondrial abnormality caused by mitochondrial DNA. The biology of mitochondrial disease means that for any woman carrying mutant mitochondrial DNA (mtDNA), even if very low levels of affected mtDNA are present, there is almost a 100% risk that her eggs will have mitochondrial abnormalities caused by mitochondrial DNA. Therefore the presence of a mutation in the female patient's mtDNA alone is sufficient to satisfy the test for 'particular risk.'

2.16. The second step is the assessment of whether there is a 'significant risk' that a child with those abnormalities will have, or develop, a 'serious' mitochondrial disease. The assessment of 'seriousness' should be based on the most severe symptoms that could be expected for a particular case. To support an application, a clinic will need to submit patient-specific information to enable an assessment of 'significant risk' and 'seriousness' to be made. This will include:

- the patient's medical history
- the patient's mutant mtDNA load and mutation threshold
- the patient's family medical history of the mtDNA mutation or disease
- scientific literature relevant to the mtDNA mutation or disease, and
- any additional information which the clinician may consider is relevant to the application.

Recommendation

2.17. The Authority is asked to approve the proposed approach to assessing individual patient applications set out at paragraphs 2.14-2.16, including the information that clinics need to submit as set out in General Directions 0008 (at annex four).

3. How to run a good quality service

3.1. For a clinic licensed to carry out mitochondrial donation to run a good service, it will need to follow new guidance set out in the Code of Practice and directions, use new consent forms, and submit the prescribed information to the HFEA. This section sets out how a clinic should run a good quality service in line with the new regulatory requirements.

Registration process

3.2. Clinics must submit information to us on their patients, donors and treatments, according to General Directions 0005 (at annex four). In addition to the patient and partner (or sperm donor) registration information submitted for standard IVF cycles, registration of the mitochondrial donors and pronuclear transfer only sperm donors (where applicable) will also be required.

3.3. The PNT-only registration will apply to a small number of cases where the male donor is only providing sperm for part of the PNT process (involving the creation of embryos with the mitochondrial donor) where he will not be genetically related to the child. This may happen if the male partner of the patient undergoing treatment cannot be used for this part of the PNT process because he is a close genetic relative of the mitochondria donor.

Obtaining consent to treatment and donation

3.4. Another step that must take place before treatment is offered is obtaining properly informed consent from the egg and sperm provider(s) and the mitochondrial donor. We have developed separate forms so that the questions

are tailored to these specific type of treatments, recognising the different information needs of the patients and donors, and reflecting the consent provisions in the Regulations.

3.5. Female patients can consent to their eggs undergoing MST and embryos created from eggs following MST being used in their treatment, and/or for their eggs to be used to create embryos which will undergo PNT. The male partner of a woman having treatment can also either consent to his sperm being used to create embryos with eggs that have undergone MST, and/or for his sperm to be used in PNT. He can consent to both stages of the technique (creating embryos with his partner's eggs (the first stage) and the donor's eggs (the second stage), or consent to the first stage only. Again, each stage of the MST and PNT technique is explained before he is asked to give his consent. In both forms we explain what MST or PNT involves beneath each question and they broadly mirror the 'standard' fertility patient/partner treatment form.

3.6. We have also developed a form for women donating their eggs and/or embryos created with their eggs for use in other women's mitochondrial donation treatment. They can consent to their eggs undergoing MST and for embryos created from eggs following MST being used for the treatment of others, and/or to their eggs being used to create embryos outside of the body which will undergo PNT. If a man is donating his sperm for use in PNT only (and not for 'standard' donation) he can provide consent to both stages of the PNT process (including creating embryos with the intended mothers eggs and donor eggs), or for the second stage only (with the donor eggs). Alternatively, we have developed a form which allows a man to consent to the use of his sperm for PNT in addition to 'standard' donation. These forms have been developed to reflect the different information needs of PNT donors as opposed to 'standard' donors.

3.7. We propose that before any consents or samples are obtained from a prospective mitochondrial donor and patient, the recruiting clinic should provide information about screening and its implications, the procedure, legal parenthood, what information will be collected and held by the HFEA and what will be potentially disclosed to any person born following their donation (paragraphs 33.28-29). The consent requirements are outlined at paragraphs 33.30-33.32.

3.8. In developing the consent forms we have sought legal advice and feedback from stakeholders, including from patient organisations, professional bodies and licensed clinics, to make sure they meet the requirements of the Regulations and Schedule 3 of the Human Fertilisation and Embryology Act 1990 and are as patient friendly as possible.

3.9. The Authority is asked to approve this approach to consent to treatment and donation. The consent forms are for information (at annex five), and are as follows:

- Women's consent to mitochondrial donation treatment and storage form (WMT form)

- Men's consent to mitochondrial donation treatment and storage form (MMT form)
- Your consent to mitochondrial donation (WDM form)
- Your consent to donating sperm for mitochondrial donation (for pronuclear transfer only) (MD - PNT only)
- Your consent to donating sperm, including for use in pronuclear transfer (MD including PNT)

Code of Practice guidance

3.10. We propose to introduce a standalone guidance note on mitochondrial donation and make a number of minor consequential changes to our existing guidance and requirements to cover the use of mitochondrial donation in clinical treatment. We sought stakeholder feedback on the key policy areas, which is incorporated in the summaries below. The mitochondria guidance note is at annex three.

Staff to be involved in mitochondrial donation

3.11. New Code of Practice guidance (paragraphs 33.1-33.8) sets out the licensing process outlined in stage one of this paper, including who should be involved in deciding whether a particular patient should receive mitochondrial donation treatment, who can perform the treatment, and who the treatment can be offered to.

3.12. Paragraphs 33.9-33.11 describe how embryos following mitochondrial donation can be used. They state that embryos that have undergone either MST or PNT should not be transferred with any other embryos that have not undergone the same technique in the same treatment cycle. A clinic should not perform embryo biopsy (such as for the purpose of preimplantation genetic diagnosis (PGD) or preimplantation genetic screening (PGS)) on embryos that have undergone MST or PNT. It also states that a clinic should use the same sperm provider for both steps of PNT unless there is a good reason for not doing so (eg, if the mitochondria donor is a close genetic relative of the intended father).

Provision of counselling and information

3.13. New Code of Practice guidance (paragraphs 33.12-33.13) advises clinics that people seeking treatment should have access to mitochondrial disease specialists, clinical geneticists, genetic counsellors and, where appropriate, infertility counsellors. The clinic should work closely with the local genetics/mitochondrial disease clinic of those seeking treatment.

3.14. The guidance also sets out what information clinics should provide to patients seeking mitochondrial donation (paragraphs 33.14-33.20). Most stakeholders agreed that these patients should receive similar information to other types of fertility patients but that they should also receive information specific to this form of treatment, including genetic and clinical information about the mitochondrial disease, the possible impact (if known) of the mitochondrial

disease on those affected and their families, and the experience of the clinic in carrying out the techniques.

3.15. Similarly to sperm, egg and embryo donation, (paragraphs 33.21-33.22) clinics should tell people who seek mitochondrial donation treatment that it is best for any resulting child to be told about their origin early in childhood. We also propose that clinics inform patients of the potential risk of mitochondrial disease in future generations and the potential ways to avoid this (eg, that any female born following MST or PST that, should she wish to have children of her own, could have her eggs or early embryos analysed by PGD in order to select for embryos free of abnormal mitochondria).

Disclosing non-identifying information about mitochondrial donors to patients and parents

3.16. The Authority is asked to consider whether to allow certain non-identifying information about the mitochondrial donor to be accessed by patients and/or parents of children born following mitochondrial donation before the child reaches the age of 16. This would mirror the access policy for sperm, egg and embryo donation.

3.17. The Regulations require clinics to submit the following information about the mitochondria donor:

(a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history

(b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and

(c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section.

3.18. This information can be accessed by a mitochondrial donor-conceived person, should they decide to access the information they are entitled to from the age of 16. Just as with standard gamete and embryo donation, there is no provision in the Act or Regulations to release this information to patients or parents of the resulting child. Legal advice suggests that if the Authority were to allow the disclosure of this information, it could disclose information about screening tests and medical history (see (a) above) and any description given by the donor ((b) above), but not information provided for the mitochondria donor-conceived person ((c) above).

3.19. A key reason for encouraging clinics to disclose non-identifying donor information to patients and parents of donor-conceived people is to help parents share information about their child's genetic origins, and to prepare them for potentially meeting their donor once they can receive donor identifying information at 18. These Regulations introduce a different system for mitochondria donor-conceived children because it is recognised that a mitochondria donor does not determine the characteristics of a child in the

same way as with gamete donation and will not be the genetic parent of any child born. The Regulations specify that mitochondria donors cannot be identified, reflecting the policy view that mitochondrial donation is more akin to organ donation than egg or sperm donation.

3.20. However, it is possible that patients or parents might find it beneficial to access certain information via the clinic or the HFEA about their mitochondrial donor. For example, the parent of a child born following mitochondrial donation with a medical condition may want to access information about their mitochondrial donor's family medical history. The Authority may wish to allow patients and parents to access this type of information, if they so wish. However, to recognise the clear differences with sperm and egg donation, we would not advise clinics to provide information about the mitochondria donor to prospective patients, in the same way as we do for egg and sperm donation.

Mitochondrial donor screening

3.21. Mitochondrial donors will provide their eggs in the same way as egg donors for treatment and as such the risk of infectious diseases being transmitted is likely to be the same. New mandatory requirements set out in box 33B requires clinics to follow the same requirements for laboratory tests and storage set out in **licence condition T52** (for sperm and egg donors), except for genetic screening. This part of T52 is not relevant because it relates to nuclear DNA based conditions. Instead, stakeholders suggested mitochondrial donors are screened for pathogenic mitochondrial DNA mutations to ensure, as far as possible, that the donor doesn't carry a mitochondrial disease. Clinics should therefore carry out genetic screening for pathogenic mitochondrial DNA mutations and carry out an assessment of the risk of transmitting inherited conditions known to be present in the maternal line, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation should be communicated and clearly explained to the recipient.

3.22. Following stakeholder feedback on the impact of continuing research in this area, we propose advising clinics to keep up to date with relevant literature and professional guidance, such as on refinements to the techniques, to improve their efficacy in treatment. Also, consistent with a recommendation of the scientific expert panel, clinics should keep up to date with emerging research relevant to mitochondria haplotype matching and consider matching the haplotypes of donors with recipients where possible.

3.23. In addition, before accepting a mitochondrial donor, clinics should follow the broadly same requirements and guidance as set out in guidance note 11 Donor recruitment, assessment and screening (such as on assessing their suitability and the provision of information and counselling). This is proposed in paragraph 33.25 of the new guidance note.

Age limit for mitochondrial donors

3.24. Age should be a consideration when selecting mitochondrial donors as there is some evidence to suggest that mitochondrial DNA has a high mutation rate

resulting in numerous new mutations over a person's lifetime, and potentially resulting in decreased mitochondrial function. The age of the donor may also affect the number of viable eggs that are collected. Stakeholders had mixed views on our proposal to apply the same age limit for egg donors to mitochondrial donors. It was agreed that any limit applied needs to be scientifically justified.

3.25. There is some evidence to suggest that mitochondria in a woman's eggs accumulate damage over time meaning the eggs of older donors may have reduced mitochondrial function. Age should therefore be taken into consideration (paragraph 33.26) when determining the suitability of a woman donating her eggs, in conjunction with an assessment of her reproductive health, such as an assessment of ovarian reserve.

The 10 family limit

3.26. The family limit refers to the number of families a single donor can help to create. The current limit is based on the perceived social and psychological interests of donors and donor-conceived people in maintaining a relatively small number of siblings/children. It is also there to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related.

3.27. We proposed that the 10 family limit should also apply to women donating their mitochondria. The reasons for the limit, referred to above, do not apply in the case of mitochondrial donation, but we nevertheless felt that the limit should apply in order to keep the number of offspring from one donor low to mitigate against the impact of one of those donors later being found to have a transmissible disease or condition.

3.28. However, stakeholders argued that the risk of a donor transmitting a disease or condition to the child is very low because mitochondrial donors do not donate their nuclear genetic material and will have undergone genetic screening for pathogenic mitochondrial DNA mutations. This, coupled with the fact that the main reasons for the limit do not apply to mitochondrial donation, means that we propose introducing guidance (paragraph 33.27) that the family limit will not apply to those who only donate their mitochondria and those sperm donor's who's gametes are used to produce embryos with donor eggs in PNT (and are thus not genetically related to the child).

Compensating donors

3.29. Under the current system of donor compensation, clinics can compensate egg donors a fixed sum of up to £750 per cycle of donation and compensate sperm donors a fixed sum of up to £35 per clinic visit. Paragraph 16 in General Directions 0001 (at annex four) will specify that the system for compensating people providing eggs or sperm for mitochondrial donation should be consistent with that of gamete and embryo donation. People donating for the purposes of PNT and/or MST will be required to undergo the same process for providing

their sperm or eggs as egg or sperm donors. For the same reason, the current benefits in kind system for egg and sperm donors should equally apply.

Import of eggs or embryos which have undergone mitochondrial donation

3.30. New mandatory requirements set out in box 33C explain the statutory provisions which prohibit UK clinics from importing eggs or embryos for treatment in the UK which have undergone MST or PNT abroad. Eggs or embryos which been created abroad using either MST or PNT do not fall within the statutory definition of 'permitted' because they will not have been created within the circumstances prescribed by the Regulations.

3.31. A clinic is prohibited by Section 3 of the 1990 Act from using eggs or embryos unless they fall within the definition of permitted. There is no statutory power for the Authority to retrospectively authorise the use of PNT or MST. Consequently, the new guidance reflects the fact that, even if it were lawful to import eggs or embryos created abroad using PNT or MST, there would be little point in doing so because the use of the material in the UK would not be lawful. This has been highlighted in the import and export guidance note.

3.32. In relation to the import of eggs, embryos or sperm for use in treatment involving mitochondrial donation (ie, where PNT or MST using the donor gametes takes place in the UK), the Regulations do not prevent this. However, as with any other import, clinics need to ensure that there is compliance with the requirements for information provision, screening and consent etc., specific to mitochondrial donation.

Follow-up of children born following mitochondrial donation

3.33. Clinics offering mitochondrial donation must have a documented process for monitoring children born following mitochondrial donation, including long-term medical follow-up, where patients have consented. New guidance (at paragraph 33.34) proposes that clinics should explain to patients the benefits of participating in follow-up. The majority of stakeholders agreed that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but that this should not be mandatory. There is no legal power to mandate follow-up studies.

3.34. Proposed guidance (at 33.33) also states that clinics should establish links with mitochondrial disease clinics to facilitate follow-up. If the patient is not a UK resident, the clinic should decide whether to establish links with either a mitochondrial disease clinic based in the UK or an overseas clinic. Plans for follow-up must be submitted with a clinic's application to vary its licence to perform mitochondrial donation as stated in Direction 0008 (paragraph 7(iiv)) at annex four.

3.35. Proposed guidance (paragraph 33.35) states that if a clinic becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or other adverse outcome (such as a miscarriage), the clinic must regard this as an adverse

incident and report this in line with the requirements on adverse incidents set out in guidance note 27. This is to capture information about any abnormalities that may occur as a result of carrying out the MST or PNT treatment.

Recommendation

3.36. The Authority is asked to approve the proposed approach for clinics running a good quality service, including the:

- Registration process, as set out in General Directions 0005 - Collecting and recording information for the HFEA (at annex four).
- The proposed approach to obtaining consent set out at paragraphs 3.4-3.9 above, guidance within the new Mitochondrial donation guidance note, paragraphs 33.28-33.32 (at annex three) and the General Directions 0007 - Consent (at annex four).
- Staff to be involved in mitochondrial donation, as set out in the Mitochondrial donation guidance note, paragraphs 33.1 to 33.11 (at annex three).
- Provision of counselling and information, as set out in the Mitochondrial donation guidance note, paragraphs 33.12 to 33.22 (at annex three).
- Mitochondrial donor screening, as set out in the Mitochondrial donation guidance note, 33B Mandatory requirements box and paragraphs 33.23-33.25 (at annex three).
- Age limit for mitochondrial donors, as set out in the Mitochondrial donation guidance note, paragraph 33.26 (at annex three).
- The 10 family limit, as set out in the Mitochondrial donation guidance note, paragraph 33.27 (at annex three).
- Compensating donors, as set out in General Directions 0001 - Gamete and Embryo donation (at annex four).
- Import of eggs or embryos which have undergone mitochondrial donation, as set out in the Mitochondrial donation guidance note, mandatory requirements set out in box 33C (at annex three).
- Follow-up of children born following mitochondrial donation, as set out in the Mitochondrial donation guidance note, paragraphs 33.33-33.35 (at annex three).

3.37. The Authority is also asked to consider whether to allow certain non-identifying information about the mitochondrial donor to be accessed by patients and/or parents of children born following mitochondrial donation prior to the child reaching the age of 16. This decision will affect the Mitochondrial donation guidance at paragraphs 33.28-29 (at annex three).

4. What to do after treatment

4.1. Following treatment clinics must ensure that they continue to comply with their obligations under this new regulatory framework.

Submitting outcome of treatment

4.2. The same data submission requirements that apply to other treatment outcomes will also apply to mitochondrial donation treatments. This involves informing the HFEA of the outcome of treatment 14 weeks after the treatment cycle completion date and the outcome of any pregnancy where there is foetal pulsation.

Follow-up reporting

4.3. As mentioned above in 3.33, clinics will be required to have in place a documented process for monitoring children born following mitochondrial donation, where patients have consented to follow-up. In addition clinics should submit an annual report on patient uptake of follow-up studies and (non-patient specific) information on the outcomes. These requirements are outlined in General Directions 0005 (at annex four) and the Mitochondrial donation follow-up information sheet that must be submitted for your information (at annex five).

Export of eggs or embryos which have undergone mitochondrial donation

4.4. The Regulations do not prevent post MST or PNT eggs or embryos (created following authorisation by the Authority) from being exported. The Authority's current policy is that within the UK, only clinics licensed to undertake mitochondrial donation are permitted to also use those eggs or embryos in treatment once PNT or MST is completed. General Directions 0006 currently require a receiving clinic abroad to be licensed, authorised, accredited or designated before a UK clinic can export to it (a requirement arising from EU legislation). However, they do not require the clinic abroad to be specifically accredited to do mitochondrial donation nor its embryologists to be accredited to undertake the two processes.

4.5. It is therefore possible that post MST or PNT eggs or embryos could be exported to a clinic with little or no experience of treatment involving mitochondrial donation and with overseas clinics there would be no mechanisms in place to follow up any child born following mitochondrial donation treatment. We propose that the Authority agrees, in principle, that clinics should not export post MST or PNT eggs or embryos under general directions.

4.6. Pending legal advice, we think that it will be possible to include specific requirements in General Directions 0006 to reflect the need for clinics abroad to have equivalent expertise and mechanisms in place – either by an addition to requirements for general directions or by requiring clinics wishing to export to apply for special directions. If the Authority agrees with this approach, we will amend General Directions 0006 – Imports and exports and invite the Authority to delegate the approval thereof to the sub-group of members that will also be approving the final version of General Directions 0008.

Record keeping

4.7. Additions have been made to the General Directions 0012 to require licensed clinics to retain copies of the 'Mitochondrial donation follow-up information sheets' for a period of at least 30 years from the date on which any gametes or embryos were used in treatment.

Recommendation

4.8. The Authority is asked to approve the proposed approach to what clinics must do following treatment, including follow-up reporting and record-keeping:

- General Directions 0005 - Collecting and recording information for the HFEA on outcome reporting and the 'Other submissions' section (at annex four).
- General Directions 0012 - Retention of records, at paragraph 1(k) (at annex four).

4.9. The Authority is also asked to approve the proposed approach to the export of eggs or embryos following mitochondrial donation at paragraphs 4.4-4.6 of the paper.

5. Consequential amendments to the Code of Practice

5.1. Consequential changes following the introduction of the new Regulations have been made to existing guidance in the Code of Practice (see separate document). These changes are not substantial but are required to ensure accuracy across the Code of Practice.

Recommendation

5.2. The Authority is asked to approve the consequential changes following the introduction of mitochondrial donation.

6. Implementation

6.1. On the 29 October we will issue a Clinic Focus article and Chair's letter setting out the final processes, systems and guidance for regulating mitochondrial donation. All forms and guidance will be published on the HFEA website.

6.2. At the same time we will publish patient information on our website with information for those who may be interested in finding out more about the treatment, the approval process and the first steps that should be taken.

Human Fertilisation & Embryology Authority

Annex 1: Regulating mitochondrial donation: stakeholder feedback report

1. Introduction

1.1. In February 2015 Parliament approved The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 to permit the use of maternal spindle transfer (MST) and pronuclear transfer (PNT) to avoid serious mitochondrial disease. The regulations will come into force on 29 October 2015.

1.2. Since Parliament approved the regulations we have been designing a regulatory system to develop a robust framework for licensing mitochondrial donation. As part of this process we have sought expert stakeholder views on a number of our draft processes and guidance, which were set out in the 'Regulating mitochondrial donation: seeking expert views. Background document'

1.3. This report summarises stakeholder feedback on the:

- Clinic licensing process and how to demonstrate competency
- Patient approval process for mitochondrial donation
- Eligibility criteria for mitochondrial donors
- Process by which the HFEA will collect information about mitochondrial donation
- Information patients undergoing mitochondrial donation and mitochondrial donors need
- Follow-up process for clinics carrying our mitochondrial donation.

2. Methodology

2.1. We sought stakeholder views throughout June 2015, on some of the operational aspects of regulation through an online survey and a workshop held in Central London.

2.2. The workshop was attended by 30 stakeholders and we received 28 completed responses to the online survey. Both the workshop and the survey attracted contributions from a broad spectrum of stakeholders, including but not limited to staff from HFEA licensed clinics and mitochondrial disease centres, experts in mitochondrial genetics and inheritance, and patient groups and charities.

3. The clinic licensing process and how to demonstrate competency

3.1. Before an HFEA-licensed clinic can undertake treatments using mitochondrial donation, they will need to apply to the HFEA to vary their licence to include the 'express provision' required by the regulations, which will allow clinics to carry out the techniques. As part of this process the competency of the proposed embryologist to perform mitochondrial donation will need to be assessed.

3.2. We asked stakeholders to consider the appropriateness of the proposed approach for assessing the competency of a clinical embryologist to perform mitochondrial donation techniques. The proposal suggested that clinics should submit evidence of the clinical embryologist having experience in performing micro-manipulation on human or animal (eg, mice) eggs or embryos, performing MST and PNT techniques in treatment, training or research and also submission of supporting references of the embryologist's knowledge and experience. In addition stakeholders were asked if they had suggestions for alternative or additional evidence that could demonstrate the competency of a clinical embryologist intending to perform one or both of the recognised techniques

Stakeholder views

3.3. In general stakeholders thought that due to the highly specialised techniques it was essential for a clinical embryologist to have previously carried out PNT and MST on human gametes and embryos (either under a research licence or from overseas experience) before carrying out the technique in clinical treatment.

3.4. Encouraging clinics to first obtain a research licence prior to applying to varying a treatment licence was seen as advantageous for the scientific community at large, as this would encourage a greater number of clinics to independently reproduce published data. An opportunity to replicate and adapt previous research was seen as a chance to improve knowledge and methodologies based on published results.

3.5. Aside from an embryologist demonstrating an ability to carry out the technique using human embryos, there was a broad consensus of what would evidence competency. A competent practitioner would demonstrate a low carryover of mitochondria from the patient's egg or embryo comparable with published results and obtain good quality blastocysts. However, it is not known how blastocyst quality could be evaluated, some suggested considerations of morphology or gene expression could be taken into account.

3.6. Onward monitoring of competency assessments for the clinical embryologist was seen as paramount. Suggestions of monitoring competency included assessing against key performance indicators (KPIs) derived from published literature regarding safety and efficacy as well as advice from practicing/publishing research centres. It was suggested that the competency frameworks should recognise competencies of embryologists who had been trained overseas.

3.7. Some stakeholders thought that it would be unnecessary for the HFEA to conduct an onsite inspection for every licence variation, but instead suggested that it would be desirable for the HFEA to conduct an onsite inspection if there is a belief it is necessary (e.g. change in the premises or lab used) on a case by case basis. Others thought onsite inspections were necessary due to the novel nature of PNT and MST.

3.8. A few stakeholders highlighted the importance of providing genetic counselling for women undergoing mitochondrial donation treatment. However, there were mixed views on competency requirements for counsellors. Some thought that it is important to have counsellors who are associated with a mitochondrial diagnostic service with considerable experience of genetic counselling, whilst others thought counsellors competent for fertility counselling would have appropriate skills to counsel mitochondrial donation patients. One stakeholder said that: *"Linkage to a mitochondrial diagnostic service with substantial experience of genetic counselling for mitochondrial disease is essential until experience is gained and standard operating procedures fully established and success rates known."- Clinical lead of the Oxford mitochondrial genetics service.*

Summary

- Clinical embryologists should have previously carried out PNT and MST on human gametes and embryos before carrying out the technique in clinical treatment. Key performance indicators (KPIs) and performance metrics for clinical embryologists performing mitochondrial donation should be developed.
- Patients should have access to a genetic counselling service to explore their treatment options, including alternative options to MST and PNT. Mixed views on different competency requirements for counsellors seeing people affected by mitochondrial disease.

4. The patient approval process for mitochondrial donation

4.1. Stakeholders were asked to firstly consider the proposed approach for assessing the particular risk of a patient passing on abnormal mitochondria to their embryos. Secondly stakeholders were asked to consider how we should assess significant risk and seriousness, including whether the draft application form allows for the capture of all the information that would be necessary for the HFEA to make this assessment.

Stakeholder views

4.2. Generally, stakeholders agreed with the proposed approach for assessing the 'particular' risk by reference to the presence of mutant mitochondria. Some stakeholders thought the assessment should be 'stricter' as women with lower mitochondria load may not be affected. However, others were of the view that women with lower mutant mitochondria load were still at risk of having an affected embryo. One stakeholder said that: *"If a women goes forward for this technique she should have evidence to say her mitochondrial DNA is effected - any level should make her suitable for the technique." - The Lily Foundation.*

4.3. Some stakeholders thought the current process used by the HFEA to peer review applications from clinics wishing to carry out preimplantation genetic diagnosis (PGD) for a new condition, should be used as a model in the assessment of particular risk. Others were concerned that the proposal for each application to be peer reviewed may delay decisions on cases.

Stakeholders thought that the HFEA Statutory Approvals Committee should have some guidance in determining seriousness as this would be important for consistency.

4.4. The majority of stakeholders agreed that the proposed process took into account all aspects relevant to the risk of, and seriousness, of the disease as well as mitochondria disease biology. However, a few emphasised that we should be flexible to account for rare or unknown mitochondrial diseases and suggested allowing room for other evidence to be submitted. One stakeholder stated that "…*mutation threshold is much more difficult to assess and may vary between different families. Often family trees are small and thus being precise about the threshold is NOT possible. Even for relatively common mtDNA mutations the threshold causing disease can be challenging with differences between different families. For rarer mutations where there is less information this will be even more challenging" – Newcastle Fertility Centre.*

4.5. Stakeholders had mixed views on using published literature to help assess seriousness. Some highlighted that existing literature would be important (both as evidence for the application and to aid putting the patient case into context), but others thought that this would be difficult where the literature on a patient's condition was inadequate. Some had significant reservations about assessing seriousness based on the worst possible symptoms for a given mutation. This is because many mutations have significant variability in their symptoms, with some manifesting very severe symptoms but only rarely. Therefore an application could put down symptoms that are very unlikely to be seen. However, it was pointed out that while these worst case symptoms might be rare it is still possible and would have serious consequences for this resulting child.

4.6. Some suggested that assessment of seriousness is subjective and different for each family. Patient views and familial risk should be taken into account through an impact statement of the disease and this should be presented by geneticists with experience in mitochondrial disease. One stakeholder said *"It is important that the patient perspective of choice is also considered following appropriate implications discussions."- The British Fertility Society.*

4.7. A small number of stakeholders expressed a desire to only allow mitochondrial donation treatment to women who had previously undergone unsuccessful preimplantation genetic diagnosis (PGD). Others reasoned that having PGD as a pre-requisite could potentially undermine the very purpose of PNT and MST. One group of stakeholders stated that *"mitochondrial donation has the potential to be used for women whose eggs contain very high levels of, or exclusively, mitochondrial DNA mutation, which are not suitable for PGD. Mitochondrial donation is likely to be a safer option than PGD when levels of mitochondrial DNA mutation are borderline, both for the child born, but particularly for subsequent generations if the child is female. " - The Association of Medical Research Charities, The Academy of Medical Sciences, Medical Research Council, Wellcome Trust and The Royal Society.*

4.8. Stakeholders suggested that it may be preferable in some circumstances for PGD to be offered as an option to patients but should not be made a pre-requisite.

Summary

- Stakeholders broadly agreed on the proposed approach to the patient approval process, which will involve take into account all aspects relevant to the risk of, and seriousness, of the disease as well as mitochondria disease biology of assessing particular risk.

5. The eligibility criteria for mitochondrial donors

5.1. Mitochondrial donors will provide their eggs in the same way as egg donors for fertility treatment (the same will apply to men who provide sperm for mitochondrial donation). As their eggs will be collected and used to create embryos, the risk of infectious diseases being transmitted is likely to be the same. For this reason we proposed that most of the same requirements for laboratory tests and storage in relation to sperm and egg donors should apply to mitochondrial donors, except for genetic screening and assessment of mitochondrial donors' medical history.

5.2. We also examined the extent to which mitochondrial donor recruitment is comparable to egg donor recruitment for fertility treatment. In particular we focused on whether the existing age limit for egg donors (36 and under, unless there are exceptional circumstances) should also apply to mitochondrial donors and if the ten family limit should also apply to mitochondrial donors.

5.3. Another specific issue we considered is whether clinics should attempt to match the haplogroup/haplotype of the mitochondria donor with that of the patient undergoing treatment. Some scientists have suggested that if the patient and the mitochondria donor have different mitochondrial haplotypes, there is a theoretical risk that the donor's mitochondria won't be able to 'communicate' properly with the patient's nuclear DNA, which could cause problems in the embryo and resulting child. We asked stakeholders whether consideration should be given to mitochondria haplotype matching in the process of selecting donors and how this might affect the availability of donors.

Stakeholder views

5.4. The majority of stakeholders favoured mitochondrial donors being screened in the same way as egg donors with the addition of next generation sequencing of the donors' mitochondrial genome. In addition, some suggested screening the mitochondria DNA from blood or urine samples to detect levels of abnormal mitochondria DNA and determine risk. Some also thought that consideration should be given to heteroplasmy levels of common pathogenic mutations in the blood as they may not always be linked to phenotypes.

5.5. There were mixed views on the value of applying the same age limit of 36 for women donating their mitochondria. Stakeholders recognised that mitochondrial mutations accumulate over time and may therefore indirectly affect the quality of eggs; however they acknowledged the lack of evidence in this area. Some thought that the age limit was too restrictive and suggested instead a broader assessment of a donor's reproductive health (for example, their ovarian reserve) could be more useful to determine the eligibility of a mitochondria donor. It was suggested that any age limit should be justified and regularly reviewed in light of any new evidence.

5.6. Similarly, stakeholders had mixed views on the proposed approach to applying the ten family limit for gamete donors to women donating their mitochondria. The family limit is based on the perceived social and psychological interests of donors and donor-conceived people in maintaining a relatively small number of siblings/children. It is also to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related. It could be argued that the reasons for setting the limit at ten do not apply in the same way to children born from mitochondrial donation.

5.7. The majority of stakeholders agreed that this rationale for the ten family limit for gamete donors does not apply in the same way for mitochondria donors. One group of stakeholders said that: *"Although mitochondria donors will ostensibly undergo the same process as gamete donors, namely egg retrieval, the purpose and genetic relatedness is very different. Directly transposing provisions from one technology to another may bring unnecessary restrictions, and could also risk that unique considerations for licensing mitochondrial donation could be overlooked".* *- The Association of Medical Research Charities, The Academy of Medical Sciences, Medical Research Council, Wellcome Trust and The Royal Society.*

5.8. Some stakeholders however did agree with the proposed rationale for having a family limit to limit inadvertent disease transmission from a donor who has a previously undetected genetic condition. Others thought it was not relevant for mitochondrial donors as the mitochondrial genome would be screened to detect most diseases. Some stakeholders also suggested that in order to protect the health of donors there should be a limit on the number of egg collection cycles they could undergo.

5.9. The majority of stakeholders agreed with the proposed approach of encouraging clinics to keep a watching brief on emerging evidence concerning haplogroup matching and for clinics to consider haplogroup matching were appropriate, as some studies with inbred laboratory animals have shown some mild adverse health effects associated with mitochondrial donation between divergent mtDNA backgrounds**.** Given the lack of current evidence to support haplotype matching, most thought this should not be a requirement and were concerned that if it was this would add unnecessary delays to treatment, especially for ethnic minority patients who could potentially have more rare haplotypes.

Summary

- Stakeholders recommended mitochondrial genome sequencing for prospective mitochondria donors. Genetic testing for nuclear based conditions is not necessary and it would only be necessary to take maternal family medical history.
- Stakeholders had mixed views on applying the same age limit and family limit for egg donors to mitochondrial donors. It was agreed that any limit applied needs to be scientifically justified.
- Most stakeholders thought clinics should be responsible for monitoring emerging evidence on haplogroup matching.

6. The process by which the HFEA will collect information about mitochondrial donation

6.1. The HFE Act 1990 (as amended) requires UK licensed clinics to submit information to the HFEA on their patients, donors, treatments and outcomes. These data are collected via electronic forms and are held on the HFEA Register. We collect information on each patient (the woman who is treated), their partner (if there is one), all donors and every licenced treatment and its outcome.

6.2. The HFEA will collect different information about mitochondrial donation because the regulations that apply, particularly to disclosure of information, are different. For example, mitochondria donor-conceived people will not be able to access information that could identify the mitochondrial donor. Instead, they will be able to access non-identifying information from HFEA register at the age of 16. Mitochondrial donors will also be able to find out how many children have been born using their eggs, their sex and year of birth.

6.3. We asked stakeholders to consider how the HFEA could collect information about mitochondrial donors. We also asked if there should be any differences in the information we require from mitochondrial donors as compared to information requirements from egg donors as well as entitlement to accessing this information. A proposed mitochondrial donor registration form was also considered at the workshop.

Stakeholder views

6.4. Some stakeholders emphasised that only necessary information that will be useful to mitochondrial donor-conceived people should be collected about a donor's family history in accordance to data protection laws. Some thought that following 'standard' donation, parents generally show greater interest in a donor's medical history, whereas the children are more interested in the donor's personal information.

6.5. Stakeholders fed back their views on the draft mitochondrial donor registration form. Some thought that the form should have separate sections for medical history relating to their mitochondria and a general medical history section.

Stakeholders also agreed that both the clinic and the donor should complete the form together.

7. The information patients undergoing mitochondrial donation and mitochondrial donors need

7.1. Before clinics obtain consent we propose that they should i) provide patients with information about the potential risks of mitochondrial donation, the importance of follow-up studies and ii) encourage patients to be open with any resulting children regarding their conception. We propose that donors should be provided with information in accordance to best practice guidelines which apply to sperm and egg donors as well as information regarding unsuspected heritable conditions. This would mean that if a clinic learns, through the birth of an affected child, that a mitochondria donor carries a previously unsuspected mitochondrial disease, the donor should be notified (if they have indicated that they wish to be notified).

7.2. We asked stakeholders to explore the extent to which information provided to patients receiving treatment involving mitochondrial donation, and to mitochondrial donors, should mimic or differ that given to those undergoing fertility treatment/gamete donation. We examined what specific information clinics should provide and collect at what stage, and also guidance that should be offered to clinics about how to discuss with parents the best methods of informing children about their origins.

Stakeholder views

7.3. The majority of stakeholders stated that patients should be provided with information on risks of treatment. One stakeholder said that patients should be given *"information about the potential risks of mitochondrial donation, appropriate alternatives, the importance of follow-up studies and encouraging openness with any resulting children" - Newcastle Fertility Centre*

7.4. One stakeholder thought it would be logical to ask patients to confirm that they have been advised by experts in mitochondrial disease on the procedure and any associated risks after visiting a clinic. This guidance could be revised after five years if mitochondrial donation proves to be safe and effective in practice.

7.5. Stakeholders were in general agreement that it would be reasonable for clinics to provide patients with information to inform their child about circumstances of their conception whilst they are still young. This would be of particular benefit for families participating in routine follow up after they have received treatment involving mitochondrial donation. Stakeholders reasoned that any child who grows up experiencing frequent interactions with healthcare professionals, as part of clinical follow-up and research, would be able to have a greater understanding of their experiences as a child, and in the longer term the child may be more willing to consent to continue participation in follow up as an adult.

7.6. In terms of information provided to the mitochondrial donor, some stakeholders emphasised the importance of explaining the legal position of the mitochondrial donor. The information should explain that donors are not identifiable to recipients or to anyone conceived via their donation and donating mitochondria does not make the donor legally or financially responsible for the resulting child.

Summary

- The majority of stakeholders agreed that mitochondrial donors and patients receiving treatment involving mitochondrial donation should be given similar information as those donating/receiving eggs, sperm or embryos for fertility treatment.
- In particular, they should receive information about the risks, any follow up processes and success rates before they give consent to treatment. Some also thought that mitochondrial donors should receive information on their legal status and relationship to donor conceived child.

8. The follow-up process for clinics carrying out mitochondrial donation

8.1. The HFEA proposes that clinics should have in place a documented process for monitoring children born following mitochondrial donation, where patients have consented to follow-up. We propose introducing guidance that clinics should encourage their patients to take part in follow-up studies, whilst also acknowledging the rights of patients and their children not to participate in such studies. The topic examined here was how to encourage patients to take part in the clinical follow-up of children born following mitochondrial donation. Proposals included requiring clinics to submit a documented process for monitoring children born following mitochondrial donation (and any future changes to this process) and annual reports to the HFEA.

Stakeholder views

8.2. Stakeholders acknowledged that clinical follow up of children born following mitochondrial donation was important and distinct from broader medical or social research that may take place in the future, for example from researchers accessing data from the HEFA Register. There was consensus that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but consent should be freely given. A small number of stakeholders felt that follow-up should be mandatory and legally binding at least until the donor conceived child is sixteen years old.

8.3. Some stakeholders stated that follow-up should be made easy for patients and resulting children to encourage continued participation. The majority of stakeholders thought that children should not feel medicalised by the process. They felt it would be important for children to be told they were born following mitochondrial donation so they can decide whether or not to continue to consent to follow up in adult years.

One stakeholder said that*: "we must be careful not to be overbearing on this subject - the whole reason for this is to have a "normal child" any parent involved will want protect their very wanted child and ensure that they are ok but not to the point where they feel like an experiment - I cannot imagine any family not wanting follow up" – The Lily Foundation*

8.4. Stakeholders felt that follow-up, where possible, should be done locally via GPs and Health Visitors and trips to clinics kept to a minimum. They felt it would be essential for GPs and clinics to work together closely. Stakeholders had mixed views on the frequency of check-ups made during follow-up. Some recommended annual assessments of physical health and mental health were appropriate; other stakeholders recommended check-ups at certain ages of the child's life. One stakeholder highlighted that the NHS already has established facilities and procedures to allow for appropriate follow-up care during and after pregnancy for women who carry certain mitochondrial DNA mutations.

8.5. Most stakeholders agreed that clinics should make arrangements with mitochondrial disease centres. One stakeholder said that: *"…whilst there is an emphasis on licenced centres to ensure that appropriate follow up is available this should be provided by specialist paediatric mitochondrial services to an agreed program. The BFS believes this process should be established through specialist services with a consideration to long term follow-up." – The British Fertility Society*.

8.6. Some also highlighted that submitting follow-up plans to the HFEA could help standardise the quality of information collected by clinics and help standardise provision of information.

Summary

- The majority of stakeholders agreed that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but that this should not be mandatory.
- Mixed responses on how frequently the check-ups should take place for consenting families.
- Most agreed that clinics should make arrangements with mitochondrial disease centres to carry out follow-up and some stakeholders agreed that these plans should be submitted to the HFEA in an annual update report.

Annex 2: Summary of Standing Orders changes

3. The Statutory Approvals Committee

Purpose of the committee

3.1 The purpose of the Statutory Approvals Committee is to keep under review and to authorise the use of embryo testing; to authorise the use of mitochondrial donation treatment; to issue Special Directions for the import/export of gametes; and to authorise the use of novel processes in licensed activities.

Delegated powers and functions of the Statutory Approvals Committee

3.2 The Authority delegates to the Statutory Approvals Committee the following powers:

a) the authorisation of the use of embryo testing for conditions not previously authorised by the Authority (under Schedule 2, paragraph 1ZA(1)(a), (b) and (c) of the Act)

b) the authorisation of the use of embryo testing to establish whether the tissue of any resulting child would be compatible with that of a sibling that suffers from a serious medical condition (under Schedule 2, paragraph 1ZA(1)(d)

c) the authorisation of the use of embryo testing to establish whether an embryo is one of those whose creation was brought about by using the gametes of a particular person (under Schedule 2, paragraph 1ZA(1)(e)

d) the authorisation of the use of maternal spindle transfer (MST) and/or pronuclear transfer (PNT) for a named patient (under The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015)

e) the issuing of Special Directions for the import/export of gametes or embryos (under section 24 of the Act), and

f) the authorisation of the use of novel processes in licensed activities.

3.3 The functions of the Statutory Approvals Committee shall include:

a) keeping under review the genetic conditions authorised by the Authority for embryo testing.

Membership of the Statutory Approvals Committee

3.4 The Statutory Approvals Committee shall consist of no more than six members, which shall include:

a) a Committee Chair (who shall be a lay Authority member)

b) a Deputy Committee Chair (who shall be a lay Authority member);

c) up to four other Authority members.

3.5 The Chair of the HFEA shall appoint the members of the Statutory Approvals Committee.

3.6 Members of the Statutory Approvals Committee shall usually be appointed for a term of three years.

Meetings of the Statutory Approvals Committee

3.7 The quorum for a meeting of the Statutory Approvals Committee shall be three including the Committee Chair or Deputy Committee Chair and two other members.

3.8 The Statutory Approvals Committee shall usually meet 12 times per year. At the discretion of the Chair, the committee may meet additionally at short notice (and, if necessary, by telephone- or video-conference) if the Chair considers there is an item (or items) which cannot be delayed until the next meeting.

3.9 No member of the Statutory Approvals Committee present at a meeting shall abstain from voting.

3.10 Decisions of the Statutory Approvals Committee to authorise embryo testing or novel processes, or to issue Special Directions, require a simple majority (and in the event of a tie, the Committee Chair shall have a casting vote).

Attendance at meetings of the Statutory Approvals Committee

3.11 In addition to members of the Statutory Approvals Committee, the following persons shall usually attend its meetings:

a) a legal adviser

b) a specialist adviser

a) the Head of Governance and Licensing

b) the Committee Secretary.

3.12 The Committee Chair may invite such other persons (including employees) as he/she considers appropriate, to attend the meetings of the Statutory Approvals Committee and/or to provide advice to inform the deliberations of the Statutory Approvals Committee.

3.13 The Committee Chair may determine when and whether it is necessary or desirable for any non-members of the committee to withdraw from the meeting to enable the committee to deliberate in private.

Human Fertilisation & Embryology Authority

Annex 3: Draft Mitochondrial donation Code of Practice guidance note

33. Mitochondrial donation

Version 1.0

On this page:

Mandatory requirements

Human Fertilisation and Embryology (HFE) Act 1990 (as amended)

Amended section 31ZA Request for information as to genetic parentage or mitochondrial donors etc

(1) A person who has attained the age of 16 ("the applicant") may by notice to the Authority require the Authority to comply with a request under subsection (2) or (2A).

(2) The applicant may request the Authority to give the applicant notice stating whether or not the information contained in the register shows that a person ("the donor") other than a parent of the applicant would or might, but for the relevant statutory provisions, be the parent of the applicant, and if it does show that—

(a) giving the applicant so much of that information as relates to the donor as the Authority is required by regulations to give (but no other information), or

(b) stating whether or not that information shows that there are other persons of whom the donor is not the parent but would or might, but for the relevant statutory provisions, be the parent and if so—

(i) the number of those other persons,

(ii) the sex of each of them, and

(iii) the year of birth of each of them.

(2A) The applicant may request the Authority to give the applicant notice stating whether or not the information contained in the register shows that a person is the applicant's mitochondrial donor, and if it does show that, giving the applicant the following information contained in the register —

(a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history,

(b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and

(c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section,

but not giving any information which may identify the mitochondrial donor or any person who was or may have been born in consequence of treatment services using genetic material from the applicant's mitochondrial donor, by itself or in combination with any other information which is in, or is likely to come into, the possession of the applicant.

(3) The Authority shall comply with a request under subsection (2) if—

(a) the information contained in the register shows that the applicant is a relevant individual, and

(b) the applicant has been given a suitable opportunity to receive proper counselling about the implications of compliance with the request.

(3A) The Authority must comply with a request under subsection (2A) if—

(a) the information contained in the register shows that the applicant is a mitochondrial donor-conceived person, and

(b) the applicant has been given a suitable opportunity to receive proper counselling about the implications of compliance with the request.

(4) Where a request is made under subsection (2)(a) and the applicant has not attained the age of 18 when the applicant gives notice to the Authority under subsection (1), regulations cannot require the Authority to give the applicant any information which identifies the donor.

(5) Regulations under subsection (2)(a) cannot require the Authority to give any information as to the identity of a person whose gametes have been used or from whom an embryo has been taken if a person to whom a licence applied was provided with the information at a time when the Authority could not have been required to give information of the kind in question.

(6) The Authority need not comply with a request made under subsection (2)(b) by any applicant if it considers that special circumstances exist which increase the likelihood that compliance with the request would enable the applicant—

(a) to identify the donor, in a case where the Authority is not required by regulations under subsection (2)(a) to give the applicant information which identifies the donor, or

(b) to identify any person about whom information is given under subsection (2)(b).

(7) In this section—

"relevant individual" has the same meaning as in section 31;

"the relevant statutory provisions" means sections 27 to 29 of this Act and sections 33 to 47 of the Human Fertilisation and Embryology Act 2008.

(8) In this section and sections 31ZB to 31ZE—

"mitochondrial donor-conceived person" means a person who was or may have been born in consequence of treatment services using—

(a) an egg which is a permitted egg for the purposes of section 3(2) by virtue of regulations under section 3ZA(5), or

(b) an embryo which is a permitted embryo for those purposes by virtue of such regulations;

the "mitochondrial donor" in respect of a person who was or may have been born in consequence of treatment services using such a permitted egg or such a permitted embryo is the person whose mitochondrial DNA (but not nuclear DNA) was used to create that egg or embryo.

Amended section 31ZD Provision to donor of information about resulting children

(1) This section applies where a person ("the donor") has consented under Schedule 3 (whether before or after the coming into force of this section) to—

(a) the use of the donor's gametes, or an embryo the creation of which was brought about using the donor's gametes, for the purposes of treatment services provided under a licence, or

(b) the use of the donor's gametes for the purposes of non-medical fertility services provided under a licence.

(2) In subsection (1)—

(a) "treatment services" do not include treatment services provided to the donor, or to the donor and another person together, and

(b) "non-medical fertility services" do not include any services involving partner-donated sperm.

(3) The donor may by notice request the appropriate person to give the donor notice stating—

(a) the number of persons of whom the donor is not a parent but would or might, but for the relevant statutory provisions, be a parent by virtue of the use of the gametes or embryos to which the consent relates,

(ab) the number of persons in respect of whom the donor is a mitochondrial donor,

(b) the sex of each of those persons, and

(c) the year of birth of each of those persons.

(4) Subject to subsections (5) to (7), the appropriate person shall notify the donor whether the appropriate person holds the information mentioned in subsection (3) and, if the appropriate person does so, shall comply with the request.

(5) The appropriate person need not comply with a request under subsection (3) if the appropriate person considers that special circumstances exist which increase the likelihood that compliance with the request would enable the donor to identify the persons falling within paragraphs (a) to (c) of subsection (3).

(6) In the case of a donor who consented as described in subsection (1)(a), the Authority need not comply with a request made to it under subsection (3) where the person who held the licence referred to in subsection (1)(a) continues to hold a licence under paragraph 1 of Schedule 2, unless the donor has previously made a request under subsection (3) to the person responsible and the person responsible—

(a) has notified the donor that the information concerned is not held, or

(b) has failed to comply with the request within a reasonable period.

(7) In the case of a donor who consented as described in subsection (1)(b), the Authority need not comply with a request made to it under subsection (3) where the person who held the licence referred to in subsection (1)(b) continues to hold a licence under paragraph 1A of Schedule 2, unless the donor has previously made a request under subsection (3) to the person responsible and the person responsible—

(a) has notified the donor that the information concerned is not held, or

(b) has failed to comply with the request within a reasonable period.

(8) In this section “the appropriate person” means—

(a) in the case of a donor who consented as described in paragraph (a) of subsection (1)—

(i) where the person who held the licence referred to in that paragraph continues to hold a licence under paragraph 1 of Schedule 2, the person responsible, or

(ii) the Authority, and

(b) in the case of a donor who consented as described in paragraph (b) of subsection (1)—

(i) where the person who held the licence referred to in that paragraph continues to hold a licence under paragraph 1A of Schedule 2, the person responsible, or

(ii) the Authority.

(9) In this section "the relevant statutory provisions" has the same meaning as in section 31ZA.

Amended paragraph 4 of Schedule 3

Variation and withdrawal of consent

(1) The terms of any consent under this Schedule may from time to time be varied, and the consent may be withdrawn, by notice given by the person who gave the consent to the person keeping the gametes, human cells, embryo or human admixed embryo to which the consent is relevant.

(1A) Sub-paragraph (1B) applies to a case where an egg is used in the process set out in regulation 4 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (and "egg A" and "egg B" have the same meanings in this paragraph as in that regulation).

(1B) The terms of the consent to that use of egg A or egg B cannot be varied, and such consent cannot be withdrawn, once all the nuclear DNA of egg B which is not polar body nuclear DNA is inserted into egg A.

(2) Subject to sub-paragraphs (3) to (3B), the terms of any consent to the use of any embryo cannot be varied, and such consent cannot be withdrawn, once the embryo has been used—
(a) in providing treatment services,
(aa) in training persons in embryo biopsy, embryo storage or other embryological techniques, or
(b) for the purposes of any project of research.

(3) Where the terms of any consent to the use of an embryo ("embryo A") include consent to the use of an embryo or human admixed embryo whose creation may be brought about in vitro using embryo A, that consent to the use of that subsequent embryo or human admixed embryo cannot be varied or withdrawn once embryo A has been used for one or more of the purposes mentioned in sub-paragraph (2)(a) or (b).

(3A) Sub-paragraph (3B) applies to a case where an embryo is used in the process set out in regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (and "embryo A" and "embryo B" have the same meanings in sub-paragraph (3B) as in that regulation).

(3B) The terms of the consent to that use of embryo A or embryo B cannot be varied, and such consent cannot be withdrawn, once all the nuclear DNA of embryo B which is not polar body nuclear DNA is inserted into embryo A.

(4) Subject to sub-paragraph (5), the terms of any consent to the use of any human admixed embryo cannot be varied, and such consent cannot be withdrawn, once the human admixed embryo has been used for the purposes of any project of research.

(5) Where the terms of any consent to the use of a human admixed embryo ("human admixed embryo A") include consent to the use of a human admixed embryo or embryo whose creation may be brought about in vitro using human admixed embryo A, that consent to the use of that subsequent human admixed embryo or embryo cannot be varied or withdrawn once human admixed embryo A has been used for the purposes of any project of research.

Definition of the mitochondrial donor eg, for consent and surrogacy purposes

Schedule 3 Amended paragraph 22

(A1) For the purposes of this Schedule, neither of the following is to be treated as a person whose gametes were used to create an embryo ("embryo E")—

(a) where embryo E is a permitted embryo by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of embryo E;
(b) where embryo E has been created by the fertilisation of an egg which was a permitted egg by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

(3B) For the purposes of this Schedule, in a case where an egg is a permitted egg by virtue of regulations under section 3ZA(5) the egg is not to be treated as the egg of the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

(1) In this Schedule references to human cells are to human cells which are not—
(a) cells of the female or male germ line, or
(b) cells of an embryo.

(2) References in this Schedule to an embryo or a human admixed embryo which was used to bring about the creation of an embryo ("embryo A") or a human admixed embryo ("human admixed embryo A") include an embryo or, as the case may be, a human admixed embryo which was used to bring about the creation of—
(a) an embryo or human admixed embryo which was used to bring about the creation of embryo A or human admixed embryo A, and
(b) the predecessor of that embryo or human admixed embryo mentioned in paragraph (a), and
(c) the predecessor of that predecessor, and so on.

(3) Reference in this Schedule to an embryo or a human admixed embryo whose creation may be brought about using an embryo or a human admixed embryo are to be read in accordance with sub-paragraph (2).

(4) Reference in this Schedule (however expressed) to the use of human cells to bring about the creation of an embryo or a human admixed embryo include the use of human cells to alter the embryo or, as the case may be, the human admixed embryo.

(5) References in this Schedule to parental responsibility are—
(a) in relation to England and Wales, to be read in accordance with the Children Act 1989,
(b) in relation to Northern Ireland, to be read in accordance with the Children (Northern Ireland) Order 1995, and
(c) in relation to Scotland, to be read as references to parental responsibilities and parental rights within the meaning of the Children (Scotland) Act 1995.

(6) References in this Schedule to capacity are, in relation to England and Wales, to be read in accordance with the Mental Capacity Act 2005.

(7) References in this Schedule to the age of 18 years are, in relation to Scotland, to be read as references to the age of 16 years.

Regulations

Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015

Permitted eggs and permitted embryos

Permitted egg
3. An egg ("egg P") is a permitted egg for the purposes of section 3(2)(b)(a) of the Act if—
(a) egg P results from the application of the process specified in regulation 4 to two eggs, each of which—
(i) is a permitted egg as defined in section 3ZA(2)(b) of the Act (not an egg which is a permitted egg by virtue of these regulations), and
(ii) was extracted from the ovaries of a different woman;
(b) that process has been applied to those eggs in the circumstances specified in regulation 5; and
(c) there have been no alterations in the nuclear or mitochondrial DNA of egg P since egg P was created by means of the application of that process.

Permitted egg: process
4.—(1) The process referred to in regulation 3(a) consists of the following two steps.
(2) In step 1—
(a) either—
(i) all the nuclear DNA of an egg ("egg A") is removed, or
(ii) all the nuclear DNA of egg A other than polar body nuclear DNA is removed; and
(b) either—
(i) all the nuclear DNA of another egg ("egg B") is removed, or
(ii) all the nuclear DNA of egg B other than polar body nuclear DNA is removed.
(3) In step 2 all the nuclear DNA of egg B which is not polar body nuclear DNA is inserted into egg A.

Permitted egg: circumstances
5. The circumstances referred to in regulation 3(b) are that—
(a) the Authority has issued a determination that—
(i) there is a particular risk that any egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA; and
(ii) there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease; and
(b) egg B was extracted from the ovaries of the woman so named.

Permitted embryo
6. An embryo ("embryo P") is a permitted embryo for the purposes of section 3(2)(a) of the Act if—
(a) embryo P results from the application of the process specified in regulation 7 to two embryos, each of which—
(i) is a permitted embryo as defined in section 3ZA(4) of the Act (not an embryo which is a permitted embryo by virtue of these regulations), and
(ii) was created by the fertilisation of a permitted egg as defined in section 3ZA(2) of the Act (not an egg which was a permitted egg by virtue of these regulations) extracted from the ovaries of a different woman;
(b) that process has been applied to those embryos in the circumstances specified in regulation 8; and
(c) since embryo P was created by means of the application of that process—
(i) there have been no alterations in the nuclear or mitochondrial DNA of any cell of embryo P, and
(ii) no cell has been added to embryo P other than by the division of embryo P's own cells.

Permitted embryo: process
7.—(1) The process referred to in regulation 6(a) consists of the following two steps.
(2) In step 1—
(a) either—
(i) all the nuclear DNA of an embryo ("embryo A") is removed, or

(ii) all the nuclear DNA of embryo A other than polar body nuclear DNA is removed; and

(b) either—

(i) all the nuclear DNA of another embryo ("embryo B") is removed, or

(ii) all the nuclear DNA of embryo B other than polar body nuclear DNA is removed.

(3) In step 2 all the nuclear DNA of embryo B which is not polar body nuclear DNA is inserted into embryo A.

Permitted embryo: circumstances

8. The circumstances referred to in regulation 6(b) are that—

(a) the Authority has issued a determination that—

(i) there is a particular risk that any embryo which is created by the fertilisation of an egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA; and

(ii) there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease; and

(b) embryo B was created by the fertilisation of an egg extracted from the ovaries of the woman so named.

Licence conditions

T124 a. No clinic may carry out either the process of pronuclear transfer* (PNT) or maternal spindle transfer* (MST) or part of either process, unless express provision has been made on the clinic's licence permitting it to undertake either or both processes.

b. Neither PNT nor MST may be carried out under third party, satellite or transport agreements.

c. No clinic may provide treatment using gametes or embryos which have been created using PNT or MST unless express provision has been made on the clinic's licence permitting the clinic to undertake either or both processes;

*Wherever reference is made in this licence to PNT or MST or the process of PNT or MST, that is the process defined in Regulation 4 or Regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

T125 PNT and MST must only be carried out on premises of clinics that are licensed to undertake mitochondrial donation ('MD'). These processes must not be carried out on the premises of a clinic that is operating under a third party, satellite or transport agreement with a clinic that holds a licence to undertake MD.

T127 a. No alterations may be made to the nuclear or mitochondrial DNA of an egg created by means of the application of MST.

b. No alterations may be made to the nuclear or mitochondrial DNA of an embryo created by means of the application of PNT and no cell may be added to an embryo created by means of the application of PNT other than by the division of the embryo's own cells.

T128 a. In the case of treatment involving mitochondrial donation the clinic must ensure that it only carries out the process of PNT or MST for a particular, named patient once the Authority has issued a determination that:

- there is a particular risk that any egg extracted from the ovaries of the named woman or any embryo created by the fertilisation of an egg extracted from the ovaries of the named woman may have mitochondrial abnormalities cause by mitochondrial DNA
  and

- there is a significant risk that a person with those abnormalities will have or develop a serious mitochondrial disease.

T129 Only those embryologists assessed as competent by the Authority to undertake PNT, MST or both, and named on the front of this licence, are permitted to undertake those processes or any part thereof.

Directions

0001 – Gametes and embryo donation

0005 – Collecting and recording information for the HFEA

0007 - Consent

0008 - Information to be submitted to the HFEA as part of the licensing process

Staff to be involved in mitochondrial donation

33.1 A senior clinical geneticist/mitochondrial disease specialist should be involved in deciding whether a particular patient should receive mitochondrial donation treatment.

33.2 The centre should ensure that a multidisciplinary team is involved in providing the treatment. The team should include mitochondrial disease specialists, reproductive specialists, embryologists, clinical geneticists, genetic counsellors and molecular geneticists. It should maintain close contact with the primary care physician, the referring clinician, or the mitochondrial disease centre.

33.3 Only embryologists who have been assessed as competent by the HFEA and named on the clinic's licence can perform maternal spindle transfer or pronuclear techniques as defined in Regulation 4 and 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015. An application for an assessment of the competence of an embryologist must be submitted to the HFEA and will be considered by a Licence Committee. When submitting an application to the HFEA for a competency assessment the person responsible and the relevant embryologist should provide:

- evidence of the embryologist's experience of carrying out MST or PNT in treatment, training or research on human eggs or embryos (eg, embryo survival rates, blastocyst development, and rate of carryover of mutant mitochondria, in line with KPIs determined by the HFEA)
- references to support the embryologist's experience and knowledge, and
- any other information that may demonstrate competence (such as the embryologist's experience of performing micro-manipulation on human or animal (e.g., mice) eggs or embryos).

33.4 The PR should submit an application to the HFEA for an assessment of the competence of each embryologist who intends performing MST or PNT or any part thereof. A PR wishing to make any changes to the authorised embryologists must submit an application to the HFEA for a variation of the clinic's licence accompanied by the relevant evidence of competency for each proposed embryologist.

Mitochondrial donation for the avoidance of serious mitochondrial disease

Interpretation of mandatory requirements 33A

Maternal spindle transfer (MST) can only be carried out where the Authority has issued a determination that —

• there is a particular risk that any eggs collected from the patient named in the application form may have mitochondrial abnormalities caused by mitochondrial DNA; and

• there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease

Pronuclear transfer (PNT) can only be carried out where the Authority has issued a determination that—

• there is a particular risk that any embryos created with eggs collected from the patient named in the application form may have mitochondrial abnormalities caused by mitochondrial DNA; and

• there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease.

Treatment involving mitochondrial donation can only be carried out by a clinic that is licensed to do mitochondrial donation as evidenced by express provision on the clinic's licence permitting it to undertake either PNT, MST or both.

The process of PNT or MST (as defined in Regulation 4 and 7 of the Human Fertilisation and Embryology Authority (Mitochondrial Donation) Regulations 2015) may only be carried out by embryologists who have been assessed by the HFEA as competent to undertake these processes and who are named on the clinic's licence.

PNT and MST may only be carried out on the premises of a clinic licensed to undertake mitochondrial donation and may not be done on third party premises or the premises of any satellite centre.

Clinics that are not licensed to undertake PNT or MST for treatment purposes may not use eggs or embryos created using these techniques in treatment services.

33.5 When deciding if it is appropriate to offer MST or PNT in particular cases, the centre should consider the circumstances of those seeking treatment rather than the particular mitochondrial condition.

33.6 The centre should discuss with the patient the likely outcomes of the proposed treatment, the nature and potential risks of the treatment, and any other treatment options that may be suitable, such as pre-implantation genetic diagnosis (PGD) or egg donation.

33.7 When deciding if it is appropriate to offer MST or PNT in particular cases, the seriousness of the disease in that case should be discussed between the patient seeking treatment and the clinical team. The level of risk for those seeking treatment and any child that may be born will also be an important factor for the centre to consider and should be discussed with the patient.

33.8 The centre should consider the following factors before deciding whether it is appropriate to offer MST or PNT in particular cases. Having considered these factors, if a decision is taken to offer MST or PNT, the clinic must submit an application for authorisation to the HFEA.

The Authority's assessment of the seriousness will be made, where possible, based on the most severe symptoms that could be expected for a particular patient's case. When submitting an application to the HFEA, the PR must wherever possible, provide supporting evidence detailing:

a) the patient's medical history
b) the patient's family medical history of mitochondrial disease
c) the patient's mutant mtDNA load and threshold associated with symptoms of disease
d) scientific literature relevant to the mtDNA mutation or disease, and
e) any additional information which the clinician may consider is relevant to the application, such as a statement from a genetic counsellor.

Embryo transfer using embryos following mitochondrial donation

33.9 Embryos that have undergone either MST or PNT (or any other technique) should not be transferred with any other embryos that have not undergone the same technique in the same treatment cycle.

33.10 A centre should not perform embryo biopsy (such as for the purpose of preimplantation genetic diagnosis (PGD) or preimplantation genetic screening (PGS)) on embryos that have undergone MST or PNT.

33.11 A centre should use the same sperm provider for both steps of PNT unless there is a good reason for not doing so (i.e. if the mitochondria donor is a close genetic relative of the intended father).

Genetic consultation and counselling

33.12 The centre should ensure that people seeking treatment have access to mitochondrial specialists, clinical geneticists, genetic counsellors and, where appropriate, infertility counsellors. Patients who have been referred by one clinic to another for the purposes of mitochondrial donation must be offered specific counselling about mitochondrial donation by the clinic licensed to do mitochondrial donation regardless of whether the patient has previously been offered counselling by the referring centre.

33.13 The centre should work closely with the local genetics/mitochondrial disease centre of those seeking treatment.

Information for those seeking mitochondrial donation

33.14 The centre should ensure that people seeking MST or PNT are given the appropriate information about the treatment. Where a patient has been referred by one clinic to another for the purposes of mitochondrial donation, the clinic licensed to provide

mitochondrial donation must ensure that it provides the patient with appropriate information including:

a) information about the process, procedures and possible risks involved in mitochondrial donation including the risks for any child that may be born following the mitochondrial donation, and in the IVF treatment
b) information about the experience of the centre and embryologist(s)carrying out the techniques.

33.15 The centre should also provide information to those seeking treatment to help them make decisions about their treatment, including:

a) genetic and clinical information about the mitochondrial disease
b) the possible impact (if known) of the mitochondrial disease on those affected and their families
c) the importance of telling any resulting children of the mitochondrial donation treatment
d) information about treatment and social support available, and
e) information from a relevant patient support group or the testimony of people living with the condition, if those seeking treatment have no direct experience of it themselves.

33.16 If the person seeking treatment has already been given information about the particular mitochondrial disease, for example from a regional mitochondrial disease centre with appropriate expertise, the centre need not provide this information again. However, the centre should ensure that the information which has been provided is accurate, sufficiently detailed and that the patient fully understands the information.

33.17 Before providing mitochondrial donation treatment the centre should ensure that those seeking treatment have had sufficient opportunity to fully consider the possible outcomes and risks of these techniques and their implications.

33.18 The centre should provide information to people seeking mitochondrial donation treatment about the collection and provision of information, specifically:

a) information that centres must collect and register with the HFEA about the donors
b) what information may be disclosed to people born as a result of the mitochondrial donation and in what circumstances, and
c) that person's right to access anonymous information about the mitochondrial donor from the age of 16.

33.19 The centre should give people seeking mitochondrial donation treatment information about the screening of people providing mitochondria. This information should include details about:

a) the sensitivity and suitability of the tests, and
b) the possibility that a screened provider of mitochondria may be a carrier of a mitochondrial disease or infection.

33.20 The centre should provide information that explains the limitations of procedures and the risks of treatment to anyone seeking mitochondrial donation treatment. The centre should make available appropriate counselling.

Guidance note 20 applies to mitochondrial donation except guidance 20.1, 20.2 d)iii)-v).

See also:

Guidance note 20 – Donor assisted conception

Human Fertilisation & Embryology Authority

Guidance note 3 - Counselling

Importance of informing children of their origins

33.21 The centre should tell people who seek mitochondrial donation treatment that it is best for any resulting child to be told about their origin early in childhood.

33.22 Centres should inform patients of the potential risk of mitochondrial disease in future generations and the potential ways to avoid this (eg, that any female born following MST or PST that, should she wish to have children of her own, could have her eggs or early embryos analysed by PGD in order to select for embryos free of abnormal mitochondria).

Eligibility requirements for mitochondrial donors

Licence conditions

T52 Prior to the use and/or storage of donor gametes and/or embryos created with donor gametes the centre must comply with the selection criteria for donors and the requirements for laboratory tests and storage set out below, namely:

a. donors must be selected on the basis of their age, health and medical history, provided on a questionnaire and through a personal interview performed by a qualified and trained healthcare professional. This assessment must include relevant factors that may assist in identifying and screening out persons whose donations could present a health risk to others, such as the possibility of transmitting diseases, (such as sexually transmitted infections) or health risks to themselves (eg, superovulation, sedation or the risks associated with the egg collection procedure or the psychological consequences of being a donor).

b. the donors must be negative for HIV1 and 2, HCV, HBV and syphilis on a serum or plasma sample tested as follows, namely:

- HIV 1 and 2: Anti-HIV – 1, 2
- Hepatitis B: HBsAg and Anti-HBc
- Hepatitis C: Anti-HCV-Ab
- Syphilis: see (d) below

c. the centre must devise a system of storage which clearly separates:

- quarantined/unscreened gametes and embryos,
- gametes and embryos which have tested negative, and
- gametes and embryos which have tested positive.

d. a validated testing algorithm must be applied to exclude the presence of active infection with Treponema pallidum. The non-reactive test, specific or non-specific, can allow gametes to be released. When a non-specific test is performed, a reactive result will not prevent procurement or release if a specific Treponema confirmatory test is non-reactive. The donor whose specimen test reacted on a Treponema-specific test will require a thorough risk assessment to determine eligibility for clinical use

e. in addition to the requirements in (b) and (d) above, sperm donors must be negative for chlamydia on a urine sample tested by the nucleic acid amplification technique (NAT)

f. This requirement has been removed.

g. HTLV-1 antibody testing must be performed for donors living in or originating from high-prevalence areas or with sexual partners originating from those areas or where the donor's parents originate from those areas, and

h. in certain circumstances, additional testing may be required depending on the donor's history and the characteristics of the gametes donated (eg, RhD, Malaria, T.cruzi).

i. genetic screening for autosomal recessive genes known to be prevalent, according to international scientific evidence, in the donor's ethnic background and an assessment of the risk of transmission of inherited conditions known to be present in the family must be carried out, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation must be communicated and clearly explained to the recipient.

T126 Donors of gametes for use in PNT and or MST must be screened for pathogenic mitochondrial DNA mutations and an assessment of the risk of transmission of inherited conditions known to be present in the maternal line, must be carried out, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation must be clearly communicated and explained to the recipient.

Interpretation of mandatory requirements **33B**

Sections (a) to (h) of Licence condition T52 on medical and laboratory tests should apply to mitochondrial donors and to men providing sperm used to fertilise eggs of the mitochondrial donor in the process of PNT.

33.23 As well as taking their medical and maternal medical history (in line with T52 and T126) the recruiting centre should take details of previous donations. If a prospective donor cannot give a full and accurate maternal family history, the centre should record this fact and take it into account in deciding whether or not to accept their eggs for treatment.

33.24 Centres should ensure that they keep up to date with relevant literature and professional guidance, such as on refinements to the techniques, to improve their efficacy in treatment. Centres should also keep up to date with emerging research relevant to mitochondria haplotype matching and consider matching the haplotypes of donors with recipients where possible.

33.25 Before accepting a mitochondrial donor, centres should follow the same requirements and guidance as set out in guidance note 11, except guidance 11.2, 11.3, 11.32g,j 11.32 i)-l), 11.36, 11.37, 11.38, 11.39, 11.42, 11.46-11.52.

33.26 Guidance on the upper age limits for egg and embryo donors does not apply for mitochondrial donors. There is some evidence to suggest that mitochondria in a woman's eggs accumulate damage over time meaning the eggs of older donors may have reduced mitochondrial function. Age should therefore be taken into consideration when determining the suitability of a woman donating her eggs, in conjunction with an assessment of her reproductive health, such as an assessment of ovarian reserve.

33.27 The ten family limit guidance for those providing donor gametes (or embryos created using donated gametes) outlined at 11.46, does not apply to:

- egg donors who have donated their mitochondria only or
- sperm donors who have donated for pronuclear where they will not be genetically related to the child.

See also:

Information for prospective mitochondrial donors

33.28 Before any consents or samples are obtained from a prospective mitochondrial donor, the recruiting centre should provide information about:

a) the screening that will be done, and why it is necessary
b) the possibility that the screening may reveal unsuspected conditions (eg, mitochondrial related anomalies or HIV infection) and the practical implications
c) the scope and limitations of the genetic testing that will be done and the implications for the mitochondria donor and their family
d) the importance of informing the recruiting centre of any medical information that may come to light after donation that may have health implications for any woman who received treatment with their mitochondria or for any child born as a result of such treatment
e) the procedure used to collect gametes, including any discomfort, pain and risk to the mitochondria donor (eg, from the use of superovulatory drugs)
f) the legal parenthood of any child born as a result of their mitochondrial donation
g) what information about the mitochondrial donor must be collected by the centre and held on the HFEA Register
h) that only non-identifying information will be disclosed when the applicant is aged over 16. No identifying information about the donor will be disclosed.
i) the possibility that a child born as a result of their mitochondrial donation who is disabled as a result of an inherited condition that the donor knew about, or ought reasonably to have known about, but failed to disclose, may be able to sue the donor for damages, and
j) the ability of the mitochondrial donor to withdraw consent, procedure for withdrawal of consent for the use of their mitochondria and the point up until which the donor can withdraw consent.

Informing mitochondrial donors about information available to children born from the treatment

33.29 The centre should inform mitochondrial donors that anyone born as a result of their mitochondrial donation will have access to the following non-identifying information provided by them, from the age of 16:

a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history,
b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and
c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section.

Consent

33.30 The centre should obtain written informed consent from patients and their spouse or partner (if relevant), for mitochondrial donation treatment. Where a patient and their partner have been referred by one centre to another for the purposes of mitochondrial donation, the clinic that will be undertaking the mitochondrial donation must obtain consent specific to the treatment involving mitochondrial donation regardless of what consent the patient and their partner may have provided to the referring centre. This is because the centre doing the mitochondrial treatment will have the necessary experience and expertise in mitochondrial donation and is best placed to provide the relevant information and obtain fully informed consent.

33.31 For mitochondrial donors, the centre should obtain the donor's written informed consent to the donation of her eggs or embryos for MST or PNT.

33.32 Any prospective women donating their eggs for mitochondrial donation, or men donating sperm for PNT where they will not be genetically related to the child, should be aware that they cannot withdraw or vary their consent once the donated egg or embryo has undergone the process of MST or PNT (ie, the nuclear material has been moved from one egg or embryo to another).33.33 Centres should follow all other requirements and guidance on consent as outlined in guidance note 11 on donor recruitment, assessment and screening and in guidance note 5 on consent to treatment, storage, donation and disclosure of information.

Import of eggs or embryos which have undergone mitochondrial donation

Interpretation of mandatory requirements 33C

It is not lawful in the UK to provide treatment using gametes or embryos created abroad following the use of pronuclear transfer or maternal spindle transfer. Schedule 1(f) and 3 (i) of General Direction 0006 provides that the purpose of importing gametes or embryos must be to provide treatment services. However, as treatment using gametes or embryos created abroad following the use of pronuclear transfer or maternal spindle transfer is not lawful, it follows that the import of such gametes or embryos should not take place.

See also:

Guidance note16 - Imports and exports

See also:

Guidance note 5 - Consent to treatment, storage, donation and disclosure of information

Guidance note 11 - Donor recruitment, assessment and screening

Follow-up arrangements

33.33 Centres offering mitochondrial donation should have a documented process setting out how children born from mitochondrial donation will be followed up, where patients have consented to follow-up. These should include long-term medical follow-up of children born as a result. Centres should establish links with mitochondrial disease centres to facilitate follow-up. If the patient is not a UK resident but nevertheless wishes to participate follow-up, the centre and patient should discuss whether the patient wishes to be followed up at a mitochondrial disease centre based in the UK or a relevant centre overseas, in a location more convenient for the patient.

33.34 Centres should explain to patients the benefits of participating in follow-up.

33.35 If a centre becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or if there has been

some other adverse outcome (such as a miscarriage) following treatment involving mitochondrial donation, the centre must regard this as an adverse incident and report this to the HFEA in line with the requirements on adverse incidents set out in guidance note 27. This is to capture information about any abnormalities that may occur as a result of carrying out the MST or PNT treatment, to inform any regulatory or licensing action that the HFEA may wish to take and inform the scientific sector.

See also:

Guidance note 27 – Adverse incidents

Annex 4: Draft general directions, including:

- 0001 - Gamete and Embryo donation
- 0005 - Collecting and recording information for the HFEA
- 0007 - Consent
- 0008 - Information to be submitted to the HFEA as part of the licensing process
- 0012 - Retention of records

Ref: 0001
Version: 4

Gamete and embryo donation

These Directions are:	GENERAL DIRECTIONS
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Re-registering an anonymous donor as an identifiable donor

1. Licensed centres must use form Bv2005/1 to re-register any person who:

   (a) registered as a donor before 1 April 2005 and/or who donated gametes and/or embryos before that date; and
   (b) now wishes to be registered as an identifiable donor so that information about him or her may be disclosed to any persons born as a result of the donation.

2. Centres must use Donor Information form Dv2009 to record any additional updating information about a donor who now wishes to be re-registered as an identifiable donor. Licensed centres should ensure that the appropriate box in Part 1 is ticked to indicate that the form "Corrects or changes Details already registered". This form should be completed in addition to form Bv2005/1.

Giving and receiving money or other benefits in respect to any supply of gametes or embryos

3. Centres must not accept an individual as a donor who is known (or is reasonably suspected) by that centre to have received or to be about to receive money or other benefits not in line with these Directions.

4. Where the person responsible is aware that a person wishes to be treated using gametes obtained from a donor sourced by another agency or intermediary, including introductory agencies and internet websites, the person responsible should take reasonable steps to satisfy himself that the requirements of paragraph 3 have not been breached and must keep a record of the steps taken for this purpose.

5. Centres may compensate sperm donors a fixed sum of up to £35 per clinic visit.

6. Centres may compensate egg donors a fixed sum of up to £750 per cycle of donation. Where a prospective egg donor does not complete the cycle, the centre may compensate the egg donor on a 'per clinic visit' basis.

7. Where a person has stored gametes or embryos for use in their own treatment but then consents to donate them, a centre may compensate the donor for subsequent visits on a 'per clinic visit' basis.

8. Centres may compensate donors an excess amount in cases where expenses (such as for travel, accommodation or childcare) exceed the amounts specified in paragraphs 5 and 6 above. Centres may only provide excess expenses which:

   (a) are reasonable;
   (b) do not include loss of earnings;
   (c) have been incurred by the donor in connection with the donation of gametes provided to that centre; and
   (d) have been incurred by the donor solely within the United Kingdom.

9. Donors who are not permanent residents of the UK should be compensated in the same way as UK donors without an excess for overseas travel expenses. Centres must not directly or indirectly pay the overseas travel of a non-UK donor.

Recording excess expenses for donors

10. Where centres compensate donors an excess amount, as specified in paragraph 8 above, the centre must keep:

    (a) a record of the actual excess expenses incurred by the donor;
    (b) a record of the amount reimbursed to the donor; and
    (c) the receipts produced by the donor, and/or the steps taken by the person responsible to satisfy themselves that the excess expenses claimed by the donor have in fact been incurred.

11. The records referred to in paragraph 10 must be made available to the Centre's Inspector or provided directly to the Human Fertilisation and Embryology Authority, on request.

Giving and receiving money or other benefits in respect to any import of gametes or embryos from outside the UK

12. When considering whether to import gametes donated overseas, the centre should ensure the donor has not received compensation which exceeds:

    (a) reasonable expenses incurred by the donor in connection with the donation of gametes provided to that centre; and
    (b) loss of earnings (but not for other costs or inconveniences) incurred by the donor up to a daily maximum of £61.28 but with an overall limit of £250 for each course or cycle of donation (local currency equivalent).

13. When receiving donated gametes from overseas, the centre must keep a record (provided by the overseas centre) of:

    (a) the actual expenses incurred by the donor;
    (b) the amount reimbursed to the donor; and
    (c) the receipts produced by the donor, and/or the steps taken by the person responsible to satisfy themselves that the excess expenses claimed by the donor have in fact been incurred.

Supply of gametes or embryos from one establishment to another

14. Licensed centres that supply gametes or embryos to other licensed centres may only be given money or other benefits by the receiving centre for reimbursement of the reasonable expenses incurred in the supply of the gametes or embryos.

Benefits in kind

15. Gamete donors may receive licensed services, such as treatment, storage, or access to licensed services, in return for supplying gametes for donation. Egg donors who receive a benefit should be provided with that benefit in the course of the donation cycle unless there is a medical reason why they cannot be.

Mitochondrial donation

16. Centres may compensate those providing gametes for use in mitochondrial donation in line with paragraphs 3 to 15 above.

Definitions

17. The terms listed in these Directions are explained below:

(a) "clinic visit" means an appointment a donor attends in connection with the donation, including where the sperm sample is produced at home. This may include, but is not limited to, consultation visits, blood collection, counselling sessions and sperm sample collection.
(b) "cycle of egg donation" means the period from the first consultation until the donor's recuperation is complete.

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Collecting and recording information for the Human Fertilisation Embryology Authority

These Directions are:	GENERAL DIRECTIONS
Sections of the Act providing for these Directions:	Section 12 (1) (d) and (g)
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1. All licensed centres undertaking licensed treatments, with the exception of IUI and GIFT using partner sperm, must use the Authority's Electronic Data Interchange (EDI) to submit records relating to such activities to the Authority.

2. All licensed centres must use the following EDI forms to submit their records to the Authority:

Type of form	Purpose of form
Patient registration	To provide details of the patient receiving fertility treatment.
Partner registration	To provide details of the partner of the patient receiving fertility treatment.

Donor information	To provide identifiable details of a donor and the reasons why they are donating Licensed centres must use Donor Information form D v. 2012 to record information relating to donors and ensure that sections 1 to 20 are completed for each donor. Sections 21 to 27 of the Donor Information form (pages 3 & 4) must be submitted to the HFEA in paper format with the donor code and the centre's code referenced. Intended parents supplying gametes in a surrogacy arrangement are to be registered with the IP prefix to their donor code. When registering an intended parent as a donor, pages 3 & 4 of the donor form are not required by the HFEA.
Donor re-registration (also known as a B form)	This form enables a previously anonymous donor to register as identifiable on the HFEA Register
Intention to treat	To inform the HFEA when a cycle in which eggs are to be collected has started
IVF treatment & embryo creation and use	To inform the HFEA about the circumstances surrounding egg collection, embryo creation and /or transfer
Donor insemination treatment	To inform the HFEA when a patient has been inseminated with donor sperm
Early pregnancy outcome	To inform the HFEA of the early outcome of a treatment
Pregnancy outcome	To inform the HFEA of the outcome of any early outcome recording 'fetal pulsation seen'
Donor sperm procurement	To inform the HFEA about the quantity of sperm donated by each donor

Embryo and gamete movement - in	To inform the HFEA about the number of embryos, eggs and ampoules, straws or vials of donor sperm transferred from another UK centre or imported from outside the UK
Embryo and gamete movement - out	To inform the HFEA of the number of embryos, eggs and ampoules, straws or vials of donor sperm removed from storage at a centre and the reason for the removal
Consent Variation	To inform the HFEA of a patient's or partner's variation of their preferences set out in the 'Consent to the disclosure of identifying information form' (CD form); to inform the HFEA of the initial completion of the CD form by a patient or partner registered for treatment prior to 1 October 2009; to inform the HFEA of preferences regarding the disclosure of information about children born as a consequence of treatment

3. All licensed centres must submit the relevant EDI forms to the Authority within the following timescales:

Category of information	Timescale for records to be submitted to the Authority
Patient registration details	10 working days after the patient has confirmed intention to undergo treatment
Partner registration details	10 working days after the patient has confirmed intention to undergo treatment
Intention to treat	3 **calendar** days after last menstrual period or stimulatory drugs being administered to/taken by a patient with the intention to perform IVF treatment

Donor information	10 working days after confirmation of sperm being released for use by the clinic, the harvesting of oocytes or in the case of imports, receipt of the imported eggs, sperm or embryos
IVF treatment & embryo creation and use	10 working days after the treatment cycle completion date
Donor insemination treatment	10 working days after the last insemination of the cycle
Early pregnancy outcome	8 weeks after the treatment cycle completion date
Pregnancy outcome	14 weeks after the predicted outcome date
Embryo and gamete movement - in	Within 10 working days of gametes or embryos coming into storage
Embryo and gamete movement - out	Within 10 working days of gametes or embryos being removed from storage
Consent variation	10 working days after the patient has completed the CD form

4. All licensed centres must ensure that EDI forms submitted to the Authority are completed according to the guidance issued by the Authority (the most recent versions of which are available, alongside the forms, on the HFEA website). Where an error is identified, centres must correct the error within 2 calendar months.

5. Any licensed centre wishing to amend records that it has previously submitted to the Authority must do so via EDI on a “correcting form”. This must be the same as the original form supplied to the Authority, but must be clearly marked as a correcting form, and must reference the number of the original form that is to be corrected.

6. Licensed centres must notify the HFEA within 10 working days of any change to the patient or partner consent decision in relation to disclosure of HFEA Register information for research purposes. To do so, for patients registered after 1 October 2009 the centre must amend previously submitted Patient registration or Partner registration forms via EDI on a “correcting form”. This must be the same as the original form supplied to the Authority, but must be clearly marked as a correcting form, and must reference the number of the original form that is to be corrected. For patients registered before 1 October 2009 the centre must submit a Consent Variation form.

7. Where a licensed centre has submitted duplicate forms, that clinic must submit a deletion request to the Authority via the EDI system, clearly referencing the form to be deleted and stating the reasons for the request.

8. When a Person Responsible is satisfied with the accuracy of the data for their licensed centre, they must sign off this data. To do this, the Person Responsible must sign and date a hard copy of the draft 'Choose a Clinic' entry and return it to the Authority no later than 5pm on the date notified to the centres by the Authority (the sign-off deadline). The draft entry can be returned by post, fax or by email with a scanned image of the signed document.

9. Persons Responsible must ensure that, before they sign off their data, they are satisfied that:

a) the number of treatment cycles (both generic IVF and DI) completed within the reporting period is 100% accurate;

(b) all early outcome forms relating to cycles in a) above and all outcome forms relating to clinical pregnancies in a) above have been submitted to the Authority and have been filled in accurately; and

(c) all registration forms relating to patients undergoing treatment received in a) above have been submitted to the Authority and have been filled in accurately.

Other Submissions

10. All licensed centres undertaking Intra Uterine Insemination (IUI) or Gamete Intra-Fallopian Transfer (GIFT) with partner sperm must submit an annual return to the Authority no later than 28 February in each calendar year. The annual return must be in the format set out. Guidance is available on the HFEA website at http://www.hfea.gov.uk/2508.html

11. All licensed centres undertaking maternal spindle transfer (MST) and/or pronuclear transfer (PNT) must use the following paper or EDI forms to submit their records to the Authority within the following timescales:

Type of form	Purpose of form	Mechanism and timescales for submission
Patient Registration	To provide identifying information about the female patient having treatment.	To be submitted via EDI 10 working days after the patient has confirmed intention to undergo treatment.
Partner Registration	To provide identifying information about the partner (sperm provider) of the patient.	To be submitted via EDI 10 working days after the patient has confirmed intention to undergo treatment.
Mitochondrial donor registration	To provide identifying information about the mitochondrial donor. This is required even if the mitochondrial donor is also registered as a patient or egg donor.	To be submitted in paper* form 10 working days after the patient has confirmed intention to undergo treatment.
Pronuclear ONLY Sperm Donor Registration	To provide identifiable details of a donor whose sperm will ONLY be used in pronuclear transfer mitochondrial donation treatment for fertilisation of the mitochondrial donor's eggs. NB. This form is not required if the individual is already registered as a sperm donor or is the partner of the woman being treated.	To be submitted in paper* form 10 working days after confirmation of sperm being released for use by the clinic, the harvesting of oocytes or in the case of imports, receipt of the imported eggs, sperm or embryos.
Intention to treat	To inform the HFEA when a cycle in which eggs are to be collected has started	To be submitted via EDI 3 **calendar** days after the last menstrual period or stimulatory drugs being administered to/taken by a patient with the intention to perform IVF treatment.
IVF egg donation /storage	To inform the HFEA about the egg donation by the mitochondrial donor. The number of eggs donated for mitochondrial donation are to be recorded in the comments section of the form.	To be submitted via EDI 10 working days after the treatment cycle completion date.

Mitochondrial donation treatment	To inform the HFEA of a treatment cycle involving mitochondrial donation	To be submitted using a paper* form 10 working days after the treatment cycle completion date.
Early pregnancy outcome	To inform the HFEA of the early outcome of a treatment	To be submitted via EDI 8 weeks after the treatment cycle completion date.
Pregnancy outcome	To inform the HFEA of the outcome of any early outcome recording 'fetal pulsation seen'	To be submitted via EDI 14 weeks after the predicted outcome date.

*All paper forms submitted should be sent by recorded delivery addressed to the HFEA's Register Information Team.

12. All licensed centres must ensure that paper forms submitted to the Authority are completed according to the guidance issued by the Authority (the most recent versions of which are available, alongside the forms, on the HFEA website). Where an error is identified, centres must correct the error within 2 calendar months.

13. All licensed centres undertaking maternal spindle transfer and/or pronuclear transfer must complete and submit to the Authority a copy of the 'Mitochondrial donation follow-up information sheet', available on the HFEA website, no later than 29 October each year. Licensed centres holding these records must be able to produce copies upon request from an HFEA member or employee.

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Consent

These Directions are:	GENERAL DIRECTIONS
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1. Licensed centres must record any consent of a person whose consent is required under:

   (a) Schedule 3 and Section 33B of the Human Fertilisation and Embryology Act 1990 as amended; and

   (b) Sections 37 (1) and 44 (1) of Part 2 of the Human Fertilisation and Embryology Act 2008

   in the appropriate form listed in the Schedule to these Directions.

2. Where the storage period of a person's gametes or embryos has been extended, in accordance with the Human Fertilisation and Embryology (Statutory Storage Period for Embryos and Gametes) Regulations 2009, the PR of the licensed centres at which those gametes or embryos are stored must maintain a record of evidence that the conditions for extended storage of those gametes or embryos have been fulfilled.

3. Licensed centres must maintain a record of any withdrawal of consent by a person who has previously given a consent required under Schedule 3 to the Human Fertilisation and Embryology Act 1990, as amended, or under sections 37 (1) or 44 (1) of Part 2 of the Human Fertilisation and Embryology Act 2008. This consent should be recorded in the WC form, or in the case of surrogacy, the SWC form, as listed in the Schedule to these Directions.

4. Licensed centres holding any of the records referred to in these Directions must be able to produce a copy of those records (either electronically or as a hard copy) upon request from an HFEA member or employee.

5. From 1 May 2010, anyone receiving treatment at a licensed centre must complete a 'Consent to the disclosure of identifying information form' (CD Form)

if they have not already done so, regardless of when they first registered for treatment.

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Schedule

Storage

GS	Your consent to the storage of your eggs or sperm
LGS	Your consent to extending the storage of your eggs or sperm beyond 10 years
ES	Your consent to extending the storage of your embryos beyond 10 years

Donation

MD	Your consent to donating your sperm
WD	Your consent to donating your eggs
ED	Your consent to donating embryos

Treatment

WT	Women's consent to treatment and storage form (IVF and ICSI)
MT	Men's consent to treatment and storage form (IVF and ICSI)
MGI	Your consent to the use of your sperm in artificial insemination
WGI	Your consent to the use of your eggs in GIFT

Surrogacy

MSG	Men's consent to the use and storage of sperm or embryos for surrogacy
WSG	Women's consent to the use and storage of eggs or embryos for surrogacy
SPP	Your consent to being the legal parent in surrogacy
SWP	Your consent (as a surrogate) nominating an intended parent to be the legal parent

Mitochondrial donation

WMT	Women's consent to mitochondrial donation treatment and storage form
MMT	Men's consent to mitochondrial donation treatment and storage form
WDM	Your consent to mitochondrial donation
MD - including PNT	Your consent to donating sperm, including for use in pronuclear transfer
MD - PNT only	Your consent to donating sperm for mitochondrial donation (for pronuclear transfer only)

Disclosure of information

CD	Your consent to disclosing identifying information

Parenthood

WP Your consent to your partner being the legal parent
PP Your consent to being the legal parent

Withdrawal or stating lack of consent

WC Withdrawing your consent
SWC Surrogacy - withdrawing your consent
LC Stating your spouse or civil partner's lack of consent

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Information to be submitted to the Human Fertilisation and Embryology Authority as part of the licensing process

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General requirement relating to all applications to the Authority

1. Applications to the Authority relating to categories A-M must be made by completing and submitting the relevant on-line application, together with relevant supporting information detailed below, via the 'electronic portal' located on the Authority's website (www.hfea.gov.uk). An application fee (details of current fees payable are available on the Authority's website) must also be submitted.

2. Failure to submit a fully completed application form, pay the application fee or provide all the necessary information set out below will, in normal circumstances, result in the application not being considered until such times as these requirements have been satisfied.

3. Persons Responsible for centres which are licensed by the Authority to carry out licensed activities (treatment, storage, non-medical fertility services or research) must at all times have available the information set out in iv-xiv of paragraph 4 of this Direction and submit this information to the Authority when requested no later than 10 working days after the date of any written request.

Information to be supplied with applications

A. Applications for a new (initial) treatment, storage and non-medical fertility services licence

4. An application for a new licence authorising:

   (a) activities in the course of providing treatment services; and/or

(b) the storage of gametes, embryos or human admixed embryos; or
(c) activities in the course of providing non-medical fertility services,

must be accompanied by the information specified below:

i. where the proposed Person Responsible is not the applicant, a written confirmation from the proposed Person Responsible that the application is made with his or her consent;
ii. a current CV of the proposed Person Responsible listing academic and professional qualifications; work experience and registration details with the relevant professional body;
iii. a current CV of the proposed Licence Holder listing academic and professional qualifications; work experience and registration details with the relevant professional body;
iv. the Person Responsible Entry Programme ("PREP") certificate number confirming satisfactory completion of the PREP by the proposed Person Responsible;
v. a floor plan of the premises to be referenced on the licence;
vi. a suite of information documents to be provided to patients undergoing treatment at the centre once licensed;
vii. a completed self-assessment questionnaire submitted via the electronic portal;
viii. a copy of the centre's organisational chart clearly defining accountability and reporting relationships for named individuals;
ix. evidence that staff are registered with a professional or statutory body and are appropriately qualified and trained in techniques relevant to their work, or are in a programme of supervised training;
x. a copy of the centre's induction and training programme that ensures that staff have adequate knowledge of the scientific and ethical principles, together with the regulatory context, relevant to their work;
xi. evidence that a robust quality management system is in place;
xii. a statement that all the equipment and processes to be used in activities authorised by a licence, and in other activities carried out in the course of providing treatment services that do not require a licence, have been validated;
xiii. a detailed list of the quality indicators, a schedule of the audit programme and the reporting arrangements established for all activities authorised by a licence, and other activities carried out in the course of providing treatment services that do not require a licence; and
xiv. a copy of the centre's multiple birth minimisation strategy (where applicable).

B. Applications to renew a treatment, storage or non-medical fertility services licence

5. An application for the renewal of a licence authorising:

(a) activities in the course of providing treatment services; and/or
(b) the storage of gametes, embryos or human admixed embryos; or
(c) activities in the course of providing non-medical fertility services,

must be accompanied by the information specified below:

i. where the Person Responsible is not the applicant, a written confirmation from the Person Responsible that the application is made with his or her consent;
ii. a completed self-assessment questionnaire; and
iii. a suite of information documents to be provided to patients undergoing treatment at the centre (if different to those submitted with the original or previous renewal application).

C. Applications to vary the activities authorised by a current treatment, storage or non-medical services licence

6. An application to vary the activities authorised by a current licence in the course of providing treatment services or non-medial fertility services must be accompanied by the information specified below:

i. copies of information provided to patients relating to the new activity;
ii. evidence that the process(es) and, where applicable, the equipment used in carrying out the new activity have been validated; and
iii. a schedule of the quality indicators, and reporting arrangements, established for this activity.

7. An application to vary a licence to authorise mitochondrial donation through maternal spindle transfer (MST) or pronuclear transfer (PNT) must be accompanied by the information specified below:

i. copies of information provided to patients and donors relating to treatment involving mitochondrial donation;
ii. information to demonstrate the competence of the embryologist(s) proposed to conduct the technique(s) being applied for, as follows:

a) a CV and references of the embryologist(s), to support their experience and knowledge
b) key performance indicator data relating to the proposed embryologist's/embryologists' experience in carrying out the technique(s) on human eggs or embryos as follows:
    i) whether they have carried out the techniques in treatment, training or research
    ii) embryo survival rates (which must exceed [insert kpi 1])
    iii) blastocyst development rates (which must exceed [insert kpi 2])
    iv) rate of carryover of mtDNA (which must not exceed [insert kpi 3])
c) any other information that may demonstrate competence (such as their experience of performing micro-manipulation on human or animal (eg, mice) eggs or embryos)

iii. evidence that the equipment, and process(es) where applicable, used in carrying out the new technique(s) has been validated;
iv. a schedule of the quality indicators, and reporting arrangements, established for the new treatments;
v. procedures for the follow-up of children born as result of mitochondrial donation, including the arrangements the centre has in place with a mitochondrial disease expert centre.

An application to add or vary the name of the embryologist(s) practicing MST or PNT need only include section 7ii)(a-c).

D. Application to carry out a licensed activity using a 'novel' process

8. Where centres want to carry out a licensed activity using a process that has not been authorised by the Authority, an application must be accompanied by the information specified below:

i. copies of information provided to patients relating to the new activity;
ii. evidence that the process and, where applicable, the equipment used in carrying out the new activity have been validated; and
iii. a schedule of the quality indicators, and reporting arrangements, established for this process.

E. Applications for a new (initial) research licence

9. An application for a new licence authorising activities for a research project must be accompanied by the information specified below:

   i. where the proposed Person Responsible is not the applicant, a written confirmation from the proposed Person Responsible that the application is made with his or her consent;
   ii. the PR Entry Programme ("PREP") certificate number confirming satisfactory completion of the PREP (for Person Responsible appointed after 1 October 2009);
   iii. a floor plan of the premises to be specified on the licence;
   iv. copies of all information provided to patients and/or donors relating to the proposed research project;
   v. copies of the consent forms to be used to authorise the use of gametes, embryos or human cells in the research project;
   vi. evidence of ethics approval of the research project from a properly constituted research ethics committee; and
   vii. a completed self-assessment questionnaire.

10. For applications for a new licence authorising activities in connection with the derivation from embryos of stem cells that are intended for human application, the following additional information must be submitted with the application:

   i. evidence that the proposed Person Responsible possesses a diploma, certificate or other evidence of formal qualifications in the field of medical or biological sciences, awarded on completion of a university course of study, or other course of study recognised in the United Kingdom as equivalent and has at least two years' practical experience which is directly relevant to the activity to be authorised by the licence; and
   ii. evidence that the centre has, or is obtaining, a licence from the Human Tissue Authority.

F. Applications to renew a research licence

11. An application for the renewal of a licence authorising activities for a research project must be accompanied by the information specified below:

   i. a completed self-assessment questionnaire;
   ii. evidence of ethics approval of the research project from a properly constituted research ethics committee;

iii. copies of all information provided to patients and/or donors relating to the proposed research project (if different to those submitted with the original or previous renewal application); and
iv. copies of the consent forms to be used to authorise use of gametes, embryos or human cells in the research project (if different to those submitted with the original or previous renewal application).

12. For applications to renew a licence authorising activities in connection with the derivation from embryos of stem cells that are intended for human application, the following additional information must be submitted with the application:

i. evidence that the centre has a licence from the Human Tissue Authority.

G. Applications to vary a research licence to vary the purposes for which the research is licensed

13. An application to vary a research licence to vary the purposes for which the current research is licensed must be accompanied by the information specified below:

i. evidence of ethics approval of the research project from a properly constituted research ethics committee;
ii. copies of all information provided to patients and/or donors relating to the proposed research project (if different to those submitted with the original or previous renewal application); and
iii. copies of the consent forms to be used to authorise use of gametes, embryos or human cells in the research project (if different to those submitted with the original or previous renewal application).

H. Applications to vary a licence to either relocate to new premises or change existing premises

14. An application to vary a licence to either relocate to new premises not authorised by a current licence for the conduct of licensed activities (treatment, storage, research and non-medical fertility services) or to alter premises authorised by a current licence for the conduct of licensed activities (treatment, storage, research and non-medical fertility services) must be accompanied by the information specified below:

i. where the Person Responsible is not the applicant, a written confirmation from the Person Responsible that the application is made with his or her consent;
ii. a floor plan of the premises to be referenced on the licence, and;
iii. confirmation that any re-commissioned equipment has been tested and validated.

I. Applications to change the Person Responsible or the Licence Holder

15. An application to change the Person Responsible or the Licence Holder of a licence authorising licensed activities (treatment, storage, research and non-medical fertility services) must be accompanied by the information specified below:

i. a current CV of the proposed Person Responsible listing academic and professional qualifications; work experience and registration details with the relevant professional body;
ii. a current CV of the proposed Licence Holder listing academic and professional qualifications; work experience and registration details with the relevant professional body; and
iii. the PR Entry Programme ("PREP") certificate number confirming satisfactory completion of the PREP (applications for a change of PR only).

J. Applications to authorise pre-implantation genetic diagnosis

16. An application to authorise pre-implantation genetic diagnosis (PGD) for a condition which has not previously been authorised by the Authority is subject to an application as per paragraph 1.

K. Applications to authorise human leukocyte antigen tissue typing

17. An application to authorise human leukocyte antigen (HLA) tissue typing, in isolation or in conjunction with PGD must be accompanied by the information specified below:

i. a copy of a signed letter of support from a clinician responsible for the care of the sibling child providing information on the:

(a) degree of suffering associated with the disease of the affected sibling,
(b) speed of degeneration in progressive disorders,

(c) prognosis for the affected sibling in relation to all treatment options available,
(d) availability of alternative sources of tissue for the treatment of the affected sibling, now and in the future, and
(e) availability of effective therapy for the affected sibling now and in the future.

L. Applications to authorise mitochondrial donation for a specific patient

18. Applications for authorisation of mitochondrial donation for a specific patient must be made by completing the relevant application and submitting this to the HFEA.

M. Applications for Special Directions to export gametes or embryos

19. An application for a Special Direction to export gametes or embryos must be accompanied by the information specified below:

    i. a letter from the intended export destination centre/clinic confirming that it is willing to accept the gametes or embryos for the purpose specified in the application form.

Notifying the Authority of information relating to licensed activities

20. Persons Responsible must notify the Authority, through the electronic portal located on the Authority's website, of all processes undertaken in the licensed centre in carrying out a licensed activity.

Additional information to be submitted to the Authority as part of on-going compliance

21. Persons Responsible for centres licensed by the Authority must complete and submit to the Authority the self-assessment questionnaire (SAQ) published on the Authority's website no later than six weeks prior to the date on which the Authority has confirmed it will carry out an inspection visit. Before submitting the SAQ, Persons Responsible must confirm that the information they have provided on that document is true and accurate.

22. Where a member of the Authority's Compliance Department requests the Person Responsible to submit a further SAQ in addition to that required by paragraph 21 above, the Person Responsible must submit this to the

Authority no later than 15 working days after the date of the written request.

23. Where a member of the Authority's Compliance Department requests the Person Responsible to submit a further PREP, the Person Responsible must submit this to the Authority no later than 21 working days after the date of the written request.

Version control	
Directions name:	Information to be submitted to the Human Fertilisation and Embryology Authority as part of the licensing process
Reference number:	0008
Date version 1 came into force:	1 October 2009

Date version 2 comes into force:	1 October 2011
Chair's letter reference:	CH(11)06

Date version 4 comes into force:	29 October 2015
Chair's letter reference:	CH(15) 02

Ref: 0012
Version: 3

Retention of records

These Directions are:	GENERAL DIRECTIONS
Sections of the Act providing for these Directions:	Section 13(4), 14(2), 15(3) and 24(1)
These Directions come into force on:	1 October 2009
These Directions remain in force:	Until revoked
This version issued on:	29 October 2015

1. Subject to paragraph 2, licensed centres must retain a record of the following information for a period of at least 30 years from the date on which any gametes or embryos were used in treatment or, if not so used, the date on which any gametes or embryos were removed from storage:

(a) patient or donor identifying information (first name; surname; date of birth; age and sex);

(b) how, and by whom, the patient or donor has been reliably identified, where necessary;

(c) the services provided to the patient or donor;

(d) the medical history of the patient or donor;

(e) the outcome of the welfare of the child assessment, where appropriate;

(f) all consent forms and any specific instructions relating to the use and/or disposal of gametes and embryos;

(g) all clinical data (including administration of medicine and the results of any tests carried out) necessary for traceability;

(h) all laboratory data necessary for traceability, including records relating to any taking of an embryo from a woman or other acquisition of an embryo; the use and storage of any gametes or embryos; any testing of an embryo; consumables, drug treatments, equipment and environment (including servicing, cleaning, testing and monitoring); what equipment was used (and by whom) and staff training;

(i) any child born as a result of treatment provided to the patient; and

(j) all other information necessary for traceability;

(k) copies of the 'Mitochondrial donation follow-up information sheets',

2. The record of information specified in paragraph 1 must be kept for a period of at least 50 years from the date on which information about the treatment was first recorded if:

(a) a patient has undergone treatment (other than basic partner treatment) at a licensed centre; and

(b) the Person Responsible for that licensed centre is unable to confirm whether or not that patient has given birth to a child as a result of the treatment undertaken at that centre.

3. Licensed centres must retain a record of any information not specified in paragraph 1, which relates to the safety and quality of gametes and embryos, for a period of at least 10 years after the use of gametes or embryos in treatment or, if not so used, the date on which any gametes or embryos were removed from storage.

4. The Person Responsible for a research project must retain a record of the following information for a period of at least 3 years from the date the final report of any research project is submitted to the Authority:

(a) the total number of embryos or human admixed embryos created, used or disposed of during the research project;

(b) the results of the research project; and

(c) the conclusions drawn from the research project.

5. Where a research project involves the derivation of stem cells for human application, a record of the information specified in paragraph 4 and relevant information specified in paragraph 1 must be retained for a period of at least 30 years from the date the final report of any research project is submitted to the Authority.

6. Centres licensed by the Authority to undertake preimplantation genetic diagnosis (PGD) must, in respect of each case of PGD, retain information in the patient records which fully details the reasons why the Person Responsible considered PGD to be appropriate in that particular case, in line with guidance in the Code of Practice (at 10.5, 10.6). This information shall include an explanation of why the Person Responsible

considered there to be a particular risk that the embryo tested may have a gene, chromosome or mitochondrion abnormality.

Version control	
Directions name:	Retention of records
Reference number:	0012
Date version 1 issued:	1 October 2009

Date version 2 issued:	6 April 2010
Chair's letter reference:	CH(10)03

Date version 3 issued:	29 October 2015
Chair's letter reference:	CH(15)02

Annex 5: Draft forms and guidance, including:

- Licence variation form
- Mitochondrial donation follow-up information sheet
- Patient application form
- Clinical expert review form
- Decision trees for the Statutory Approvals Committee
- Mitochondrial donation: explanatory note for Statutory Approvals Committee
- Consent forms

Variation of HFEA treatment and storage licence to allow mitochondrial donation

1. Introduction

Please use this form to apply to vary a licence to allow mitochondrial donation through either maternal spindle transfer and/or pronuclear transfer.

To make changes to the embryology staff you only need to complete section 8.

Once complete submit to your inspector.

2. Centre contact information

Person responsible	
Centre name	
Centre number	

3. Corporate information

Are there any changes being made to the corporate status of the centre?

Is the centre a NHS facility or a private operation? ☐ NHS ☐ Private ☐ Both

4. Registration

Are any changes being made to the registration status of the centre?

Will the centre be registered with a regulator other than the HFEA?

5. Licensed activities

Please tick which additional authorised processes you are applying to add to your licence:

☐ Maternal spindle transfer (under the authorised activities of 'processing gametes' and 'creation of embryos').

☐ Pronuclear transfer (under the authorised activities of 'processing embryos' and 'creation of embryos')

6. Reason

Please provide reasons for the change in licensed treatments and the expected volume of any additional services.

7. Processes

Please provide details of any critical new equipment that will be used or processes that will be revalidated as a result of the variation

8. Key staff

Please list key staff responsible for the new treatment activities. Note, only an embryologist who has been assessed by the Authority as competent to undertake pronuclear transfer, maternal spindle transfer or both is permitted to undertake those processes or any part thereof.

Name	Role	Professional body registration (HCPC, GMC, NMC etc)

9. Third party agreements

Will there be any new third party agreements as a result of the variation? This could include for example laboratories that complete genetic testing. Note that licence conditions restrict what activities can take place under a third party agreement for treatments involving mitochondrial donation.

Company	Goods/services provided

10. Additional information

Is there any additional information you wish to bring to the attention of the HFEA, which is pertinent to this application and which has not been addressed on this form?

11. Attachments

☐ An index of all documents in the quality manual revised as a result of the variation of licensed activities

☐ All patient information revised as a result of the variation of licensed activities

☐ A functional organisational chart, if changed as a result of the variation of licensed activities

☐ The procedures for the follow-up of children born as result of mitochondrial donation, including the arrangements in place with a mitochondrial disease expert centre.

12. Declarations

I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing my data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that my data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.

I further understand that the HFEA will not disclose my data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

The information provided on this form is to the best of my knowledge true and accurate

Check the box to confirm acceptance of the above statement I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing my data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that my data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.

I further understand that the HFEA will not disclose my data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

The information provided on this form is to the best of my knowledge true and accurate

Check the box to confirm acceptance of the above statement ☐

Admin use only

Form received from	
Reference number	
Submitted date	

Mitochondrial donation follow-up information sheet

Centre name(s)	
Centre number(s)	

How many patients have received treatment at your centre involving maternal spindle transfer or pronuclear transfer?

	Number of patients
Current year, ending 28 October:	
Previous years beginning 29 October 2015 (cumulative):	

How many of these patients consented to being followed-up after their treatment?

	Number of patients
Current year, ending 28 October:	
Previous years beginning 29 October 2015 (cumulative):	

As far as you are aware how many of these patients attended follow-up appointments (relevant to the outcome of their mitochondrial donation treatment)?

	Number of patients
Current year, ending 28 October:	
Previous years beginning 29 October 2015 (cumulative):	

For these patients was treatment successful in avoiding the inheritance of mitochondrial disease (eg, if known what is the outcome of early tests on the child eg, mutant load)?

Please provide in a non-identifying format.

Current year, ending 28 October:

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Previous years beginning 29 October 2015 (cumulative):

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Detail any birth abnormalities

[Note: If a centre becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or other adverse outcome (such as a miscarriage), the centre must regard this as an adverse incident and report this in line with the requirements on adverse incidents set out in guidance note 27 of the Authority's Code of Practice]

Current year, ending 28 October:

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Previous years beginning 29 October 2015 (cumulative):

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Any other outcome information the centre is able to provide in a non-identifying format

Current year, ending 28 October:

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Previous years beginning 29 October 2015 (cumulative):

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

Mitochondrial donation: new case application form

1. Introduction

Please use this form if you wish to carry out a mitochondrial donation technique to treat a patient not previously authorised by the HFEA.

Before you begin your application please make sure the following statements are true:

- You hold a licence to carry out the mitochondrial donation technique (PNT and/or MST) intended for use in the treatment of this patient.
- You have identified a pathogenic mutation in the mtDNA of the patient
- You have evidence that the patient has a significant risk of having a child who will have or go on to develop serious mitochondrial disease.

It is important that the language used in this application is clear and as far as possible, understandable to non-specialists.

All abbreviations should be explained.

The application form has been designed to ensure that applying centres provide all of the information required to enable the Authority's Statutory Approvals Committee to make its decision. If the form is completed incorrectly or does not provide sufficient information it could delay the decision-making process.

The Committee is aware that not all pieces of evidence asked for will be relevant to every case.

An independent assessment of the application may also be sought from clinical experts and may inform the Statutory Approvals Committee's decision-making process

The guidance has been developed for centres licensed to carry out maternal spindle transfer (MST) and/or pronuclear transfer (PNT) that wish to apply for approval perform mitochondrial donation on a new patient. Please refer to this as you fill in the application form. These applications are all considered on a case-by-case basis.

2. Current centre information

Person responsible	
Centre name	
Centre number	

3. Regulatory requirements

Is this application from a centre licensed to carry out maternal spindle transfer (MST) and/or pronuclear transfer (PNT)?

Only centres licensed to carry out mitochondrial donation (MST and/or PNT) are permitted to make an application. Please state whether or not the application is from an assisted reproduction clinic, licensed by the HFEA.

☐ MST ☐ PNT ☐ No

Which technique is intended for the treatment of this patient?

☐ MST ☐ PNT

Has all the diagnostic genetic testing taken place in an accredited laboratory?

Genetic testing should only be carried out by an accredited laboratory.

If not, please provide an explanation as to why the genetic testing will not be carried out in an accredited laboratory.

☐ Yes ☐ No

As the Person Responsible I confirm that the purpose of the application is to treat a patient with an mtDNA mutation, and there is a significant risk of this resulting in a serious mitochondrial disease in their children.

Please confirm that the reason you want to carry out mitochondrial donation is for the statutory purposes.

Please tick the box to confirm acceptance of the above statement: ☐ Confirmed

4. Patient details

Surname	
Forename	
Patient number	

I wish to apply for authorisation for this patient/case ☐ Yes

5. Genetic cause

Has a pathogenic genetic alteration to the mtDNA been identified in the female patient?

Only patients for whom a pathogenic mtDNA genetic alteration has been identified are considered to be at particular risk of passing on abnormal mtDNA to their children.

☐ Yes ☐ No

Please give a description of this genetic alteration, i.e. point mutation deletion, rearrangement.

Please describe the pathogenic genetic alteration present in the patient's mtDNA, e.g. T8993G in ATP synthase subunit 6 (MTAPT6)

Please list any OMIM numbers associated with this mitochondrial disease

If applicable also provide the OMIM (On Line Mendelian Inheritance in Man System) number for this mitochondrial disease. This is indicated by a hash (#) for phenotypes and a plus sign (+) for the description of a gene of known sequence and a phenotype.

6. Seriousness and significant risk: general information

In this section of the form we would like you provide information based on scientific literature, which is **not patient specific**, about the disease(s) caused by this genetic change and about the relationship between mutant mitochondrial load and disease manifestation.

When considering the seriousness of a condition, the **Statutory Approvals Committee** will consider non-case specific evidence from the scientific literature, which you will provide in this section, as well as the case-specific information given in section 5. The Committee will take the following factors into account. Please provide as much information as possible under each of these sections.

Please include references.

Where information about the disease(s) or genetic abnormality listed above is available please provide:

Please provide a summary of the genetic condition and, if applicable, all the types of the condition in non-technical / lay language in no more than 200 words. This should include a description of how the condition affects a person, if known, how mutant mitochondrial load correlates to clinical symptoms and, if applicable, whether any treatments for the condition are available.

Lay summary

Please describe the range of symptoms which an individual with this mitochondrial disease might have, indicating the worst possible outcomes.

Symptoms of the disease

At what age will the symptoms of the condition start to develop. Is the condition apparent at birth or does it manifest later in life? If so, at what stage, for example, childhood, early adulthood, later?

Age symptoms are likely to develop

In this section, please include evidence about the effect the condition has on the quality of life on a child/adult (this might include the speed of degeneration in progressive disorders together with the extent of any physical and / or intellectual impairment).

Effect on quality of life

If there is any evidence from the scientific literature to indicate the effect of mutant mtDNA load on the severity of disease, please include this information here. How does the mutant mtDNA load correlate to clinical symptoms? What is the mutant mtDNA load above which clinical symptoms become manifest? Are there any studies indicating how high the mutant mitochondrial loads were in women that have had children affected by mitochondrial disease? What is the lowest mutant mitochondrial load in a woman that has had a child affected by serious mitochondrial disease?

Threshold level of mutant mitochondria necessary to cause symptoms

Please list any treatment options available. How invasive is the treatment or likely treatment?

Available treatments

7. Significant risk and seriousness: patient information

It is important that you explain to the patient why they are being asked to provide the information on their own medical history and that of their family. Explain to the patient that this information will be disclosed to the HFEA to assist in the Statutory Approval Committee's decision making process and that all information will be treated in a confidential fashion by those to whom it is disclosed.

In this section please provide evidence that is **specific to the patient** named in this application.

The Committee may only authorise mitochondrial donation if it is satisfied that there is a significant risk that a person with the abnormality will have or will develop a serious physical or mental disability, a serious illness or another serious medical condition.

Please explain why you think the patient's child, if conceived naturally, is at significant risk of having or developing a mitochondrial disease causing a serious physical or mental disability; a serious illness; or another serious medical condition.

When considering risk and seriousness, the **Statutory Approvals Committee** will take the following factors into account. Please provide as much information as possible under each of these sections.

Is there a significant risk that a child born without mitochondrial donation will have or go on to develop a serious mitochondrial disease?

☐ Yes ☐ No

What's the patient's medical history? How does it provide evidence of risk and seriousness? You may wish to consider the following questions:

- Does the patient have any symptoms? If so, how severe are they?
- Has the patient previously had any children affected by mitochondrial disease? If so, what were their symptoms? What was the age of onset? What was the effect on quality of life? Were any treatments available and what effect did they have? Would this manifestation of mitochondrial disease pass the seriousness test?
- Has the patient previously been treated with preimplantation genetic diagnosis (PGD) to avoid transmission of mitochondrial disease? Was the PGD successful? What was the mutant mitochondrial load of the embryos tested? Did any of the embryos have a mutant mitochondrial load above the threshold level usually necessary for clinical manifestation of serious mitochondrial disease?

Please provide information on the patient's medical history

Has the patient's mutant mtDNA load been assessed? How does it provide evidence of risk and seriousness? You may wish to address the following questions:

- Is the patient is homoplamsic or heteroplasmic for the mutation?
- What is the patient's mutant mtDNA load and in which tissues?
- Have patients with similar mutant mtDNA loads have had children affected by serious mitochondrial disease?
- How the patient's mutant mitochondrial load compares to the threshold level for clinical manifestation, if known.

Please provide information on the patient's mutant mtDNA load

What's the patient's family history? How does it provide evidence of risk and seriousness? You may wish to consider the following questions:

- Does the patient have a family history of mitochondrial disease? How prevalent is mitochondrial disease in the family ie, which family members are/have been affected by mitochondrial disease? For each affected family member, how serious was their disease: what were the symptoms, what was the age of onset, what was the effect on quality of life, were any treatments available and effect did they had?
- What were the mutant mitochondrial loads of affected family members with severe mitochondrial disease and what were the mutant mitochondrial loads of their mothers? Are the mutant mitochondrial loads of female family members who have had severely affected children comparable to the patient?
- For each family member, their symptoms, age of onset, effect on quality of life, their mutant mitochondrial load, if any treatment was available, what it was and what effect it had.

A family pedigree may also be useful.

Note: Please ensure that you either have consent before providing disclosure of family medical history that is capable of identifying an individual or take measures to ensure that confidentiality is not breached, such as by anonymising the family tree.

Please provide information on the patient's family history

If there is any additional information you feel provides evidence of risk and seriousness, please include it here. For example you may wish to include a statement from the patient's genetic counsellor, outlining the impact that mitochondrial disease has had on them and why they feel mitochondrial donation is the most appropriate treatment for them.

Please provide any additional information to support this

8. Declarations

I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing this data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that this data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.

I further understand that the HFEA will not disclose this data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertilisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

The information provided on this form is to the best of my knowledge true and accurate

Please tick the box to confirm the declaration. This must be completed by the person responsible of the licensed centre applying for the treatment. The form should then be submitted to the HFEA by recorded delivery.

Check the box to confirm acceptance of the above statement ☐

Mitochondrial donation: clinical expert review form

1. Introduction

The law in the United Kingdom permits the use of the mitochondrial donation techniques, pronuclear transfer (PNT) and maternal spindle transfer (MST), to prevent the transmission of serious mitochondrial diseases caused by mutations to the mtDNA.

However, the use of mitochondrial donation is only permissible if a patient meets certain criteria and this must be assessed on a case by case basis. The responsibility for deciding whether the necessary requirements have been met rests with the Human Fertilisation and Embryology Authority (HFEA) and in particular its Statutory Approvals Committee.

The purpose of this form is to enable clinical experts, who may be called upon to act as an independent source of advice, to inform the Statutory Approvals Committee's decision-making process.

When deciding whether to authorise mitochondrial donation for a particular patient the committee must be satisfied that the patient's embryos are at risk of inheriting abnormal mitochondria caused by mutations to the mtDNA and that the patient's child, if conceived without the use of mitochondrial donation, would be at significant risk of having or developing a serious mitochondrial disease.

The committee considers the particular circumstances for each individual application and makes an assessment based on a range of sources of evidence, including the patient's medical history, family history, patient mutant mtDNA load, as well as more general information about the mitochondrial disease/genetic alteration from the scientific literature.

To aid the committee in considering whether to authorise mitochondrial donation for a particular case the HFEA would like your opinion on how serious the mitochondrial disease is, based on your own knowledge and from the scientific literature. We would also like to know whether you feel the patient-specific information provided in the application is sufficiently detailed to enable the committee to make an assessment of the likely risk of transmission of a serious mitochondrial disease from patient to child.

In providing your opinion we would ask you to outline the range of symptoms associated with the mitochondrial disease/genetic alteration, highlighting the most severe clinical outcomes.

The HFEA does not expect you to be expert in the particular mitochondrial disease but instead it would value your opinion as a clinician/clinical geneticist with experience of mitochondrial disease.

2. Seriousness: general information

When considering the seriousness of a condition, the Statutory Approvals Committee will frame its discussion by taking into account information from the scientific literature (which is **not** case specific) on these factors, in addition to evidence specific to the patient.

Please provide as much information as possible under each heading based on evidence from the scientific literature and your experience of mitochondrial disease pathology.

Please include references.

2.1 When are symptoms likely to develop?

☐ At birth ☐ Infancy ☐ Childhood

☐ Teenage years ☐ Early adulthood ☐ Middle age

☐ Later life

2.2 What symptoms would an individual with this mitochondrial disease/caused by this alteration to the mitochondrial DNA (mtDNA) have?

Please describe the range of symptoms, highlighting the worst possible outcomes.

2.3 What effect does this mitochondrial disease/genetic alteration to the mtDNA have on the quality of life of an affected individual?

Please include the rate of any degenerative aspect and the extent of any physical and/or intellectual impairment.

2.4 Is there a treatment currently available that modifies the underlying disease process?

☐ Yes ☐ No

If yes, please describe

Please list any treatment options available. How invasive is the treatment?

3. Risk: general information

When considering how significant the risk would be to a patient's child if conceived without the use of mitochondrial donation, the Statutory Approvals Committee will take into account information from the scientific literature (which is **not** case specific) on the effect of mutant mitochondrial load on the clinical presentation of disease.

3.1 Is there any evidence from the scientific literature to indicate the effect of mutant mtDNA load on the severity of disease?

☐ Yes ☐ No

3.2 If so, how does the mutant mtDNA load correlate to clinical symptoms and what is the mutant mtDNA load above which clinical symptoms are likely to manifest?

4. Seriousness and risk: patient information

The committee may only authorise mitochondrial donation if it is satisfied that there is a significant risk that a person with the abnormality will have or develop serious mitochondrial disease.

4.1. Please review the information provided by the applying clinic in Section 5 of 6 of the 'Mitochondrial donation – New case application form'. Is sufficient information provided to make an assessment of the significance of the risk?

☐ Yes ☐ No

In Section 5 of the 'Mitochondrial donation – New case application form', the applying clinic has been asked to provide information specific to the patient, that suggests there is a significant risk that a child born without mitochondrial donation will have or go on to develop a serious mitochondrial disease.

In making its decision on whether to authorise mitochondrial donation, the Statutory Approvals Committee will rely heavily on this evidence.

We understand that it will not be possible for applicants to provide every piece of evidence for each individual patient's case; however we would like to know whether, in your expert opinion, the evidence provided is sufficiently complete to make an assessment of significant risk and seriousness.

Note: we do not require your assessment of the risk or seriousness, only of the level of information provided.

4.2. If no, what additional information should be provided?

5. Any other comments

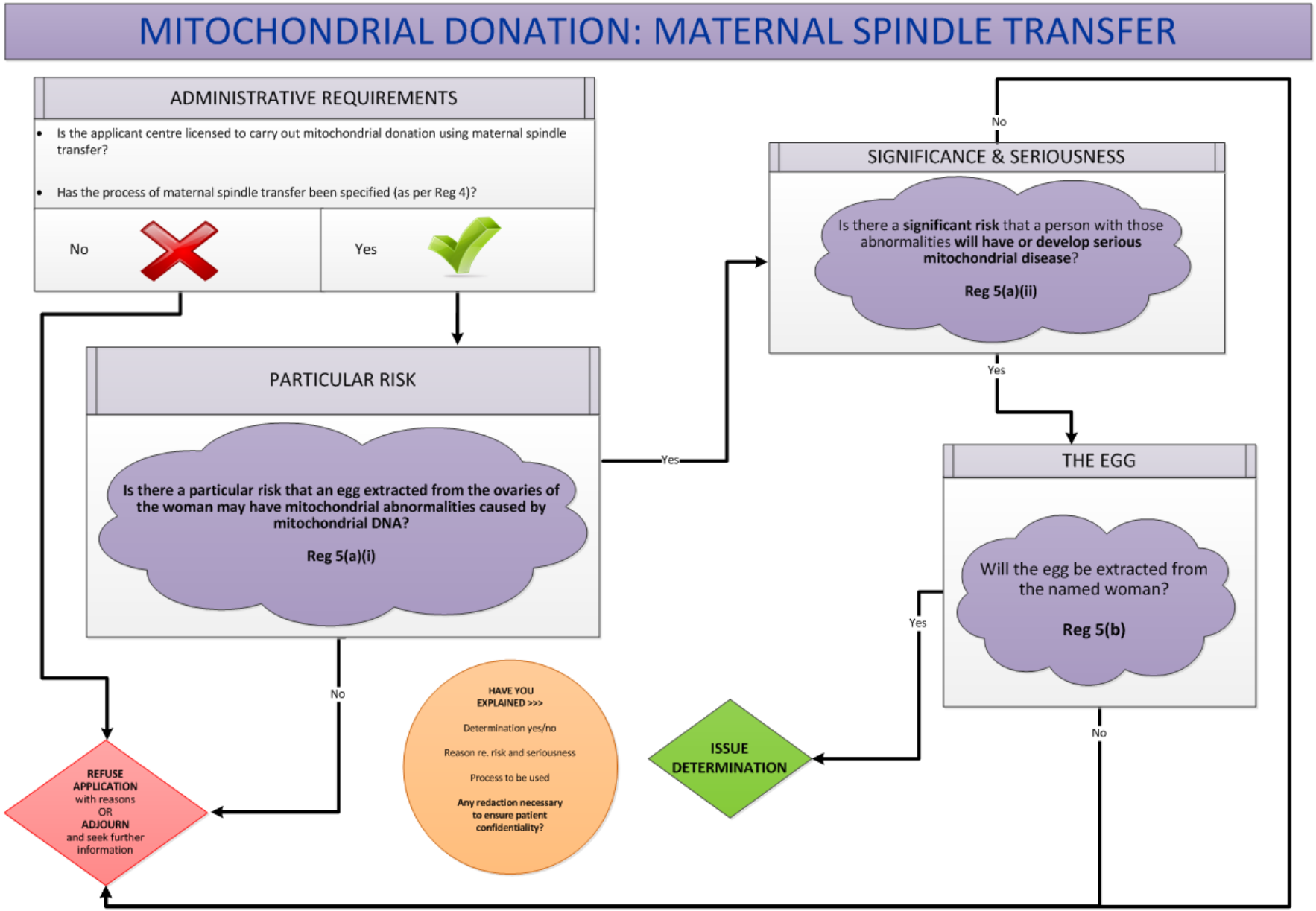
6. Personal details of clinical expert

Name	
Position held/area of work	

Signature

Date

Statutory Approvals Committee decision tree



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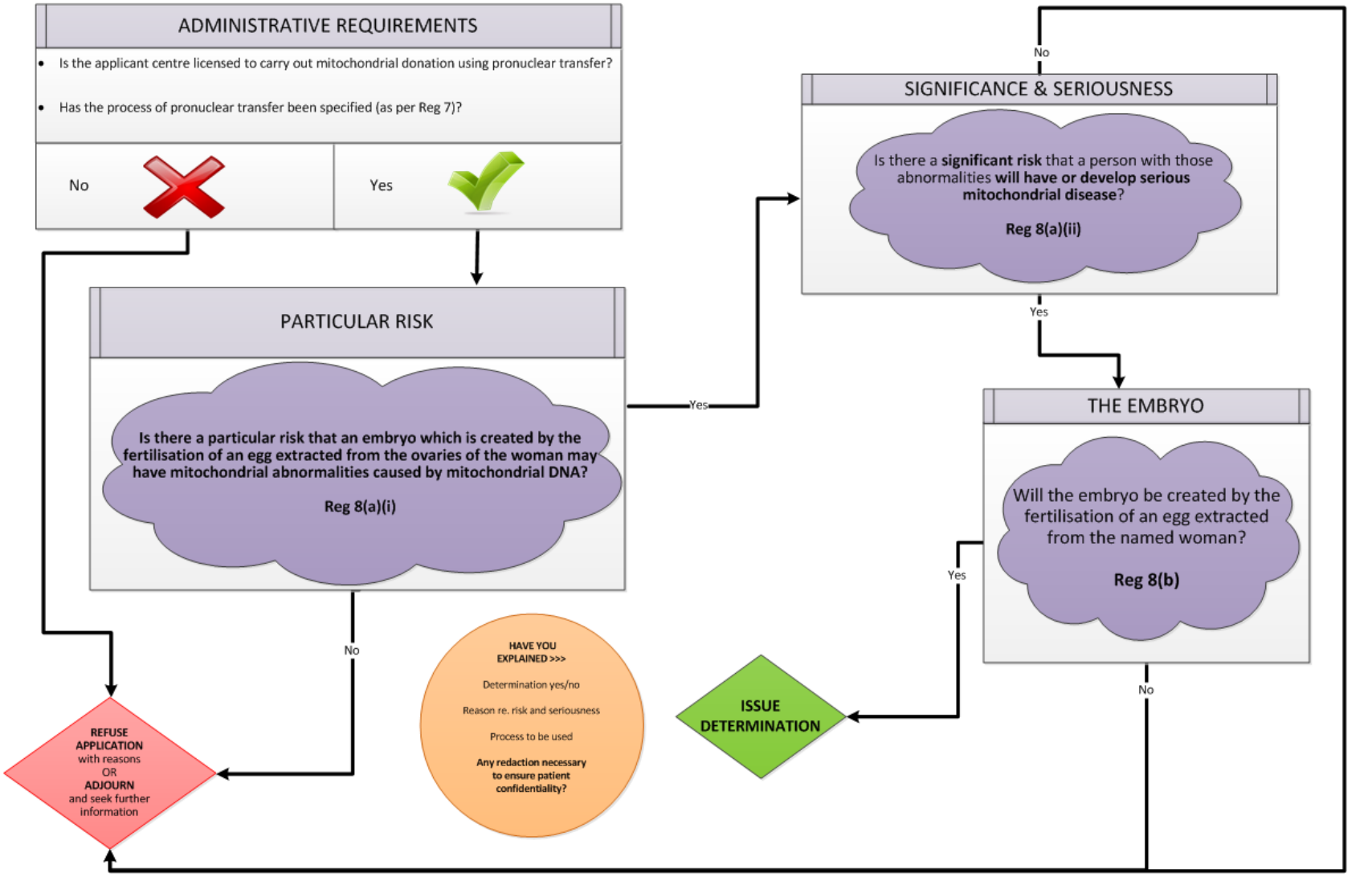
MITOCHONDRIAL DONATION: PRONUCLEAR TRANSFER



Mitochondrial donation: explanatory note for Statutory Approvals Committee

1. Overview

1.1. The Statutory Approvals Committee of the Human Fertilisation and Embryology Authority has produced this explanatory note to set out its approach to the statutory criteria of 'risk' and 'seriousness' which it is required to assess when considering applications to undertake mitochondrial donation. This explanatory note should be read in conjunction with the mitochondrial donation decision tree.

1.2. The approach set out in this explanatory note was approved by the Authority on [DD Month].

1.3. This explanatory note is effective for the Statutory Approvals Committee from [DD Month].

2. Introduction

2.1. Following the introduction of The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (the Regulations) on 29 October 2015 the Authority has delegated the function of considering mitochondrial donation applications to the Statutory Approvals Committee. The Regulations require the Authority to adopt a case by case based approach to the approval of applications which means that the Statutory Approvals Committee will consider applications to perform mitochondrial donation with reference to the particular circumstances of the patient.

2.2. Only clinics that have express provision on their licence to undertake mitochondrial donation can apply to undertake the process on behalf of a particular patient, and only those embryologist(s) approved by the HFEA are permitted to carry out the procedure.

2.3. When making applications to carry out mitochondrial donation, centres will need to assess, on an individual patient basis, whether the particular request for mitochondrial donation is appropriate. The Code of Practice provides guidance on how such decisions should be made.

2.4. When considering mitochondrial donation applications, the Statutory Approvals Committee will take into account material provided with the application, including evidence from the applicant, and any evidence from independent clinical experts and patient groups.

3. Statutory requirements

3.1. Paragraphs 5(a) and (b) and 8(a) and (b) of the Regulations (Annex A) prescribe the criteria that must be met before the Statutory Approvals Committee can issue a determination permitting the application of two mitochondrial donation techniques, pronuclear transfer (PNT) or maternal spindle transfer (MST).

3.2. These criteria include the requirements that:

- there should be a particular risk that an egg or embryo may have mitochondrial abnormalities caused by mitochondrial DNA, and

- there should be a significant risk that the person with the abnormalities will have or develop serious mitochondrial disease.

4. Particular risk

4.1. When considering whether or not there is a particular risk that an embryo may have mitochondrial abnormalities caused by mitochondrial DNA (mtDNA), the Statutory Approvals Committee will take into account evidence of the genetic basis of the inherited disorder.

4.2. This is an objectively measurable criterion. Only a woman with an identified, pathogenic genetic alteration to her mtDNA can be determined to have a particular risk of transmitting this to her embryos.

4.3. Due to the intrinsic variability in the inheritance of those mitochondrial diseases caused by mutations to the mtDNA, the HFEA has determined that any woman harbouring such a genetic alteration is at particular risk of transmitting abnormal mitochondria to her eggs and embryos.

5. Seriousness: general information

5.1. Before the Statutory Approvals Committee can authorise mitochondrial donation treatment for a particular patient it must consider the risk to the patient's child, conceived in the absence of mitochondrial donation, of developing a serious mitochondrial disease.

5.2. In order to frame its assessment of this seriousness the Statutory Approvals Committee will first consider information from the scientific literature relating to the following factors:

a. Symptoms of the disease

It is important for the committee to recognise that the symptoms associated with the same genetic alteration to the mtDNA, can vary from family to family, and person to person, and can range from mild to severe.

The committee should therefore take into account the range of symptoms associated with the mitochondrial disease/genetic alteration, ensuring that they understand the symptoms that manifest when the disease is in its most severe form.

If the symptoms in this worst case scenario are not judged to be sufficiently serious, the Committee will not authorise mitochondrial donation for this patient.

b. Age of onset

As part of its consideration of the seriousness the committee should consider whether symptoms usually manifest at birth or later in life. If the symptoms do manifest later, at which stage (childhood, early adulthood, later)? If the disease is degenerative, how quickly does it progress?

c. Effect of the disease on quality of life of the patient

This will include any evidence about the speed of degeneration in progressive disorders and the extent of any physical and/or intellectual impairment.

d. Are treatments available for the disease or any of its symptoms?

If so, what is the type and extent of the treatments available? How invasive is the treatment or likely treatment?

6. Significant risk: general information

6.1. Mutations to the mtDNA can be present in all mitochondria or in only a proportion. Where all the mitochondria are affected this is known as homoplasmy. While if only a subset are affected this is known as heteroplasmy.

6.2. Where the mutation is heteroplasmic, the proportion of affected mitochondria versus unaffected mitochondria (known as the mutant mitochondrial load) often correlates with the symptoms, with higher loads associated with more severe symptoms. However this is not always the case.

6.3. Before the Statutory Approvals Committee can authorise mitochondrial donation treatment for a particular patient it must consider how significant the risk of developing a serious mitochondrial disease to is to the patient's child, if conceived in the absence of mitochondrial donation.

6.4. This risk will be influenced by the mutant mitochondrial load a child might inherit from its mother as well as the threshold beyond which the mutant mitochondrial load needs to pass in order to cause clinical symptoms.

6.5. In order to understand this risk the Statutory Approvals Committee will first consider information from the scientific literature, which provides information on:

- The usual threshold mutant mitochondrial load necessary to cause clinical manifestation of the mitochondrial disease.
- The degree to which mutant mitochondrial load usually correlates with severity of symptoms of the mitochondrial disease.
- Any cases indicating what the mutant mitochondrial loads were in women who have had children affected by the mitochondrial disease.

6.6. Due to the rare nature of some mitochondrial diseases and the paucity of publications characterising them, information on the threshold level of mtDNA harbouring a pathogenic genetic alteration required to result in the development of a mitochondrial disease may not be available.

6.7. This information is intended to provide a foundation upon which a judgement, based on the patient's individual circumstances, can be made.

6.8. The committee should bear in mind that the mutant mitochondrial load of the patient may not be the same as the load present in her eggs and embryos. This is because the inheritance of mitochondria between a woman and the eggs she produces is unpredictable. This results in women with heteroplasmic mutations producing eggs with a wide range of mutant mitochondrial loads, some of which would be sufficiently high to cause disease while some of which would not.

7. Significant risk and seriousness: patient information

7.1. Based on the information from the scientific literature the Committee should hopefully have an understanding of the possible symptoms a particular mitochondrial disease/alteration to the mtDNA can cause, as well as the mutant mitochondrial load usually necessary to cause a clinical manifestation of disease.

7.2. However, in its assessment of 'significant risk' and 'seriousness', the Statutory Approvals Committee must take into account the circumstances of the individual patients.

7.3. The Committee should consider the following questions:

a. Does the patient's medical history provide evidence of risk and seriousness?

- Does the patient have any symptoms? If so, how severe are they?
  - A patient with symptoms herself may be at significant risk of transmitting a mitochondrial disease with comparable or more serious symptoms to her children.
- Has the patient previously had any children affected by mitochondrial disease? If so, what were their symptoms? What was the age of onset? What was the effect on quality of life? Were any treatments available and what effect did they have? Would this manifestation of mitochondrial disease pass the seriousness test?
  - A patient who has had a child/children affected by a serious mitochondrial disease may be at significant risk of having another child affected by a mitochondrial disease of similar severity.
- Has the patient previously been treated with preimplantation genetic diagnosis (PGD) to avoid transmission of mitochondrial disease? Was the PGD successful? What was the mutant mitochondrial load of the embryos tested? Did any of the embryos have a mutant mitochondrial load above the threshold level usually necessary for clinical manifestation of serious mitochondrial disease?
  - A patient who has had an unsuccessful PGD cycle because no embryos with sufficiently low mutant mitochondrial loads were found may be at significant risk of having eggs with mutant mitochondrial loads sufficiently high to cause a serious mitochondrial disease.
- Likewise a patient who has had a successful PGD cycle in which embryos were found to have mutant mitochondrial loads sufficiently high to cause a serious mitochondrial disease may be at significant risk of transmitting a serious mitochondrial disease to any children conceived in the absence of mitochondrial donation.

b. Does the patient's mutant mtDNA load provide evidence of risk and seriousness?

- Is the patient homoplasmic or heteroplasmic for the mutation? What is the patient's mutant mitochondrial load?
  - A patient who is homoplasmic for the mutation will only have eggs that are homoplasmic for the mutations. Therefore all her children are at risk of developing mitochondrial disease. Her children may have mitochondrial disease similar in severity to her own or that of her relatives.

- A patient who is heteroplasmic for the mutation is likely to have eggs which are also heteroplasmic. However, the mutant mitochondrial load of the patient may not be the same as the load present in her eggs and embryos, which are likely to have considerable variability in mutant mitochondrial load. The committee should consider whether there is evidence from the scientific literature and/or family medical history showing that women with comparable mutant mitochondrial load have had a severely affected child.

c. Does the patient's family history provide evidence of risk and seriousness?

- Does the patient have a family history of mitochondrial disease? How prevalent is mitochondrial disease in the family ie, which family members are/have been affected by mitochondrial disease? For each affected family member, how serious was their disease: what were the symptoms, what was the age of onset, what was the effect on quality of life, were any treatments available and effect did they had?
- What were the mutant mitochondrial loads of affected family members with severe mitochondrial disease and what were the mutant mitochondrial loads of their mothers? Are the mutant mitochondrial loads of female family members who have had severely affected children comparable to the patient?
  - A patient with a family history of serious mitochondrial disease may be at significant risk of having a child with a similar severity of symptoms. This is especially the case if she has a comparable mutant mitochondrial load to that of her female relatives who have had an affected child.
- For each family member, their symptoms, age of onset, effect on quality of life, their mutant mitochondrial load, if any treatment was available, what it was and what effect it had.

8. Decision-making

8.1. The Statutory Approvals Committee will give reasons for the decisions it makes. The reasons will set out clearly the matters that the Statutory Approvals Committee took into account in deciding whether or not to grant approval to perform mitochondrial donation.

9. Publication of minutes

9.1. It is important for transparency that wherever possible documentation of the committee's decision-making process is published and available for public scrutiny. However it is vital that patient confidentiality is upheld.

9.2. Some mitochondrial disease and genetic alterations to the mtDNA are very rare and as such it may be possible to identify a patient by some of the details recorded in the Statutory Approvals Committee minutes.

9.3. The committee should weigh up these two competing principals when deciding whether or not its minutes should be made publicly available, and consider publishing redacted minutes to preserve patient confidentiality where necessary, stating this as the reason.

Annex A: Regulations

5. Permitted egg: circumstances

The circumstances referred to in regulation 5(b) are that

a) The Authority has issued a determination that

1. there is a particular risk that any egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA and
2. there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease; and

b) Egg B was extracted from the ovaries of the woman so named.

8. Permitted embryo: circumstances

The circumstances referred to in regulation 8(b) are that

a) The Authority has issued a determination that

i. there is a particular risk that any embryo which is created by the fertilisation of an egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA,

3. and

ii. there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease,

4. and

b) Embryo B was created by the fertilisation of an egg extracted from the ovaries of the woman so named.

Mitochondrial donation: women's consent to treatment and storage

WMT

About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit www.hfea.gov.uk.

Who should fill in this form?

Fill in this form if you are a woman having mitochondrial donation treatment to avoid passing on an inheritable mitochondrial disease to your child, using embryos created outside the body (in vitro) with your eggs. This may be by in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

What are mitochondria?

Mitochondria are present in almost all human cells, including your eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

What does mitochondrial donation involve?

Your eggs or embryos together with donated eggs, or embryos created outside the body with donor eggs will be used in technique(s) based on IVF, so you can avoid passing on an inheritable mitochondrial disease to your child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both.

Before filling out this form please speak to your clinic about which technique will be used in your treatment.

What are the MST and PNT techniques?

MST and PNT are both techniques of mitochondrial donation allowing eggs or embryos to be created containing your nuclear genetic material (the genes which make you who you are) and donated mitochondria.

In MST, your nuclear genetic material will be removed from your eggs and transferred into donated eggs once their nuclear genetic material has been removed. The eggs containing your nuclear genetic material and the donor's mitochondria will be fertilised with your partner's (or a donor's) sperm to create embryos.

In PNT, your eggs will be fertilised with your partner's (or a donor's) sperm to create embryos. The nuclear genetic material within each embryo (which contains your genetic material) will then be transferred into embryos created using donated eggs and sperm from the sperm provider, from which the nuclear genetic material has been removed.

In both MST and PNT, the resulting embryos containing your and your partner's (or a sperm donor's) genetic material and the donor mitochondria will be transferred to your womb and hopefully implant and develop into a baby. You and the sperm provider, not the egg donor, will be the genetic parents of the child.

If you're unsure of anything, please ask your clinic for more information.

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date embryos were placed in storage

Date embryos can remain in storage until

What do I need to know before filling in this form?

You should be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic.

There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid. If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your eggs, or embryos created outside the body (in vitro) with your eggs, to be used or stored (which includes mitochondrial donation).

If following MST or PNT your eggs or embryos are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage.

Once your nuclear genetic material has been transferred into the donor eggs or embryos, you (and the sperm provider) will determine what happens to them, including how long they will be stored for.

The eggs and embryos that have had your nuclear material removed will be discarded.

You are also legally required to record what you would like to happen to your eggs and embryos if you were to die or lose the ability to decide for yourself (become mentally incapacitated). While this is perhaps not something you have considered, your clinic needs to know this so that they only allow your eggs and embryos to be used according to your wishes.

If you are unsure of anything in relation to this, please ask your clinic.

Why are there questions about using my eggs for training purposes?

There may be some eggs or embryos left after treatment, which you do not wish to use (eg, because you do not want future treatment or the eggs and embryos are not viable for treatment).

This form allows you to consent to donate eggs or embryos (containing your nuclear genetic material) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF-based treatments.

What if I want to donate my eggs and/or embryos?

Unused eggs and embryos can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any eggs or embryos (containing your nuclear genetic material) to research, speak to your clinic who will provide you with any relevant consent form(s).

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.

When you have completed the form you may request a copy of it from your clinic.

1. About you

First name(s) Surname

Date of birth NHS/CHI/HCN number (please circle)

2. About your partner

Your partner's first name(s) Your partner's surname

Your partner's date of birth Your partner's NHS/CHI/HCN number

3. About your treatment

3.1. Do you consent to your eggs undergoing MST and embryos created from eggs following MST being used in your treatment?

This process will involve:

- your eggs undergoing the MST process (this means that your nuclear genetic material will be removed from your eggs and transferred into a 'new' egg containing donor mitochondria but no donor nuclear genetic material. The egg containing your mitochondria will be discarded.),
- the eggs, following the MST process (containing your nuclear genetic material and donor mitochondria), being used to create embryos outside of the body, and
- those embryos being used in your treatment (embryo transfer).

☐ Yes ☐ No

3.2. Do you consent to your eggs being used to create embryos outside of the body which will undergo PNT and be used in your treatment? This process will involve:

- your eggs being used to create embryos outside the body (those embryos will contain your and the sperm provider's nuclear genetic material),
- those embryos (containing your nuclear genetic material) undergoing the PNT process (this means that genetic material will be removed from your embryo and transferred into a 'new' embryo containing donor mitochondria but no donor nuclear genetic material. The embryonic material containing your mitochondria will be discarded), and
- those embryos (containing your nuclear genetic material and donor mitochondria), used in your treatment (embryo transfer).

☐ Yes ☐ No

Page declaration signature Date

4. Storing eggs and embryos

You may wish to store any eggs and/or embryos before or after they have undergone MST or PNT so they can be used in future treatment.

To be stored, eggs or embryos are frozen or 'vitrified'. When considering how long to store for, you may want to think about how far in the future you might want/be able to use your stored eggs and embryos and the costs of storing – ask your clinic if you are unsure.

The law permits you to store for any period up to 10 years but in cases where you or your partner are prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

Please note that any arrangements you need to make regarding the practicalities of storage with your clinic or funding body are separate from this consent. For example, your clinic may only continue to store your eggs and/or embryos for the period you have specified in this form if you, or your funding provider, continue to pay the storage fees.

4.1. Do you consent to your eggs (containing your nuclear genetic material and donated mitochondria, or your nuclear genetic material and mitochondria) being stored?

☐ Yes ☐ No

4.2. For how long do you consent to these eggs being stored? **Only complete this section if you answered yes to section 4.1.**

☐ 10 years

☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

4.3. Do you consent to embryos (containing your nuclear genetic material and donated mitochondria, or your nuclear genetic material and mitochondria) being stored? **Please note that embryos can only be stored if the sperm provider (whose nuclear genetic material is being used) has also given his consent.**

☐ Yes ☐ No

4.4. For how long do you consent to these embryos being stored? **Only complete this section if you answered yes to section 4.3.**

☐ 10 years

☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

Page declaration signature Date

4.5. *Please note here if you would like to specify different storage period for eggs or embryos before or after they have undergone MST or PNT, or if you want to restrict your consent to only eggs or embryos at a certain stage (ie, pre or post MST or PNT). Your consent to store eggs or embryos prior to the MST or PNT process is not needed on this form if you have already completed the GS or WT form.*

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your eggs and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

5. Using eggs and embryos in training

5.1. Do you consent to eggs surplus to your treatment being used for training purposes?

☐ Yes ☐ No

5.2. Do you consent to embryos (already created outside the body containing your nuclear genetic material) surplus to your treatment being used for training purposes? **Please note that embryos can only be used if the sperm provider (whose nuclear genetic material is being used) has also given his consent.**

☐ Yes ☐ No

6. In the event of your death or mental incapacity

As part of your consent, you also need to decide what you would like to happen to your eggs, or embryos containing your nuclear genetic material, if you die or lose the ability to decide for yourself (become mentally incapacitated). Please note your eggs or embryos may only be used within the storage period you consented to above. If you do not give your consent in the section below, your eggs or embryos must be allowed to perish in the event of your death or mental incapacity and cannot be used for treatment.

6.1. Do you consent to eggs being used for training purposes?

If you die	If you become mentally incapacitated
☐ Yes ☐ No	☐ Yes ☐ No

6.2. Do you consent to embryos (already created outside the body containing your nuclear genetic material) being used for training purposes? Please note that embryos can only be used if the sperm provider (whose nuclear genetic material is being used) has also given his consent.

If you die	If you become mentally incapacitated
☐ Yes ☐ No	☐ Yes ☐ No

Page declaration signature Date

If you are storing eggs or embryos following MST or PNT you may wish for them to be used in someone else's treatment if you die or become mentally incapacitated, please speak to your clinic for more information.

Depending on your circumstances, you will need to complete one of the following:

- 'Your consent to donating your eggs' (WD form),
- 'Your consent to donating embryos' (ED form), or
- 'Women's consent to the use and storage of eggs or embryos for surrogacy' (WSG form).

7. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the time of embryo transfer, use of eggs or embryos in training, or the eggs or embryos have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because she is unable to sign for herself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with her direction.

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

Mitochondrial donation: men's consent to treatment and storage

MMT

About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit www.hfea.gov.uk.

Who should fill in this form?

Fill in this form if you are a man and your partner is having mitochondrial donation treatment using embryos created outside the body (in vitro) with your sperm. This may be by in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

What are mitochondria?

Mitochondria are present in almost all human cells, including your partner's eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

What does mitochondrial donation involve?

Your sperm will be used to create embryos with donated eggs and/or your partner's eggs, by IVF or ICSI, so your partner can avoid passing on an inheritable mitochondrial disease to your child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both. Before filling out this form please speak to your clinic about which technique will be used in your partner's treatment.

What are the MST and PNT techniques?

MST and PNT are both techniques of mitochondrial donation allowing embryos to be created for you containing your and your partner's nuclear genetic material (the genes which make you who you are) and donated mitochondria.

In MST, the nuclear genetic material will be removed from your partner's eggs and transferred into donated eggs with mitochondria which have had the donor's nuclear genetic material removed. Your sperm will then be used with these eggs to create embryos containing your and your partner's nuclear genetic material and donated mitochondria.

In PNT, your sperm may be used for two stages: -

Stage one – your sperm will be used to create embryos with your partner's eggs. The nuclear genetic material will be removed and transferred into embryos created in stage two. Once the nuclear genetic material has been removed the embryonic material created in stage one will be discarded.

Stage two – either your sperm or donor sperm (for example, if you are genetically related to the egg donor) will be used to create embryos with donated eggs. The nuclear genetic material will be removed, discarded, and replaced with the nuclear genetic material removed from the embryos created in stage one, above.

Following both MST and PNT, the embryos containing your and your partner's genetic material and the donor's mitochondria will be transferred to your partner's womb and hopefully implant and develop into a baby. You

For clinic use only (optional)

HFEA centre reference	Other relevant forms

Date embryos were placed in storage	Date embryos can remain in storage until

and your partner, not the donor, will be the

What do I need to know before filling in this form?

You should be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, and embryos created using your sperm, to be used or stored. If your sperm or embryos following MST or PNT are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage.

In MST once eggs containing your partner's nuclear genetic material have been fertilised with your sperm to create embryos, you (and your partner) will determine what happens to them, including how long they will be stored for.

In PNT embryos will be created from donated eggs and your (or donor) sperm. The nuclear genetic material will be removed from those embryos and replaced with the nuclear genetic material from embryos created with your sperm and your partner's eggs.

genetic parents of the child.
Once PNT takes place you (and your partner) will determine what happens to them, including how long they will be stored for. The embryos that have had their nuclear genetic material removed will be discarded.

You are also legally required to record what you would like to happen to your sperm and embryos if you were to die or lose the ability to decide for yourself (become mentally incapacitated). While this is perhaps not something you have considered, your clinic needs to know this so that they only allow your sperm and embryos to be used according to your wishes.

If you are unsure of anything in relation to this, please ask your clinic.

Why are there questions about using my sperm and embryos for training?

There may be some sperm or embryos left after treatment, which you do not wish to use (eg, because you do not want future treatment or the sperm and embryos are not viable for treatment).

This form allows you to consent to donate sperm or embryos (containing your nuclear genetic material) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF-based treatments.

What if I want to donate my sperm/embryos?

Unused sperm and embryos can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any sperm or embryos (containing your nuclear genetic material) to research, speak to your clinic who will provide you with any relevant consent form(s).

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.

When you have completed the form you may request a copy of it from your clinic.

1. About you

First name(s) Surname

Date of birth NHS/CHI/HCN number (please circle)

2. About your partner

Your partner's first name(s) Your partner's surname

Your partner's date of birth Your partner's NHS/CHI/HCN number

3. About your treatment

3.1. Do you consent to your sperm being used to create embryos outside of the body with eggs that have undergone MST for use in your partner's treatment?

This process will involve:

- eggs undergoing the MST process (this means that your partner's nuclear genetic material will be removed from her eggs and transferred into a 'new' egg containing donor mitochondria but no donor nuclear genetic material),
- your sperm being used to create embryos (containing your and your partner's nuclear genetic material and donor mitochondria) with the eggs that have undergone MST, and
- those embryos being used for your partner's treatment (embryo transfer).

☐ Yes ☐ No

PNT - stage one

3.2. Do you consent to your sperm being used to create embryos outside of the body with your partner's eggs (eg, through IVF or ICSI, then PNT) for use in your partner's treatment?

This process will involve:

- your sperm being used to create embryos with your partner's eggs,
- the embryos undergoing the PNT process (this means that your and your partner's nuclear genetic material will be removed and transferred into the embryos created in stage two. Once your nuclear genetic material has been removed from the embryos, the embryonic material will be discarded), and
- the embryos (containing your and your partners nuclear genetic material and donor mitochondria) to be used in your partner's treatment (embryo transfer).

☐ Yes ☐ No

Page declaration signature Date

PNT - stage two

3.3. Do you consent to your sperm being used to create embryos outside of the body with donor eggs and for those embryos to undergo the PNT process? **Do not complete this section if donor sperm is used for this stage (eg, if you are genetically related to the egg donor).**

This process will involve:

- your sperm being used to create embryos with donated eggs outside the body
- the embryos undergoing the PNT process (this means that your and the donor's nuclear genetic material will be removed, discarded, and replaced with your and your partner's nuclear genetic material from the embryos created in stage one), and
- those embryos (containing your and your partners nuclear genetic material and donor mitochondria) to be used in your partner's treatment (embryo transfer).

☐ Yes ☐ No

4. Storing sperm and embryos

You may wish to store any sperm and/or embryos before or after MST or PNT so they can be used in future treatment.

To be stored, sperm or embryos are frozen or 'vitrified'. When considering how long to store for, you may want to think about how far in the future you might want/be able to use your stored sperm and embryos and the costs of storing – ask your clinic if you are unsure. The law permits you to store for any period up to 10 years but in cases where you or your partner are prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

Please note that any arrangements you need to make regarding the practicalities of storage with your clinic or funding body are separate from this consent. For example, your clinic may only continue to store your sperm and/or embryos for the period you have specified in this form if you, or your funding provider, continue to pay the storage fees.

4.1. Do you consent to your sperm being stored?

☐ Yes ☐ No

4.2. For how long do you consent to your sperm being stored? **Only complete this section if you answered yes to section 4.1.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years:

4.3. Do you consent to embryos (containing your and your partner's or donor's nuclear genetic material and your partner's or donor's mitochondria) being stored?

☐ Yes ☐ No

4.4. For how long do you consent to your embryos being stored? **Only complete this section if you answered yes to section 4.3.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years:

4.5. *Please note here if you would like to specify different storage period for embryos before or after they have undergone PNT, or if you want to restrict your consent to only embryos at a certain stage (ie, pre or post PNT). Your consent to store sperm, or embryos prior to the PNT process, is not needed on this form if you have already completed the GS or MT form.*

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

5. Using sperm and embryos in training

5.1. Do you consent to sperm surplus to your treatment being used for training purposes?

☐ Yes ☐ No

5.2. Do you consent to embryos (already created outside the body which contain your nuclear genetic material) surplus to your treatment being used for training purposes? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

☐ Yes ☐ No

6. In the event of your death or mental incapacity

As part of your consent, you also need to decide what you would like to happen to your sperm, or embryos containing your nuclear genetic material, if you die or lose the ability to decide for yourself (become mentally incapacitated). Please note that if you would like your partner to use your sperm or embryos in the event of your death or mental incapacity, your partner should be named on this form. Your embryos may only be used within the storage period you consented to above. If you do not give your consent in the below section, your sperm or embryos must be allowed to perish in the event of your death or mental incapacity and cannot be used for treatment.

6.1. Do you consent to your sperm being used to create embryos outside the body for your partner's treatment? **Please note that the egg provider also has to give her consent for embryos to be created.**

If you die ☐ Yes ☐ No If you become mentally incapacitated ☐ Yes ☐ No

Page declaration signature Date

6.2. Do you consent to embryos (already created outside the body which contain your nuclear genetic material) being used for your partner's treatment? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

If you die ☐Yes ☐No If you become mentally incapacitated ☐Yes ☐No

6.3. Do you consent to your sperm being used for training purposes?

If you die ☐Yes ☐No If you become mentally incapacitated ☐Yes ☐No

6.4. Do you consent to embryos (already created outside the body which contain your nuclear genetic material) being used for training purposes? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

If you die ☐Yes ☐No If you become mentally incapacitated ☐Yes ☐No

If you are storing sperm or embryos following MST or PNT (containing your genetic material and donor mitochondria) you may wish for them to be used in someone else's treatment if you die or become mentally incapacitated, please speak to your clinic for more information. Depending on your circumstances, you will need to complete one of the following:

- 'Your consent to donating your sperm' (MD form)
- 'Your consent to donating embryos' (ED form), or
- 'Men's consent to the use and storage of sperm or embryos for surrogacy' (MSG form).

Consent to birth registration

Complete this part of section six if you consented to your sperm, or embryos created outside the body which contain your nuclear genetic material, being used in your partner's treatment after your death. If you have given your consent to your sperm or embryos (to be created outside the body which contain your nuclear genetic material) being used after your death, you may also wish to consent to being registered as the legal father of any child that is born as a result of your partner's treatment.

6.5. Do you consent to being registered as the legal father of any child born as a result of your partner's treatment after your death?

By ticking yes, you consent to the following:

- I consent to my name, place of birth and occupation being entered on the register of births as the legal father of any child born from my partner's treatment. This register is kept under the Births and Deaths Registration Act 1953, or the Births and Deaths Registration (Northern Ireland) Order 1976, or the Registration of Births, Deaths and Marriages (Scotland) Act 1965.
- I also consent to information about my or my partner's treatment being disclosed to my partner and one of the following registrars:
  - the Registrar General for England and Wales
  - the Registrar General for Scotland
  - the Registrar for Northern Ireland.

Please note that being recorded in the register of births as the legal father of a child born from your partner's treatment does not transfer any inheritance or other legal rights to the child.

☐Yes ☐No

Page declaration signature Date

7. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the time of embryo transfer, use of sperm or embryos in training, or the sperm or embryos have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction.

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

Mitochondrial donation: your consent WDM

About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit www.hfea.gov.uk.

Who should fill in this form?

Fill in this form if you are a woman donating eggs and/or embryos created with your eggs for use in other women's mitochondrial donation treatment so that she can avoid passing on an inheritable mitochondrial disease to her child.

What are mitochondria?

Mitochondria are present in almost all human cells, including your eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

What does mitochondrial donation involve?

You will be donating eggs (containing your mitochondria) to other women who have mitochondria containing gene abnormalities, for use in IVF-based treatment so that they can avoid passing on an inheritable mitochondrial disease to their child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both.

What are the MST and PNT techniques?

In MST, your nuclear genetic material (the genes which make us who we are) will be removed from your eggs and replaced with the nuclear genetic material from the intended mother's egg. The nuclear genetic material removed from your eggs will be discarded.

Following MST, the eggs containing your mitochondria will be fertilised with the intended father's (or a donor's) sperm to create embryos which will be used in the intended mother's treatment.

This means that the intended mother, not you, will be the genetic parent of any child that is born.

In PNT, your eggs will be fertilised with the intended father's (or a donor's) sperm to create embryos. The nuclear genetic material within these embryos will then be removed and discarded. It will be replaced with the nuclear genetic material removed from embryos created using the intended mother's eggs and father's (or donor's) sperm. This means that they, not you, will be the genetic parents of the child.

If you're unsure of anything, please ask your clinic for more information.

What do I need to know before filling in this form?

Before you fill in this form, you should have completed the 'Mitochondrial donor registration form'.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date eggs were placed in storage

Date eggs can remain in storage until

  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your eggs, or embryos created outside the body (in vitro) with your eggs, to be used or stored.

If your eggs or embryos containing your nuclear genetic material are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage. Once your nuclear genetic material has been removed and replaced with that of the intended mother and sperm provider, they will determine what happens to them, including how long they will be stored for.

Why are there questions about using my eggs and embryos for training purposes?

There may be some eggs or embryos left after treatment, eg, because they weren't viable for treatment. This form allows you to consent to donate eggs or embryos (before your nuclear genetic material is removed) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF treatment.

What if I want to donate my eggs for other purposes?

If you also wish to donate your eggs for regular egg donation (where your eggs are donated to someone to help them conceive rather than avoid passing on a mitochondrial disease), you must complete the 'Your consent to donating your eggs' (WD form). If you have entered into an egg sharing agreement, you must complete the 'Women's consent to treatment and storage form (IVF and ICSI)' (WT form).

Eggs can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially developing new treatments. If you would like to donate any eggs or embryos (before your nuclear genetic material is removed) to research, speak to your clinic who will provide you with the relevant consent form(s).

What if I want to withdraw my consent?

You can withdraw your consent at any point up until your genetic material is removed from your eggs, or in PNT, the embryos are created with your eggs. After this point you will no longer have any rights over the eggs or embryos and cannot withdraw consent to its use in treatment, storage or training.

What happens to my eggs or embryos if I die?

By consenting to mitochondrial donation, you are also agreeing to your eggs or embryos (before your nuclear genetic material is removed) being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your eggs or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.3).

Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity. If you're unsure of anything in relation to this, please ask your clinic.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given. When you have completed the form you may request a copy of it from your clinic.

1. About you

First name(s) Surname

Date of birth NHS/CHI/HCN number (please circle)

2. About your mitochondrial donation

2.1. Do you consent to your eggs undergoing MST and for embryos created from eggs following MST being used for the treatment of others?

This process will involve:

- your eggs undergoing the MST process (this means that your nuclear genetic material will be removed from your eggs and replaced with the intended mother's nuclear genetic material. Your nuclear genetic material will be discarded),
- the eggs, following MST (containing your mitochondria and the intended mother's nuclear genetic material) being used to create embryos outside of the body, and
- those embryos being used in the intended mother's treatment (embryo transfer).

☐ Yes ☐ No

2.2. Do you consent to your eggs being used to create embryos outside of the body which will undergo PNT and be used in the treatment of others?

This process will involve:

- your eggs being used to create embryos outside of the body (those embryos will contain your and the sperm provider's nuclear genetic material),
- the embryos undergoing the PNT process (this means that your nuclear genetic material will be removed from the embryo, discarded, and replaced with the intended mother's and sperm provider's nuclear genetic material), and
- those embryos (containing your mitochondria and the intended mother's and sperm provider's nuclear genetic material) being used in the intended mother's treatment (embryo transfer).

☐ Yes ☐ No

Page declaration signature Date

2.3. Do you have any restrictions you would like to apply to questions 2.1 and 2.2 above?

You may want to put restrictions on who your eggs, or in PNT, embryos created with your eggs, can be used by (eg, a specified named recipient). Another example may be that you do not wish for your eggs or embryos to be used in the event of your death or mental incapacity. If so, please state it here. Please note that you can only place restrictions on eggs or embryos that still contain your nuclear genetic material (ie, before they have undergone the MST or PNT process).

☐ Yes - specify your restrictions below then continue to section 3.

☐ No - go to section 3.

3. Using eggs and embryos in training

3.1. Do you consent to your eggs (containing your nuclear genetic material) being used for training purposes?

☐ Yes ☐ No

(For PNT only)

3.2. Do you consent to your embryos (containing your nuclear genetic material) already created outside the body with your eggs being used for training purposes?

☐ Yes ☐ No

4. Storing eggs and embryos

If your eggs or embryos are going to be stored before MST or PNT (eg, before your nuclear genetic material is removed), you must consent to this and state in writing how long you consent to them remaining in storage.

The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your eggs and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

A medical practitioner will need to certify in writing that the medical criteria for premature infertility have been met for storage to continue for more than 10 years. When the criteria have been met, the storage period will be extended by 10 years from the date the criteria are met.

The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

Once your nuclear genetic material has been removed from your eggs or embryos, the intended mother and sperm provider (together with the clinic) will determine how long the eggs or embryos will be stored for.

4.1. Do you consent to your eggs (containing your nuclear genetic material) being stored?

☐ Yes ☐ No

Page declaration signature Date

4.2. For how long do you consent to eggs (containing your nuclear genetic material) being stored? Only complete this section if you answered yes to section 4.1. **Please talk to your clinic if you're unsure of how long to store for.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

PNT only

4.3. Do you consent to embryos (containing your nuclear genetic material) being stored?

☐ Yes ☐ No

4.4. For how long do you consent to embryos (containing your nuclear genetic material) being stored? **Only complete this section if you answered yes to question 4.3. Please talk to your clinic if you're unsure of how long to store for.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your eggs and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the nuclear genetic material has been removed from my eggs, or in PNT, embryos created with my eggs.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature Date

If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because she is unable to sign for herself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with her direction.

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

Mitochondrial donation: consent to sperm donation (PNT only)

MD (PNT only)

About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit www.hfea.gov.uk.

Who should fill in this form?

If you are a man donating sperm and/or embryos created with your sperm for the treatment of others – specifically for use in mitochondrial donation treatment so that women can avoid passing on inheritable mitochondrial disease to their children.

What are mitochondria?

Mitochondria are present in almost all human cells, including in a woman's eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

What does mitochondrial donation involve?

Your sperm will be used to create embryos with donated eggs and/or the intended mother's eggs, by IVF or ICSI, so the intended mother can avoid passing on an inheritable mitochondrial disease to her child. The IVF-based technique used to achieve this is called pronuclear transfer (PNT).

What is the PNT technique?

PNT is a technique of mitochondrial donation.

It allows embryos to be created for women who have mitochondrial gene abnormalities containing their nuclear genetic material (the genes which make us who we are) and donated mitochondria.

There are two stages to the technique. A woman may need to use donor sperm for both stages of the technique (eg, if she does not have a partner who can provide sperm for her treatment), or may only need donor sperm for the second stage of PNT (eg, if the intended father is genetically related to the egg donor providing the mitochondria).

On this form you can consent to donate your sperm for both stages of the technique or for the second stage only:

Stage one – your sperm will be used to create embryos with the intended mother's eggs. Both your nuclear genetic material will be removed and transferred into embryos created in stage two below. Once your and the intended mother's nuclear genetic material is removed the embryonic material created in stage one will be discarded. If you donate sperm for this stage you will be genetically related to the child. You will not have any financial or legal obligations to the child. Your identifying information will be passed on to any child born as a result of your donation upon request after they have reached 18 years old. For more information, see www.hfea.gov.uk/egg-and-sperm-donors.html.

Stage two – your sperm will be used to create embryos with donor eggs. The genetic material will be removed, discarded, and replaced with the nuclear genetic material from the intended mother and sperm provider from the embryos created in stage one, above. If you only donate sperm for this stage you will not be genetically related to the child. No information that could identify you will be released to any child born following the mitochondrial donation treatment.

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date sperm were placed in storage

Date sperm can remain in storage until

What do I need to know before filling in this form?

Before you fill in this form, you should have completed the 'Donor information form' if you are providing sperm for both stages of the technique and going to be genetically related to the child, or the 'Mitochondrial donation:
PNT only sperm donor registration form' if you are providing sperm for stage two only and not going to be genetically related to the child.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions.

This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid. If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, or embryos created outside the body (in vitro) with your sperm, to be used or stored.

If your sperm or embryos containing your nuclear genetic material are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage. If you donate sperm for stage two only, once your nuclear genetic material has been removed and replaced with that of the intended parents, they will determine what happens to them, including how long they will be stored for.

You can make changes to or withdraw your consent to embryos created with your sperm in stage one at any point until the embryos have been transferred, used in training, or have been allowed to perish. For embryos created in stage two with your sperm, you can withdraw your consent at any point up until the nuclear genetic material has been removed from the embryos.

Why are there questions about using my sperm for training purposes?

There may be some sperm or embryos left after treatment, eg, because they weren't viable for treatment. This form allows you to consent to donate sperm or embryos (before your nuclear genetic material is removed) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF treatment.

What if I want to donate my sperm for other purposes?

If you also wish to donate your sperm for use in fertility treatment which does not involve PNT you must complete a separate form 'Your consent to donating your sperm' (MD form).

Sperm can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any sperm or embryos to research, speak to your clinic who will provide you with the relevant consent form(s).

What happens to my sperm or embryos if I die?

By consenting to the use of your sperm in PNT, you are also agreeing to your sperm or embryos being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your sperm or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.4). Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity. If you're unsure of anything in relation to this, please ask your clinic.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given. When you have completed the form you may request a copy of it from your clinic.

1. About you

First name(s) Surname

Date of birth NHS/CHI/HCN number (please circle)

2. About your sperm donation

PNT - stage one

2.1. Do you consent to your sperm being used to create embryos outside of the body (eg, through IVF or ICSI, then PNT) and for those embryos to be used for the treatment of others? **Do not complete this section if you are only providing sperm for stage two of PNT.**

This process will involve:

- your sperm being used to create embryos with the intended mother's eggs outside the body,
- the embryos undergoing the PNT process (this means that both your and the intended mother's nuclear genetic material will be removed and inserted into the embryos created in stage two). Once the nuclear genetic material has been removed from the embryos, the embryonic material will be discarded), and
- the embryos (containing your and the intended mother's nuclear genetic material and donor mitochondria) to be used in the treatment of others (embryo transfer).

☐ Yes ☐ No

PNT - stage two

2.2. Do you consent to your sperm being used to create embryos outside of the body with donor eggs and for those embryos to undergo the PNT process?

This process will involve:

- your sperm being used to create embryos with donated eggs outside the body, and
- the embryos undergoing the PNT process (this means your and the egg donor's nuclear genetic material will be removed and discarded).

☐ Yes ☐ No

Page declaration signature Date

2.3. How many families may have children using your donated sperm? **Do not complete this section if you are only providing sperm for stage two of PNT.**

The maximum number is 10 families. This is to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related.

It is also based on the perceived interests of donor-conceived people and their parents in maintaining a relatively small number of siblings. Consenting to 10 families will help the greatest number of families and maximise the potential of your donation. You should think about how many families you are comfortable donating to and the long-term implications of donation.

families may have children using my donated sperm.

2.4. Do you have any restrictions that you would like to apply to questions 2.1 and 2.2 above?

You may want to put restrictions on who can use embryos created with your sperm (eg, a specified named recipient). Another example may be that you do not wish for your embryos to be used in the event of your death or mental capacity. If so, please state it here. Please note that you can only place restrictions on embryos that still contain your nuclear genetic material (ie, before they have undergone the PNT process).

☐ Yes - specify your restrictions below then continue to section 3.

☐ No - go to section 3.

3. Using sperm and embryos in training

3.1. Do you consent to your sperm being used for training purposes?

☐ Yes ☐ No

3.2. Do you consent to your embryos (already created outside the body with your nuclear genetic material) being used for training purposes?

Please note that embryos can only be used if the female provider of the nuclear genetic material has also given her consent.

☐ Yes ☐ No

4. Storing sperm and embryos

Please note that sperm donated for the treatment of others needs to be stored.

4.1. Do you consent to your sperm being stored?

☐ Yes ☐ No

Page declaration signature Date

4.2. Do you consent to embryos (containing your nuclear genetic material) being stored?

Please note that embryos can only be stored if the female provider of the nuclear genetic material has also given her consent.

☐ Yes ☐ No

If you have answered no to both 4.1 and 4.2, sign the page declaration on this page then go to section five. If you have answered yes to 4.1 or 4.2, or both, then continue below.

Sperm and embryo storage periods

In this section you must state how long you consent to your sperm and/or embryos containing your nuclear genetic material being stored for. You may want to think about how far in the future you want others to use your stored sperm and embryos – ask your clinic if you are unsure.

The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your sperm and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

A medical practitioner will need to certify in writing that the medical criteria for premature infertility have been met for storage to continue for more than 10 years. When the criteria have been met, the storage period will be extended by 10 years from the date the criteria are met.

The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

Once your sperm or embryos have been allocated to someone else's treatment, the patient (together with the clinic) will determine how long the sperm and embryos are stored for within the boundaries of what you have consented to in this form. If you are only providing sperm for stage two of the PNT process, once your nuclear genetic material is removed the intended mother and sperm provider will determine how long the embryos will be stored for.

4.3. For how long do you consent to your sperm, being stored? **Only complete this section if you answered yes to section 4.1. Please talk to your clinic if you're unsure of how long to store for.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

4.4. For how long do you consent to embryos being stored? **Only complete this section if you answered yes to question 4.2. Please talk to your clinic if you're unsure of how long to store for.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for.

Page declaration signature Date

For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you would complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that if my sperm is used to create embryos with the intended mother's eggs (stage one of the PNT process) I can make changes to or withdraw my consent at any point until the embryos have been transferred, used in training, or have been allowed to perish.
  - I understand that if my sperm is used only to create embryos with the donor's eggs (stage two of the PNT process), I can make changes to, or withdraw, my consent at any point until my genetic material has been removed.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

Consent to donating your sperm (including for use in pronuclear transfer)

MD (including PNT)

About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit www.hfea.gov.uk.

Who should fill in this form?

Fill in this form if you are a man donating sperm for the treatment of others (by artificial insemination or IVF) or for training purposes (to allow healthcare professionals to learn about, and practice, the techniques involved in fertility treatment).

In some cases the IVF process may also involve the use of a technique called pronuclear transfer (PNT) which can be used to allow women to avoid passing on an inheritable mitochondrial disease to her child.

Mitochondria are present in almost all human cells, including in a woman's eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

What is the PNT technique?

PNT is a technique of mitochondrial donation allowing embryos to be created for women who have mitochondrial gene abnormalities containing their nuclear genetic material (the genes which make us who we are) and donated mitochondria.

There are two stages to the technique. A woman may need to use donor sperm for both stages of the technique (eg, if she does not have a partner who can provide sperm for her treatment), or may only need donor sperm for the second stage of PNT (eg, if the intended father is genetically related to the egg donor providing the normal mitochondrial).

Stage one - your sperm will be used to create embryos with the intended mother's eggs. Both your nuclear genetic material will be removed and transferred into embryos created in stage two below. Once you and the intended mother's nuclear genetic material is removed the embryonic material created in stage one will be discarded.

Stage two – your sperm will also be used to create embryos with donor eggs. The genetic material will be removed, discarded, and replaced with the nuclear genetic material from the intended mother and your sperm from the embryos created in stage one, above. These new embryos will be used in the treatment of others (embryo transfer).

If your sperm is used for both stages of the PNT process you will be genetically related to the child in the same way as if your sperm is used for IVF.

What do I need to know before filling in this form?

Before you fill in this form, you should complete the 'Donor information form'.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form

For clinic use only (optional)

HFEA centre reference	Other relevant forms
Date sperm were placed in storage	Date sperm can remain in storage until

  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how you can make changes to, or withdraw your consent.
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, or embryos created outside the body (in vitro) with your sperm, to be used or stored (for example, for in vitro fertilisation (IVF) treatment).

If you are storing your sperm or embryos, you must also state in writing how long you consent to them remaining in storage.

What if I want to donate my sperm for research?

Sperm can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. This form only allows you to consent to donate sperm for the treatment of others or for training purposes.

Your clinic can give you more information about donating for research and provide you with the relevant consent form(s).

What happens to my sperm or embryos if I die?

By consenting to donate your sperm or embryos, you are also agreeing to them being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your sperm or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.5 of this form). You may also state here that you only want your sperm or embryos to be donated in the event of your death.

Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.

When you have completed the form you may request a copy of it from your clinic.

1. About you

First name(s) Surname

Date of birth NHS/CHI/HCN number (please circle)

2. About your sperm donation

2.1. Do you consent to your sperm being used for the treatment of others, without the creation of embryos outside the body, ie, using artificial insemination?

Examples of artificial insemination include intrauterine insemination (IUI) or gamete intra-fallopian transfer (GIFT), a technique which a small number of clinics use.

☐ Yes ☐ No

2.2. Do you consent to your sperm being used to create embryos outside the body (eg, through IVF treatment) and for these embryos to be used for the treatment of others?

☐ Yes ☐ No

2.3. Do you consent to your sperm being used to create embryos outside the body (eg, through IVF treatment), for those embryos to undergo the PNT process (both stages 1 and 2 outlined above) and for resulting embryos (containing your nuclear genetic material) to be used for the treatment of others?

☐ Yes ☐ No

2.4. How many families may have children using your donated sperm?

The maximum number is 10 families. This is to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related. It is also based on the perceived interests of donor-conceived people and their parents in maintaining a relatively small number of siblings. Consenting to 10 families will help the greatest number of families and maximise the potential of your donation. You should think about how many families you are comfortable donating to and the long-term implications of donation.

families may have children using my donated sperm.

Page declaration signature Date

2.5. Do you have any restrictions that you would like to apply to any of your answers to 2.1, 2.2, and 2.3 above? You may want to put restrictions on who your sperm or embryos are used by, eg, a specified named recipient.

☐ Yes - specify your restrictions below then continue to section 3.

☐ No - go to section 3.

3. Using sperm and embryos in training

3.1. Do you consent to your sperm being used for training purposes?

☐ Yes ☐ No

3.2. Do you consent to your embryos (already created outside the body with your sperm) being used for training purposes?

☐ Yes ☐ No

4. Storing sperm and embryos

Please note that sperm donated for the treatment of others needs to be stored.

4.1. Do you consent to your sperm being stored?

☐ Yes ☐ No

4.2. Do you consent to embryos (created outside the body with your sperm) being stored? Only complete this section if you answered yes to section 2.2 or 2.3. Please note that embryos can only be stored if the egg provider has also given her consent.

☐ Yes ☐ No

If you have answered no to both 4.1 and 4.2, sign the page declaration on this page and then go to section five.

If you have answered yes to 4.1 or 4.2, or both, then continue below.

Sperm and embryo storage periods

In this section you must state how long you consent to your sperm and/or embryos being stored for. You may want to think about how far in the future you want others to use your stored sperm and embryos – ask your clinic if you are unsure.
The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your sperm and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

A medical practitioner will need to certify in writing that the medical criteria for premature infertility have been met for storage to continue for more than 10 years. When the criteria have been met, the storage period will be extended by 10 years from the date the criteria are met.

Page declaration signature Date

The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

Once your sperm or embryos have been allocated to someone else's treatment, the patient (together with the clinic) will determine how long the sperm and embryos are stored for within the boundaries of what you have consented to in this form.

4.3. For how long do you consent to your sperm being stored? **Only complete this section if you answered yes to 4.1.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

4.4. For how long do you consent to embryos (created with your sperm) being stored? **Only complete this section if you answered yes to section 4.2. Please note that the egg provider also has to give her consent to storage.**

☐ 10 years ☐ 55 years

☐ A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for.

For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you would complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

Page declaration signature Date

5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the sperm or embryos have been transferred, used in training, or have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

Business plan 2016/17: outline objectives

Strategic delivery:	☐ Setting standards	☐ Increasing and informing choice	☒ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	8		
Paper number	HFEA (16/09/2015) 765		
Meeting date	16 September 2015		
Author	Paula Robinson, Head of Business Planning		
Output:			
For information or decision?	For decision		
Recommendation	To approve the outline objectives for 2016/17, as the basis for drafting the next business plan.		
Resource implications	In budget (to be agreed with DH in the usual way).		
Implementation date	Across the 2016/17 business year		
Communication(s)	The HFEA's Business Plans, once approved by the Department of Health, are published on our website.		
Organisational risk	☒ Low	☐ Medium	☐ High
Annexes	None		

1. Business planning for strategic delivery

1.1. Three year overview

The Authority's strategy 2014-17 provides the essential context for the annual business plan. In September last year members approved an outline implementation plan which set out the activities across the three year period that will, in totality, deliver our strategy by July 2017. The current business plan (for 2015/16) was set in accordance with that implementation plan. We will also follow the plan in setting our business plan for 2016/17, and the Corporate Management Group (CMG) has started to consider what activities and resources will be needed.

1.2. Looking ahead to the next strategy

The 2016/17 business plan will cover most of the remaining strategic cycle. Before the end of this business year (ie, 2015/16), we will therefore start to consider how we would like to go about developing a new three year strategy, during 2016/17, for the period 2017 to 2020.

2. Planning timetable for 2016/17

2.1. Key dates

The business plan for 2016/17 will take shape over the next few months. The table below lists the main milestones in the process.

Date	Item
September 2015	Authority approval for outline BP for 2016/17
October 2015	2016/17 BP drafted in full
November 2015	Authority approval for full draft BP for 2016/17
December 2015	Submission of approved draft to DH; budget discussions
January 2016	DH considers draft; budget discussions continue
February 2016	DH comments on draft; budget near-final
March 2016	Near-final draft submitted to DH; budget confirmed
April 2016	Year-end figures added as relevant. Approval and publication.

3. 2016/17 business plan outline

3.1. Proposed main contents

This follows initial discussions at CMG, and is based on the earlier three year outline plan plus our usual range of statutory work. The activities proposed for inclusion are presented here in a very summarised form – there will be more descriptive detail in the ensuing draft business plan.

Quality and safety

Inspection, audit, licensing	Ensuring governance tools are effective
Incidents and complaints annual report and learning focus	Evaluating and addressing areas of regulatory concern
Processing PGD, HLA and mitochondria applications	Being the UK's competent authority for ART
Maintaining an overview of emerging developments	Ensuring internal Compliance processes and systems support quality
Identifying and implementing ways of improving the quality and safety of care, through: • Continuing regulatory focus on non-compliances • Post-IfQ, more 'right first time' data submission, to improve Register data quality • Working with commercial groups of clinics so as to improve quality on a group-wide basis when relevant	Acknowledging that treatment is often unsuccessful, and exploring with professional stakeholders how the HFEA and clinics could better address this issue, by: • Publishing more of our data to drive improvements in clinic performance (post-IfQ) • Ensuring our messaging to clinics conveys the importance of this aspect • Ensuring our information for prospective patients enables them to have realistic expectations
Counselling service pilot	Collaborating with professional stakeholders (including the British Fertility Society, BFS) to put patients in touch with better information and services when they first realise they may have a fertility issue
Implementation of EU Directives on import/export of gametes and EU coding (ongoing project`s starting in 2015/16)	Review of embryo research policies and regulation

Through the Lifecycle campaign (and through the IfQ work on CAFC), continue to provide information about donation and gamete availability	Follow-up work with commissioners of NHS services, following road-testing in 2015/16 of the HFEA's guidance leaflet for commissioners

Information and choice

Providing access to information from the Register	Publishing reports and supplying information we hold
Maintaining the Register	Facilitating access to information under various regimes
Regularly updating 'Choose a fertility clinic'	Information provision for researchers requesting access
User experience scores in place and in use on 'Choose a fertility clinic'	Enhancing the patient voice in all of our work, by seeking patients' views and by developing our communications with patients so as to help them to make choices
Annual horizon scanning for new scientific developments, to inform policy developments and website material	Ensuring patients' feedback is continuously incorporated into our core business
Improved HFEA information about treatment options, research and other subjects (on new website)	Working with clinics and experts to publish more information about new treatments

Value and efficiency

Continued collaborative and partnership working with other ALBs and health regulators	Continued sharing of services and infrastructure
Continued delivery of core internal finance and facilities work	Building our establishment staff capacity and skills, in line with our People Strategy
Continuing to run the Fees Group and ensure an annual fee review takes place	Office move (April) - to share premises with other health ALBs
Completing the work started in 2015/16 to modernise the Register function and processes (EDI, data submission and verification, portal, data dictionary etc.)	

4. Recommendation

The Authority is asked to approve the above outline as the basis for drafting the full 2016/17 business plan.

Information for Quality programme: update

Strategic delivery:	☒ Setting standards	☒ Increasing and informing choice	☒ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	9		
Paper number	HFEA (16/09/2015) 766		
Meeting date	16 September 2015		
Author	Nick Jones, Director of Compliance and Information		
Output:			
For information or decision?	For information		
Recommendation	The Authority is asked to: • Note the progress made on the Programme; • Note that Alpha stage development has now commenced and progression for the externally facing part is dependent on external approval.		
Resource implications	Significant within approved IfQ budget		
Implementation date	During 2015/16 business year		
Communication(s)	Regular throughout 2015/16		
Organisational risk	☐ Low	☐ Medium	☒ High
Annexes	N/A		

1. Background

1.1. The Information for quality (IfQ) programme encompasses:

- The redesign of our website and Choose a Fertility Clinic (CaFC) function.
- The redesign of the 'Clinic Portal' (used for interacting with clinics) and combining it with data submission functionality that is currently provided in our separate EDI (Electronic Data Interchange) system (used by clinics to submit treatment data to the HFEA)
- A revised dataset and data dictionary which will be approved by the Standardisation Committee for Care Information (SCCI)
- A revised Register of treatments, which will include the migration of historical data contained within the existing Register
- The redesign of our main internal systems that comprise the Authority's Register and supporting IT processes.

1.2. Given the importance of the programme to the Authority's strategy, updates on progress are provided to each meeting of the Authority and approval for direction and actions sought. This brief paper updates Members on key actions and emergent issues since the last meeting. Despite the holiday season, the period since the last meeting of the Authority has been a busy one.

2. Working with suppliers

2.1. The procurement process of selecting suppliers to work with us is now complete, having been on the verge of completion at the last meeting. We selected Reading Room to work with us on five outward facing contracts.

2.2. This work has mobilised successfully and three 'sprints' (usually a two-week period of activity) have now been completed, including a phase known as Discovery+ where we finalise users' expectations of the new systems. We engaged Informed Solutions to work with us on the first sprint in relation to internal systems, to establish an important suite of technical governance requirements, and to develop a detailed 'resourced plan.'

2.3. We are completing the latter aspect of the work internally as we hold most of the necessary knowledge. There will be a need to procure additional expertise – in relation to internal system work - as the programme progresses although this will be relatively small scale and will not require a lengthy procurement process. The programme is proceeding in line with budgetary expectations. That said, it is likely (although not problematic) that expenditure will extend to the next financial year.

3. 'Alpha' stage

3.1. As Members have previously been advised, the externally facing part of the programme cannot proceed beyond 'Alpha' (proof of concept) stage until approvals in line with Government Digital Standards have been granted by the Department of Health.

3.2. Alpha stage development has now commenced and is expected to be of 8 week's duration with a formal decision expected in November 2015.

3.3. That said, we are in active discussions with DH colleagues in advance of that and who are happy to provide informal indications along the way. This is a positive development.

4. Data migration

4.1. As we have previously highlighted data migration as a big risk to the programme. We have therefore taken a careful approach to this task, including commissioning a company expert in this area to help us develop a strategy and the steps that need to be put in place. As stated above, all relevant information in the current Register (20 years' of treatment data) must be transferred to the new Register structure. An important milestone has been reached relating to the current dataset.

4.2. We have identified current data fields that map to the proposed new structure, itself consistent with our new 'data dictionary.' We have also established the quality threshold required for that data to meet – that is completeness. A substantial amount of work has been undertaken by the team to quantify how much of the current dataset meets the necessary quality thresholds (circa 98%) – and the effort that will be necessary to 'cleanse' the data to this quality. We are hopeful that much of that effort can be taken care of internally.

4.3. Inevitably, though, we will require clinics to undertake some cleansing work and we are starting a process of engagement with them such they are aware of this well in advance and can schedule this around their usual activities. We expect the bulk of this work to take place from October 2015 and completed by next Spring, 2016.

4.4. The Authority is reminded that data migration is often a key feature of work such as this, and one we have categorised as high risk. We are clear that we will not implement a new system of data submission until the data migration strategy has been completely satisfied. This commitment introduces a degree of uncertainty as regards a published timetable for implementation (see below).

5. Implementation

5.1. Until the necessary procurement processes and approvals had completed - together with more detailed planning assumptions (themselves dependent on, say, Reading Room input) we have been reticent about putting a detailed timetable in to the public domain. This position is one supported by our external stakeholder group with whom we continue to engage.

5.2. At the meeting we will present a proposed timetable that will form the basis for external communications and provide clinics with a greater degree of certainty in relation to the impact on them relating to changes to the submission of treatment information. To date we have indicated a timetable of February-March 2016 for 'Beta' versions of the Website, Choose a Fertility Clinic and Clinic Portal (without treatment submission functionality) to be launched. We are confident of meeting this timetable, subject principally to Alpha stage approvals being granted. Full implementation of the Clinic Portal is dependent on data migration progressing successfully – and some resourcing issues - and further details will be provided at the meeting.

5.3. At the July 2015 meeting of the Authority the importance of seeing the programme as more than a set of 'system changes was emphasised; IfQ is an opportunity to change our ways of working.

5.4. We have begun to communicate this wider message to our staff. The detailed work on defining the impact of IfQ on our future ways of working will be led by the product teams themselves. To date the response from staff has been positive as the timing is opportune as it also prepares us for a likely office move next year.

6. Recommendation

6.1. The Authority is asked to

- Note the progress made on the Programme;
- Note that Alpha stage development has now commenced and progression for the externally facing part is dependent on external approval.

Compliance activities 2014/15: a review

Strategic delivery:	☒ Setting standards	☐ Increasing and informing choice	☒ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	10		
Paper number	HFEA (16/09/2015) 767		
Meeting date	16 September 2015		
Author	Debra Bloor, Chief Inspector		
Output:			
For information or decision?	Decision		
Recommendation	The Authority is asked to • note and comment on this paper; • review the supporting papers and evidence, • consider and agree final recommendations for the update of the Compliance and Enforcement Policy; • consider and agree the current and future direction of our regulatory activities		
Resource implications	In budget		
Implementation date	To be determined once in principle decision is made on future direction of regulatory regime		
Communication(s)	Publication of review on HFEA website to be communicated through Clinic Focus article. Conclusions of the review to be communicated through usual stakeholder engagement channels.		
Organisational risk	☐ Low	☒ Medium	☐ High
Annexes			

1. Background

1.1. Our Strategy for 2014-17 signals an ambition for high quality care for everyone affected by assisted reproduction. Within this framework our regulatory activities are directed to the improvement of the quality and safety of care.

1.2. This paper introduces a suite of papers that analyse and comment on the impact of our regulatory activities[1,2,3]. It also sets out how our working priorities have evolved to maximise the chance of our having an even more positive impact in the light of our findings and experiences..

1.3. To ensure that the Compliance and Enforcement Policy – our framework for taking action when there are concerns about quality of care – remains properly aligned to our regulatory activities and ultimately to the licensing process that our regulatory activities serve, we have undertaken a review of the policy and its supporting documents and the recommendations from that review are presented[4].

1.4. The Act (section 8ZA(2)) specifies that in carrying out its functions the Authority must have regard to the principles of best regulatory practice (transparency, accountability, proportionality, consistency) [8ZA (2)]. We also committed in our strategy to ensure the HFEA remains demonstrably good value for the public, the sector and Government. These requirements need not necessarily be in tension and our experience to date is that they are not. Equally it's important that the Authority has an opportunity to scrutinise and challenge our regulatory approach and consider recommendations for improvement so that we have the best chance of balancing all of our obligations.

1.5. To date, we have made an annual report of our regulatory activities to a *committee* of the Authority - more lately the (now dissolved) Ethics and Standards Committee, and before that its predecessor Compliance Committee. Following a review of our committee structures and in consideration of the importance of our strategy it has been decided these are matters that are now more properly considered at a full meeting of the Authority with the discussions that this prompts forming the basis of future conversations about our regulatory approach.

2. Establishing effectiveness

2.1. Our strategy commits us to measure the extent by which we have improved the quality and safety of care through our regulatory activities.

[1] Summary of Inspection Findings between April 2013 and March 21014 and April 2014 and March 2015
[2] Analysis of Risk tool outputs 2014/15: patters, lessons and future actions
[3] Clinical Governance Activities: learning and culture
[4] Review of the Compliance and Enforcement Policy and supporting documents

2.2. The cause and effect of regulatory activities is however tricky to measure. For example, our existence and the development and production the Code of Practice which provides a set of rules to guide clinics – may themselves promote compliance and with it, improvement. Further, the prospect of inspection (especially unannounced inspection) may catalyse compliance. On the whole it is our experience that clinics want to provide good quality care and to be seen to be compliant.

2.3. Taking these limitations into account we aim to keep our regime under review and to continually evolve our regulatory approach in line with our strategic goals.

3. Assessing our performance

3.1. As to criteria for assessing our own performance, a starting point might be the Regulators' Code (2014) that we are bound by. The main points of the code are set out below with a brief self-assessment of our own compliance shown in italics. The Code states that regulators should:

3.2. Carry out their activities in a way that supports those they regulate to comply and grow: Our approach is supportive. Our starting point is that clinics are compliant and inspection is an opportunity of validating that assumption. We try to work with clinics to support plans to innovate and grow although there are inevitably tensions from time to time in balancing regulatory requirements.

3.3. Provide simple and straightforward ways to engage with those they regulate and hear their views: We seek feedback; we engage using a variety of mechanisms – clinic focus, licensed centres' panel, annual conferences, Chair and Chief Executive's visits to clinics.

3.4. Base their regulatory activities on risk; the Act provides a statutory framework which we cannot vary but within this constrain we take into account the history of regulatory compliance; we adapt our themes taking into account evidence of high-frequency non-compliance; we have adopted a risk tool that flags up performance concerns at individual clinics.

3.5. Share information about compliance and risk: In the past few years we have established good links with the MHRA, CQC and GMC in particular ensuring there are no barriers to effective information sharing and we have agreements in place with our fellow regulators in each of the countries of the UK.

3.6. Ensure that their approach to their regulatory activities is transparent: We publish the basis on which we do our work; together with the outcomes of inspection including the report and the minutes of all licensing decisions – including those related to incidents (and we produce an annual report on incidents reported. We believe we can do more here - and the opportunities presented by website changes (further to IfQ) are considerable.

4. Evolution of the regulatory regime

4.1. The tone or personality we adopt in our work is influenced by many factors. Given that it is so instrumental in the work we do it is worth being more explicit within this set of papers. Whilst not easy to capture, we have attempted to characterise the tone of our regulatory approach below.

4.2. A fairly evenly balanced focus on identifying (and therefore reducing) harms, and promoting improvement.

4.3. Being resolute and using tough enforcement powers when necessary combined with being approachable, customer-facing, preventive and problem-solving when possible. We do not see a tension in adopting these different styles as the situation warrants.

4.4. We adopt a high-trust model – but a model in which trust is earned through disclosure of problems (incidents and material events); implementation of recommendations for improvements, and; that clinics strive for and are motivated by quality and improvement.

4.5. Given that the regulatory landscape in which we operate changes continually we must expect to adapt and change. A raft of new requirements was transposed into the Act in 2007. Notably at this time, it became a mandatory requirement for clinics to have *documented* and *validated* processes and procedures and to establish a quality management system (QMS) to support continuous improvement. In response the HFEA's inspection regime became focused on clinics' documentation.

4.6. Further changes to the Act in 2009 significantly updated the consent regime and introduced complex new consent requirements which in turn resulted in a continued focus on clinics' consent procedures and documentation of consent.

4.7. In 2012 the HFEA extended its remit to inspect a number of additional clinical activities (safeguarding, infection control, medicines management and the pre-,peri- and post-operative pathway) so that clinics in England that only carry out HFEA licensable activity could be exempted from the requirement to be registered with the CQC.

4.8. It was (and remains) straightforward to inspect documentation. It is harder to assess the quality of processes themselves and to evaluate the quality of services provided and experienced by patients.

4.9. Learning from our governance and inspection activities suggests that while clinics "tick the boxes" in carrying out audits and in conducting root cause analysis to identify the causes of incidents, complaints and or poor performance, in common with the healthcare sector in general, these activities may not always be effective in identifying opportunities for improvement. In consideration of this, since 2014 we have aimed to phrase recommendations for improvement to encourage clinics to consider *why* a non compliance has

evaded their QMS, *why* an incident has occurred or *why* a patient has experienced poor service. Having identified the root cause we encourage clinics to identify corrective actions *specific to their own circumstances* and then to assess the *effectiveness* of the corrective actions. We are also working one to one with clinics that see recurrence of C grade incidents or whose root cause analysis could be better. This approach aims to support the continued development of a "learning culture" that we hope will be more effective in driving improvement.

4.10. Since April 2015 we have also specifically focused on whether clinics have learned from incidents (both their own and those documented in our annual review), complaints and guidance in the course of interim inspections.

4.11. We don't anticipate that it will be easy to influence culture in clinics or that the approach will deliver fast results. However we do believe that a change in approach is warranted if we are to continue to raise the bar to encourage continuous improvement in the quality of service provided by clinics.

5. Summary

5.1. The tools we have are generally well calibrated and effective in motivating regulatory compliance. To reflect our strategy and practice however, our regulatory tools in the form of the Compliance and Enforcement Policy and associated documentation should be revised to emphasise that regulatory action will be initiated where there is considered likely to be a risk to patients, their embryos or gametes or where there are concerns about quality of service provided to patients.

5.2. Our analysis of risk tool alerts suggests that clinics had fewer alerts related to success rates in 2014/15. While it is difficult to establish a cause and effect of our regulatory activities in respect of this improvement the ongoing reduction suggests that centres are taking action to continually improve success rates. It is likely that the HFEA's proactive real time monitoring – most significantly interventions should performance trends continue on a negative trajectory - plays a role in encouraging this.

5.3. Although a small number of clinics continue to struggle to meet the 10% multiple birth target we continue to have bespoke conversations with these clinics to motivate and encourage change: ultimately however, if these interventions fail to have an impact then it is recognised that the significant risk posed by multiple births are such that regulatory action may be initiated in line with the Compliance and Enforcement Policy.

5.4. Alerts related to errors in the submission of information to the HFEA register about treatments involving donor gametes increased in 2014/15: the HFEA's IfQ programme is expected to have a significant impact on the improving the

quality of data submission although it is likely to be some time before this work has a measurable impact.

5.5. Analysis of incidents suggests that clinics may need more time to embed learning and more support to extract learning from incidents. On this basis we have refreshed our approach to inspection and our governance activities to try to support and encourage clinics in the continued development of a learning culture.

5.6. Analysis of inspection findings supports a conclusion that the sector is largely compliant. The focus of interim inspections was refreshed in April 2015 taking into account the most frequent non compliances and this will ensure that our regulatory activities continue to be risk focussed. Our analysis shows that recommendations for improvement are implemented within prescribed timescales supporting a conclusion that our inspection activities have a tangible impact.

5.7. Feedback from the sector on their experiences of inspection and inspection reports is positive with PRs reporting that inspection visits lead to improvements in service delivery and patient care.

6. Recommendation

6.1. The Authority is asked to

- note and comment on this paper;
- review the supporting papers and evidence,
- consider and agree final recommendations for the update of the Compliance and Enforcement Policy;
- consider and agree the current and future direction of our regulatory activities.

Compliance activities 2014/15: analysis of risk

Strategic delivery:	☒ Setting standards	☐ Increasing and informing choice	☐ Demonstrating efficiency economy and value

Details:	
Meeting	Authority
Agenda item	11
Paper number	HFEA (16/09/2015) 768
Meeting date	16 September 2015
Author	Sara Parlett, Senior Inspector
Output:	
For information or decision?	For information
Recommendation	N/A
Resource implications	In budget
Implementation date	N/A
Communication(s)	N/A
Organisational risk	☐ Low ☒ Medium ☐ High
Annexes	Annex 1: charts derived from analysis of risk tool alerts between April 2014 and March 2015 and comparison with data from 2013/14 and 2012/13.

1. Background

1.1. The compliance cycle, with inspection at its core, defines the HFEA's regulatory regime. We inspect every two years as required by law and follow up recommendations made during inspections to ensure necessary actions have been implemented. Our ability to undertake 'on-going' monitoring of a clinic's performance between inspection visits has been greatly enhanced by the introduction in April 2011 of the risk based assessment tool (RBAT) that provides information about licensed clinics' performance in near to real time.

1.2. Clinics have been able to access their own RBAT outputs through the clinic portal since April 2012 and information from RBAT analysis has routinely been included in inspection reports since then.

1.3. The risk tool measures performance in relation to the following indicators:

- outcomes in terms of both clinical pregnancy rates and clinical multiple pregnancy rates;
- submission of critical register information relating to treatments using donor gametes;
- timeliness of payment of monthly HFEA invoices.

1.4. Performance is based on the analysis of information submitted to the HFEA. Where the trend analysis performed by RBAT suggests that there may be a dip in performance, an automated alert is sent to the Person Responsible (PR) and clinics are expected to act on these alerts to investigate any possible causal factors and take corrective action if appropriate. Inspectors and/or members of the register information and finance teams also carry out targeted follow-up where appropriate.

1.5. This paper provides an update to the review of RBAT outputs completed in 2014 and aims to identify trends; establish performance against the benchmark analysis undertaken in 2014; and identify actions for the future in relation to the focus of our regulatory interventions.

2. Analysis of RBAT outputs April 2014 to March 2015

2.1. There is no "normal" range for the number of alerts issued to a clinic. Alerts are generated by trend analysis and do not by themselves indicate poor practice or performance. The aim of alerts is to prompt clinics to review practices **before** performance is negatively affected.

2.2. The system uses information submitted to the HFEA's register as the basis of nearly all monitoring. This limits the impact of RBAT in relation to clinics that provide only basic partner treatment services (IUI with partner sperm) as these clinics do not submit information to the HFEA register. While this limitation is acknowledged, it is also recognised that the nature of the services provided by these clinics also limits their risk factors.

2.3. It is also important to note that there is a considerable variation in the number of treatment cycles carried out by clinics. Around 36,000 treatment cycles were carried out by 19 of the 111 clinics included in the analysis. This represents approximately 50% of the treatment activity of the sector in 2014/15. Inevitably, these clinics carry out more complex treatments (involving donor gametes for example) and the volume of their activity means that the significance of any change in performance is identified quickly: this is because a certain volume of activity has to be included in any statistical analysis before it can be identified that a trend represents a true change in performance rather than the result of chance.

2.4. Annex 1 sets out a number of charts derived from analysis of RBAT alerts between April 2014 and March 2015. In summary, it shows that clinics' performance in this period has improved in relation to success rates and timeliness of payment of fees, but has worsened in relation to submission of critical register information.

2.5. Chart 1 shows that more alerts continue to be issued to clinics as a result of delayed payment of fees and invoices and inaccuracies in the reporting of treatments involving the use of donor gametes than in relation to concerns about success rates. However, the chart also shows that the number of finance alerts has decreased from the previous year.

2.6. There are various factors that contribute to clinics delaying payment of invoices. For example some clinics do not have robust processes to deal with absences of staff responsible for processing our invoices. However, in general most clinics pay invoices within the stipulated timeframes. The introduction by the HFEA of an automated debt chasing system in March 2015 has reduced the average days to payment of invoices to 34 days from 47 days before the introduction of this system.

2.7. The number of alerts related to negative trends in success rates following IVF, ICSI and FET decreased in 2014/15. This demonstrates that clinics are taking action to continually improve their success rates. The exception to this is in the number of alerts relating to clinical multiple pregnancy rates and more detailed analysis of this observation is below.

2.8. Chart 2 shows that while the majority of clinics received very few alerts, 27 clinics received more than 10 alerts in 2014/15. This is the same number as in 2013/14; approximately half of these clinics have remained in the list in 2014/15.

2.9. Chart 3 shows the 'top 10' clinics that had the highest number of alerts in 2013/14 and 2014/15. Eight clinics in the top 10 in 2013/14 have remained in the list in 2014/15. All of the clinics in this chart could be considered worthy of scrutiny, but in order to determine where risk lies, the data have been further analysed (see below).

2.10. Chart 4 again shows the 10 clinics that had the highest number of alerts in 2014/15 but divided into two alert categories. This demonstrates that the majority of alerts were either finance or register information related.

2.11. The number of alerts relating to submission of critical information to the HFEA register has increased significantly since the last reporting year. The HFEA has implemented an extensive programme (Information for Quality, IfQ) to streamline and improve systems for the submission of treatment information to the HFEA register. Information team resources have been diverted to focus on the development of new systems rather than (as previously) focusing efforts on poor performing clinics. It is expected that the new systems will have a significant impact on the quality of register submissions but that these improvements will not start to take effect until the IfQ programme is complete.

2.12. In order to aim our resources at the areas of risk associated with our strategic aims, alerts relating to success rates and multiple pregnancy rates have been further analysed.

2.13. Chart 5 shows the three clinics that had five or more alerts related to success rates in 2014/15. This chart demonstrates a negative trend in performance for one clinic and an improvement for three clinics compared to the previous year.

2.14. Success rates for one of these clinics for the period April 2014 to March 2015 show the clinic's success rates are in line with the national average. This suggests appropriate action was taken by the clinic in response to the alerts.

2.15. For the other two clinics, success rates for the period April 2014 to March 2015 are lower than average at a statistically significant level. Both clinics are being monitored closely by the Executive and the clinics are taking action to review their practices.

2.16. Chart 6 shows the clinics that had four or more alerts related to multiple pregnancies.

2.17. Two of these clinics have responded and appear to have taken effective action such that the clinics' multiple live birth rates are likely to be consistent with the 10% multiple live birth rate target.

2.18. The other two clinics have clinical multiple pregnancy rates that are likely to be significantly higher than the 10% multiple live birth rate target for the April 2014 to March 2015 time period. Both clinics are being monitored closely by the Executive.

2.19. The small increase in the number of alerts related to clinical multiple pregnancy rates in 2014/15 is surprising, as clinics have had since October 2012 to adjust to the 10% multiple live birth rate target. However, data for the sector shows that in 2013/14 19 clinics had a multiple pregnancy rate that was likely to be higher than the 10% multiple live birth rate target, whilst in 2014/15 this had decreased to 15 clinics. This reflects findings documented in our 'Improving outcomes for fertility patients: multiple births 2015' report published recently. This suggests that clinics are taking action to review the effectiveness of their multiple births minimisation strategies: it is likely that the HFEA's proactive real time monitoring through RBAT plays a role in encouraging this behaviour.

3. Conclusions and actions

3.1. This review of RBAT outputs should be interpreted cautiously because, as noted above, alerts are not indicators of poor performance per se. They are issued to prompt clinics to take action before there is an impact on performance.

3.2. The reduction in alerts related to success rates suggests that clinics are continually improving success rates. There has also been a reduction in the number of finance alerts and it is anticipated that these will continue to fall in the next year due to the new automated debt chasing system.

3.3. There was an increase in alerts relating to trends in clinical multiple pregnancy rates. This is disappointing but as documented in the 'Improving outcomes for fertility patients: multiple births 2015' report, fewer clinics had a multiple pregnancy rate that was likely to be higher than the 10% multiple live birth rate in 2014/15 compared to 2013/14. This suggests that clinics are taking effective action in relation to these alerts albeit more slowly than we might have hoped.

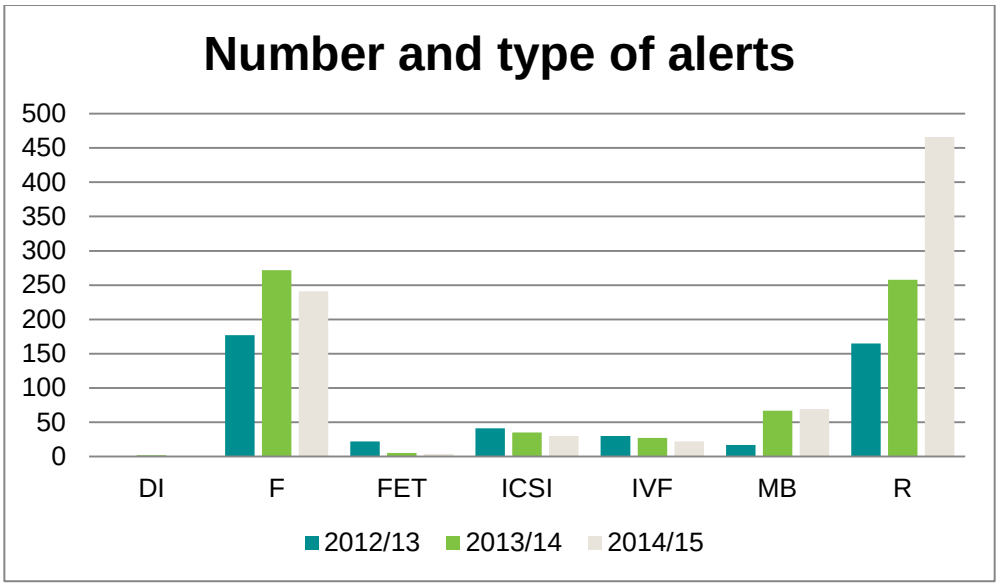
3.4. The number of alerts related to submission of information relating to donors and/or treatments using donor gametes has increased indicating clinics' performance has declined. Action is being taken by the HFEA through the IfQ programme to streamline systems and processes.

3.5. As follow up to this analysis, we will initiate a cross directorate review of the 10 clinics with the highest number of alerts to ensure that everything that can/should be done to support these clinics is being done. Other clinics' responses to alerts will continue to be monitored during the time between inspections and regulatory action taken when it is warranted.

3.6. By providing the information required for clinics to monitor their own performance in comparison to national norms, the HFEA targets and helps clinics that may be struggling to improve the quality of care given to patients. Overall, clinics respond positively to requests to act on these alerts.

Annex 1: Charts derived from analysis of RBAT alerts between April 2014 and March 2015 and compared with data from 2013/14 and 2012/13.

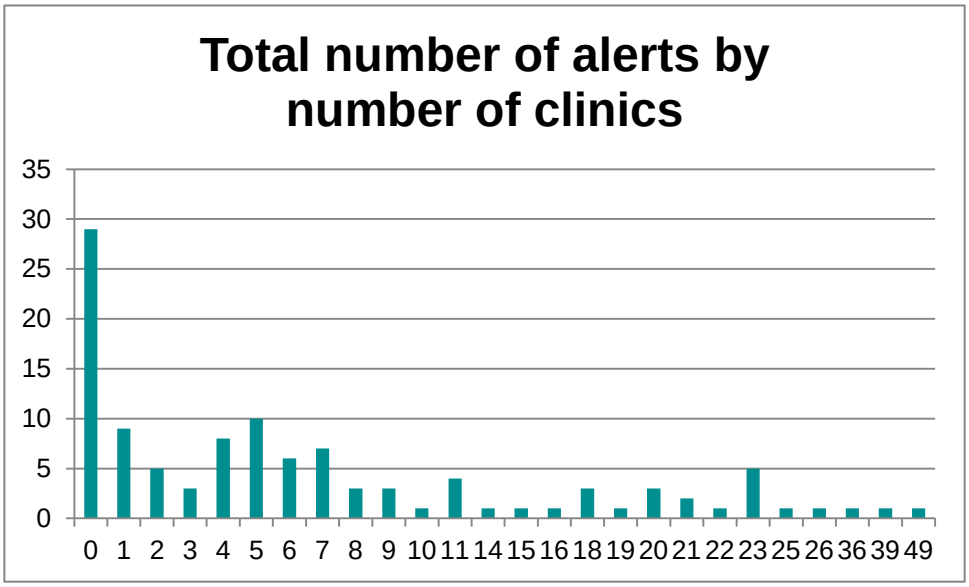
Chart 1



F, Finance; the sum of all alerts related to delay or non-payment of invoices
R, Register; the sum of all alerts related to errors in reporting of treatments involving donor gametes
MB, Multiple births; the sum of all alerts related to trends in clinical multiple pregnancy rates as measured against the relevant target
ICSI; the sum of all alerts related to trends in clinical pregnancy rates following ICSI treatments
IVF; the sum of all alerts related to trends in clinical pregnancy rates following IVF treatments
DI; the sum of all alerts related to trends in clinical pregnancy rates following DI treatments
FET; the sum of all alerts related to trends in clinical pregnancy rates following frozen treatment cycles (IVF and ICSI).

This chart shows that the sector as a whole received more alerts relating to late payment of fees and accurate reporting of treatments involving donor gametes than relating to success rates. This is unchanged from the previous two reporting years. The chart does however show a decrease in the number of finance alerts sent to clinics as compared to the previous reporting year. The number of alerts related to trends in success rates following IVF, ICSI and FET have continued to decrease.

Chart 2

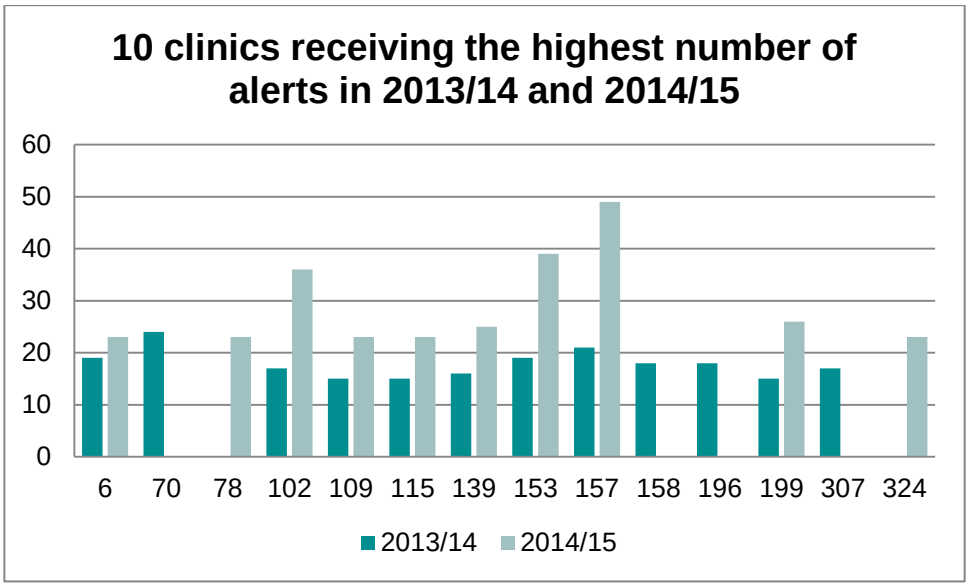


In 2014/15, 29 of the 111 clinics included in the analysis received no alerts; a further 35 had fewer than 5 alerts; 20 clinics had between 6 and 10 alerts and 27 clinics had >10 alerts.

The number of clinics receiving >10 alerts in 2014/15 is the same as that in 2013/14.

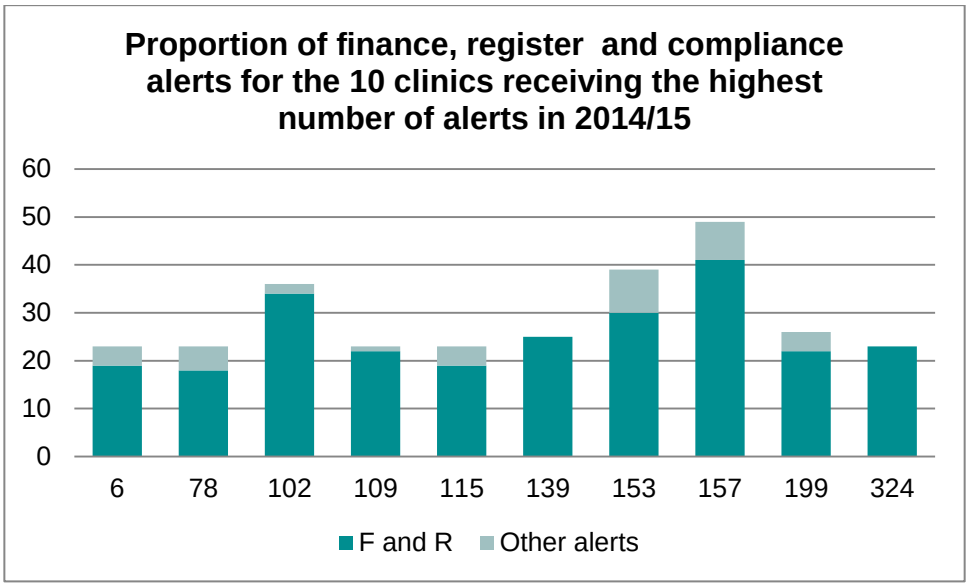
It should be noted that clinics providing basic partner services or storage only do not pay monthly fees, do not provide treatment with donor gametes and make only a single annual data submission to the HFEA recording their success rates (this means that success rates and multiple pregnancy rates are not continuously monitored through RBAT for these clinics). These clinics represent the majority of those receiving no or very few alerts.

Chart 3



This chart shows the 10 clinics that received the highest number of alerts in either 2013/14 or 2014/15. Eight clinics that were in the 'top 10' in 2013/14 have remained in the list in 2014/15. All of the clinics in this chart could be considered worthy of scrutiny but in order to determine where risk lies, the data have been analysed further below.

Chart 4

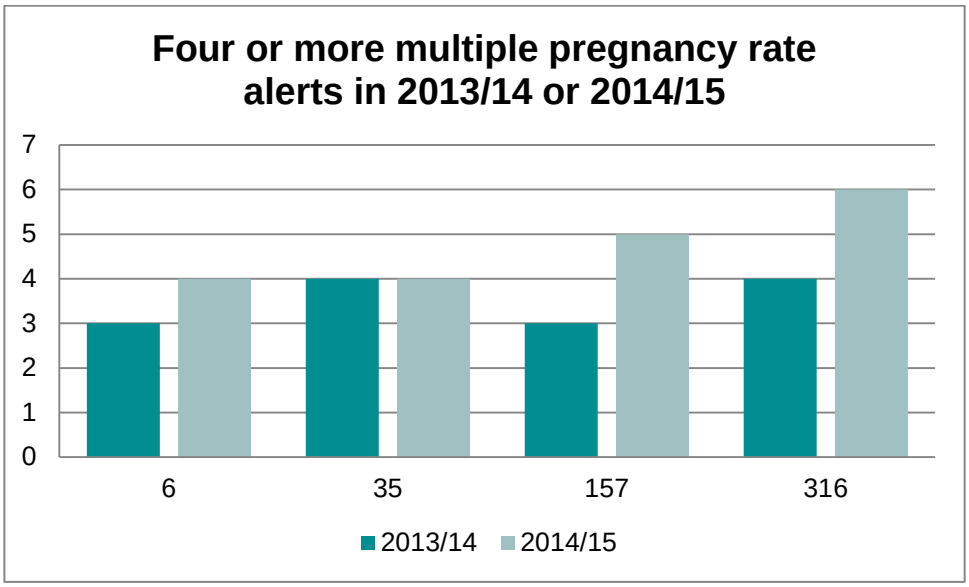


This chart shows the 10 clinics that received the highest number of alerts in 2014/15. A significant proportion of these alerts related either payment of invoices or submission of critical information to the HFEA register.

Chart 5

No clinic received more than 7 alerts related to success rates in 2014/15. This chart shows that three clinics were sent five or more alerts related to success rates in 2014/15; the same number as in 2013/14. It is important to note that all three clinics that received 5 or more alerts last year have all showed an improvement this year. It should be noted that multiple birth rate alerts are not included in this analysis.

Chart 6



Four clinics have received four or more alerts related to multiple pregnancies in 2014/15. Only two clinics received four or more alerts in 2013/14. However, sector wide data shows a decrease in the number of clinics with a multiple pregnancy rate likely to be higher than the 10% target compared to the previous year.

Compliance activities 2014/15: analysis of inspection findings

Strategic delivery:	☒Setting standards	☐ Increasing and informing choice	☐ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	12		
Paper number	HFEA (16/09/2015) 769		
Meeting date	16 September 2015		
Author	Andrew Leonard, Senior Inspector		
Output:			
For information or decision?	For information		
Recommendation	N/A		
Resource implications	N/A		
Implementation date	N/A		
Communication(s)			
Organisational risk	☐ Low	☒ Medium	☐ High
Annexes	Annex 1: Analysis of data on inspection findings		

1. Background

1.1. This report provides an analysis of non-compliances found in the course of renewal and interim inspections between 1 April 2014 - 31 March 2015 and a comparison with the 2013/14 inspection findings.

1.2. Non-compliances with the Act and requirements of the HFEA Code of Practice (CoP) observed on inspection are classified as critical[1], major[2] or 'other'[3] depending on the associated risks. Post inspection the HFEA's compliance team record the findings of inspections in an electronic system (the post inspection tool) which groups non-compliances according to the HFEA CoP guidance note they are most relevant to.

1.3. This analysis is based on information extracted from this post inspection monitoring system on 30 July 2015.

1.4. We have not included the findings from inspections of research centres in this analysis because these non compliances are very specific and observations are not more generally applicable.

2. Overview of inspection findings

2.1. In 2014/15 there were 59 inspections of treatment and/or storage clinics:

- 28 renewal inspections
- 14 interim inspections and
- 17 inspections of other types (initial/new premises/additional/clinical governance).

2.2. It is important to note the number of inspections carried out and, to some extent, the type of clinic inspected because this impacts on the number of non-compliances. Table A at annex 1 shows a breakdown of the number of inspections by clinic type and size of IVF clinic for 2014/15 and 2013/14. The table shows that fewer inspections were carried out in 2014/15 than in the preceding year. We conducted a larger proportion of inspections at large clinics compared to 2013/14 and smaller proportion at treatment only clinics. Large clinics tend to provide more complex treatments and as a result are subject to compliance with more requirements than treatment only clinics.

[1] An area of practice which poses a significant risk of causing harm to a patient, donor, embryo or to a child who may be born as a result of treatment services, or a significant shortcoming from the statutory requirements

[2] An area of practice which poses an indirect risk to the safety of a patient, donor, embryo or to a child born as a result of treatment services. This area of non-compliance may also indicate a major shortcoming from the statutory requirements and/or indicate a failure by the Person Responsible to carry out their legal duties.

[3] An 'other' area of practice that requires improvement is any area of practice, which cannot be classified as either a critical or major area of non compliance, but which indicates a departure from statutory requirements or good practice.

2.3. Only renewal and interim inspection findings are entered into the monitoring system and so only the findings of these inspections are included in this analysis. This work identified that the findings of four inspections were not recorded in the system and action has been taken to resolve the technical and training issues that led to this omission (Table A at annex 1).

2.4. All inspections in 2014/15 identified non-compliances, although three inspections identified only 'other' non-compliances. When critical and major non-compliances are considered, 32 inspections identified fewer than 10 non compliances while six inspections identified more than 10 non compliances (see Figure 1). Management review meetings were held with respect to four of the clinics where more than 10 non compliances were observed and licences of less than the usual four years were issued in all four cases. With respect to the two clinics having more than 10 non compliances but where licences for four years were issued, the risks associated with the non-compliances were not considered serious enough to warrant a management review. This gives us confidence that we are applying our compliance and enforcement policy appropriately and consistently where there are regulatory concerns.

2.5. Table B at annex 1 shows that when the data are normalised to take into account that fewer inspections were carried out in 2014/15 than in 2013/14, there has been an increase in the number of non-compliances identified per inspection in 2014/15 compared to the previous year with a significant increase in the number of critical non-compliances observed.

2.6. Some of the increase may be attributable to non compliances identified in the course of inspection of clinical areas of practice (safeguarding, infection control, medicines management and the pre-, peri- and post-operative pathway) which have only been inspected since we extended our remit when CQC introduced a policy that clinics in England that only carry out HFEA licensable activity do not need to have CQC registration in addition to their HFEA licence[4].Four of the 22 critical non-compliances identified related to these areas of practice. We have also applied additional scrutiny to inspection of viral screening requirements; the use of suitably approved medical devices; and consent on the basis of observations of non-compliance from previous analyses. Six of 22 critical non-compliances were related to consent.

2.7. It is not considered likely that clinics inspected in 2014/15 are inherently less compliant and our procedures for inspecting are unchanged (and so consistent with other years) and reports continue to be subject to considerable quality assurance to ensure consistency. We do strive continually to develop and adapt our regulatory regime based on our experiences and this is the likely cause of the observed increase in the frequency of non-compliances.

[4] Where we identify non-compliance with these requirements these are referenced against "suitable practices" in the monitoring system (see Figure 4).

3. The relationship between clinic size and type and performance

3.1. It is important for us to consider whether clinics of different size or type have a different pattern of non compliance. This is because right touch regulation requires us to apply our resources where they are most effective.

3.2. Figure 2 shows the variation in the number of non-compliances between clinics of different size or providing treatment of differing complexity[5]. The figure shows that there is an increased frequency of non-compliance observed on inspection of IVF clinics of different size with smaller clinics generally having more non-compliance. It is possible that large clinics (those providing more than 1000 cycles of treatment in a year) may have more resources available to ensure regulatory compliance with medium and small clinics having progressively fewer resources. Clinics offering only relatively basic treatment also have progressively less non-compliance than small IVF clinics but this is likely to arise because these clinics are subject to fewer regulatory requirements. While interesting, these differences are too small to usefully influence how we apply our inspection regime however.

3.3. Figure 3 shows that the five most frequently observed non-compliances are broadly seen on inspection of clinics of all sizes and types. Again, this supports a conclusion that the same inspection regime should be applied to all licensed clinics. It should be noted however that clinics offering more basic treatment services are only subject to compliance with the relevant subset of requirements so the inspection process is inherently adapted to be proportionate on the basis of centre type.

4. Types of non-compliance found on inspection

4.1. Table C and Figure 4 show the most frequently observed types of non-compliances observed in the two years from 2013 to 2015. The areas of practice most frequently observed as requiring improvement were:

- The quality management system (QMS)
- Consent
- Equipment and materials
- Procuring, processing and transporting of gametes and embryos
- Witnessing
- Traceability

[5] The frequency of non-compliances has been normalised to account for the different number of inspections in each category

4.2. Almost identical results were obtained when only critical and major non-compliances, which carry a higher risk to patients and their gametes and embryos, were considered (Table D).

4.3. Clinics have been required to have a QMS since 2007: it is the mechanism by which clinics are expected to achieve continuous improvement. Clinics struggled initially to implement all of the requirements and after 2007 inspections tended to focus on clinics' quality management systems and processes. Figure 4 shows that while there were frequent recommendations for improvement with respect to clinics' QMS, non compliances tended to be less serious with more 'other' recommendations than critical or major. Because of the pivotal role of the QMS in ensuring quality of care, we will continue to focus on this aspect of practice but since April 2015 we have refreshed our approach to consider the impact and effectiveness of clinics' audits of practice. It is likely that we will continue to make recommendations for improvement as we try to raise the bar on quality.

4.4. Consent is at the heart of our regulatory regime and consent failure is considered to be one of the two most significant risks of fertility treatment. Consent requirements are very complex and were changed significantly in 2009. As a result we continue to scrutinise clinics' procedures for taking consent and we continue to recommend improvements. Commonly we make recommendations with respect to the storage of gametes and embryos after the gamete provider's consent to storage has expired – while it is critical that clinics' store in line with consent this particular non compliance has fewer associated risks than other consent failures. Notably the absolute number of samples stored beyond the consented period has reduced significantly. More significant are problems with reporting of consent to disclosure intentions and in relation to legal parenthood. The observation of these anomalies (accounting for 6 of 22 critical non-compliances observed –see Figure 4) has had a wider impact beyond regulatory action and we held consent workshops across the country in 2014 and at the 2015 annual conference. We also implemented changes to disclosure consent forms and initiated sector wide regulatory action with respect to consent to parenthood.

4.5. Non-compliances related to equipment and materials commonly include failing to validate new and/or repaired equipment and using non-CE marked medical devices. The requirements related to CE marking were poorly understood by the sector but collaborative working with the Medicines & Healthcare products Regulatory Agency has clarified requirements in the last year, We also had a workshop on CE-marking at the HFEA annual conference in 2015. Clinics are still working through the implementations of these requirements – hence the frequency of recommendations for improvement.

4.6. In relation to procuring, processing and transporting gametes and embryos, common non-compliances include inadequacy of process validation and poor practice around the screening of gamete providers. As noted above, validation requirements were poorly understood when introduced in 2007 and we continue to try to raise the bar and encourage clinics to ensure not only that they 'tick the

boxes' with respect to validation documentation, but that they are able to demonstrate the effectiveness of their validation in leading to improvements in the quality of their services. With respect to viral screening the frequency of this non compliance has arisen as a result of changes in guidance. In response to observation of this non compliance we sought expert opinion and then issued updated guidance following consultation with the Licensed Centres Panel.

4.7. Risk of misidentification is (with consent) the most significant risk of fertility treatment and effective witnessing is key to minimising it. As a result we scrutinise this area of practice closely. Clinics all have good procedures in place to minimise these risks and common non-compliances (the absence of witnessing at the disposal of sperm after treatment and errors in the documentation of witnessing) generally carry an extremely low level of risk. Although this is a common no-compliance, there were no critical witnessing non-compliances and seven of the 16 non-compliances were low risk and classified as "other" (see Figure 4).

4.8. In relation to traceability, the most common non-compliances observed were failure to label tubes used during egg collection –as clinics generally only carry out one egg collection at a time there are no significant opportunities for misidentification, but because of the potential impact we continue to prompt clinics to be robust in the documentation of the measures they take to minimise all possible risks in respect of this non-compliance.

5. Changes in the prevalence of non-compliance, 2013/14 and 2014/15

5.1. We also looked at which critical and major non-compliance were identified more frequently in 2014/15 when compared to 2013/14 (Table E, Annex 1).

5.2. Increases were noted between 2013/14 and 2014/15 in non-compliances related to consent, data submission, equipment and materials, QMS, traceability, witnessing and procuring, processing and transporting gametes and embryos. These non-compliance types have already been identified as focus areas in this analysis.

5.3. Non-compliances related to premises and facilities and staffing also increased to a notable level in certain clinic types such that they were relatively prevalent as non-compliances in 2014/15. Our revised interim inspection methodology already focusses on these areas.

5.4. Increases were also noted with respect of non-compliances related to: counselling, donor selection, egg sharing, information provision, record keeping and document control, but these areas of non-compliance were still not notably prevalent in 2014/15 relative to other areas. They may however represent areas of potential regulatory concern in the future.

5.5. 'Suitable practices' was the seventh most prevalent critical or major non-compliance type in all inspections in 2014/15 (see Table E in Annex 1. As noted above 'Suitable practices' non-compliances are commonly cited where clinics are failing to meet the 10% target for multiple births or when poor practice is found relevant to findings of inspection of the extended clinical practices. The HFEA continues to engage with the sector with respect to compliance with the multiple births target and we have already provided clarification of requirements around the new areas of clinical practice being inspected – particularly medicines management.

6. Implementation of recommendations to resolve non-compliance

6.1. Ninety percent (436 of 484) of the recommendations for improvement made following inspection in 2013/14 were implemented within the prescribed timescales. It is likely that a small number may not have been recorded as complete in our monitoring system although they are complete and, occasionally, Persons Responsible (PRs) do not provide evidence of compliance. Where outstanding non compliance poses a risk we generally invoke the Compliance and Enforcement policy and take appropriate action if the PR does not provide evidence of improvement. So far in respect of recommendations made following inspection in 2014/15 only 78% (251 of 323) have been implemented. This is because the deadline for completing some recommendations made in 2014/15 has not yet been reached.

7. Clinic feedback regarding inspections

7.1. We ask PRs to provide feedback to the HFEA regarding the inspection process via a questionnaire on our website.

7.2. Feedback has been provided with respect to 42 renewal inspections and 36 interim inspections carried out between 2013 and 2015. Seventy two of the 78 respondents (92%) considered that their inspection visit had promoted improvement to the way the clinic carries out its work and >95% of the 78 respondents were satisfied with their inspection report and with the recommendations and timescales for implementation within it.

7.3. There was a small proportion of negative feedback. Two of 42 respondents who experienced renewal inspections and three of 29 who experienced interim inspections did not agree that patients were not inconvenienced and/or their care was not jeopardised by the inspection. Furthermore, five of 29 respondents who had experienced an unannounced interim inspection did not agree that staff were able to take the inspection in their stride and carry on with their work while the inspection took place. These respondents are in a minority however the

inspection team are mindful of this feedback and continue to endeavour to minimise any negative impact of the inspection visit on patient treatment.

7.4. Of 78 respondents, three said that they did not have enough time to discuss the inspection findings on inspection and two felt they did not understand an issue of non-compliance. It is noted that inspection team leaders telephone clinics, where required, after an inspection and all but one respondent was satisfied with this interaction.

8. Conclusions

8.1. The sector remains largely compliant and the non-compliances identified during inspection relate to either high risk or complex areas of practice.

8.2. Inspections continue to adapt to the regulatory landscape and aim to raise the bar and clinics are clearly making improvements prompted by our regulatory activities. Post inspection feedback supports a conclusion that inspection visits lead to improvements in service delivery and patient care.

Annex 1: Analysis of data on inspection findings

Table A: The numbers of renewal and interim inspections performed in 2013/14 and 2014/15, by clinic size[6] and activity[7]

Centre size/activity	2013/14			2014/15		
	Renewal	Interim	Total inspections	Renewal	Interim	Total inspections
Large IVF	7	6	13	3	9	12
Medium IVF	12	7	19	8	2	10
Small IVF	9	6	15	7	2	9
IUI/DI+IUI	7	13	20	3	1	4
Storage only	2	2	4	3	0	3
Total	37	34	71	24	14	38

[6] A clinic that provides treatments to less than 500 patients per year is categorised as small; 501–999, medium and 1000+ large.

[7] Clinics with treatment and storage licences can provide a full in vitro fertilisation service (IVF), or storage facilities allowing insemination with stored donor sperm or partner sperm (DI+IUI). Other clinics have a treatment only licence and provide insemination with partner sperm (IUI) or a storage only licence and provide facilities for gamete and embryo storage only (Storage only). In this analysis DI+IUI and IUI clinics have been amalgamated due to the low numbers in each group and the common activities between them.

Figure 1

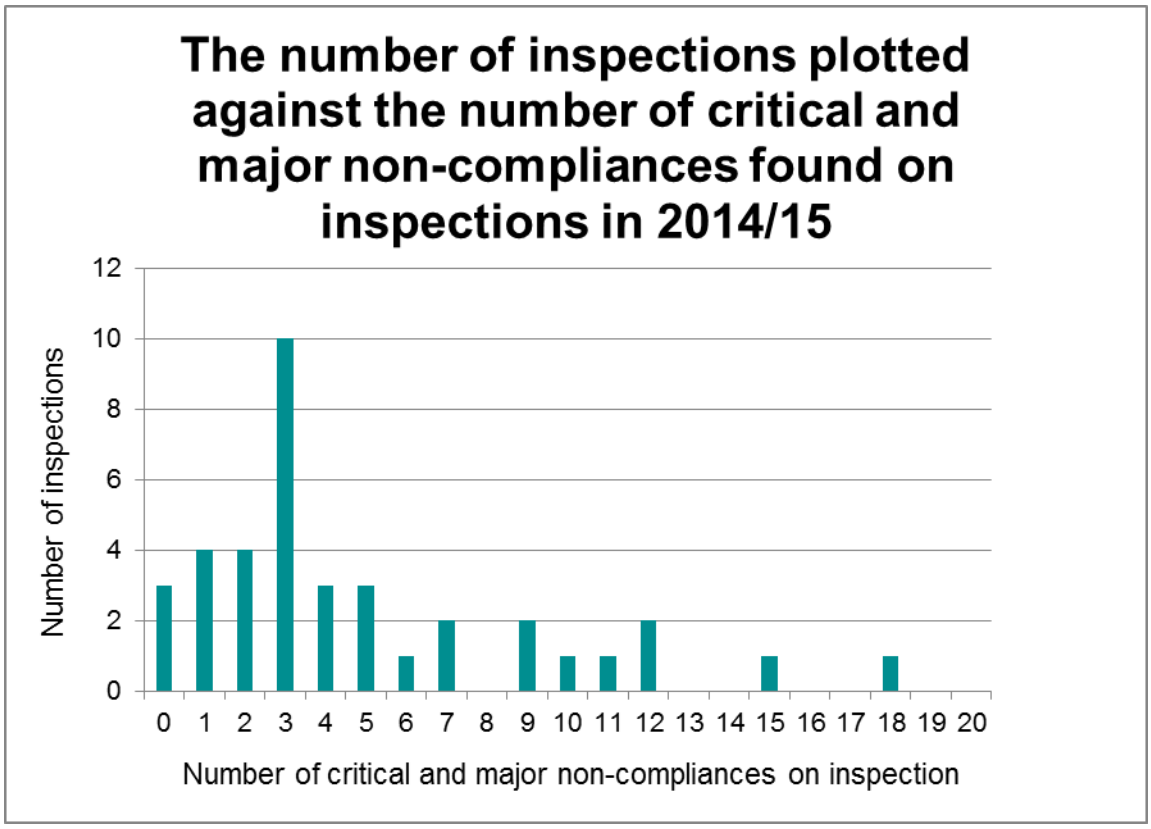

The number of inspections plotted against the number of critical and major non-compliances found on inspections in 2014/15
Number of inspections
0
2
4
6
8
10
12
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Number of critical and major non-compliances on inspection

Table B: Non-compliances grouped by severity - critical (C), major (M), other (O) - identified on renewal and interim inspections, and on all inspections to clinics of varying size and activities in 2013/14 and 2014/15. The corresponding detection rates per inspection are also shown. Increases (Red) and decreases (Green) in non-compliance detection rates in 2014/15 versus 2013/14 are highlighted to show at which types of clinic non-compliances and their severity is changing.

2013/14									
	Non-compliances found					Number per inspection			
Inspection type	C	M	O	All	Inspections	C	M	O	All
Renewal	5	118	233	356	37	0.1	3.2	6.3	9.6
Interim	3	57	68	128	34	0.1	1.7	2.0	3.8
Clinic size/activity									
Large	5	39	82	126	13	0.4	3.0	6.3	9.7
Medium	2	54	98	154	19	0.1	2.8	5.2	8.1
Small	0	43	67	110	15	0.0	2.9	4.5	7.3
DI/IUI + IUI	0	34	50	84	20	0.0	1.7	2.5	4.2
Storage only	1	5	4	10	4	0.3	1.3	1.0	2.5
Grand Total	8	175	301	484	71	0.1	2.5	4.2	6.8
2014/15									
	Non-compliance found					Number per inspection			
Inspection type	C	M	O	All	Inspections	C	M	O	All
Renewal	14	123	118	255	24	0.6	5.1	4.9	10.6
Interim	8	40	20	68	14	0.6	2.9	1.4	4.9
Clinic size/activity									
Large	4	32	40	76	12	0.3	2.7	3.3	6.3
Medium	4	50	42	96	10	0.4	5.0	4.2	9.6
Small	12	62	40	114	9	1.3	6.9	4.4	12.7
DI/IUI + IUI	2	13	11	26	4	0.5	3.3	2.8	6.5
Storage only		6	5	11	3	0.0	2.0	1.7	3.7
Grand Total	22	163	138	323	38	0.6	4.3	3.6	8.5

Figure 2: The number per inspection in 2014/15 of non-compliances of differing severity by clinic type and size

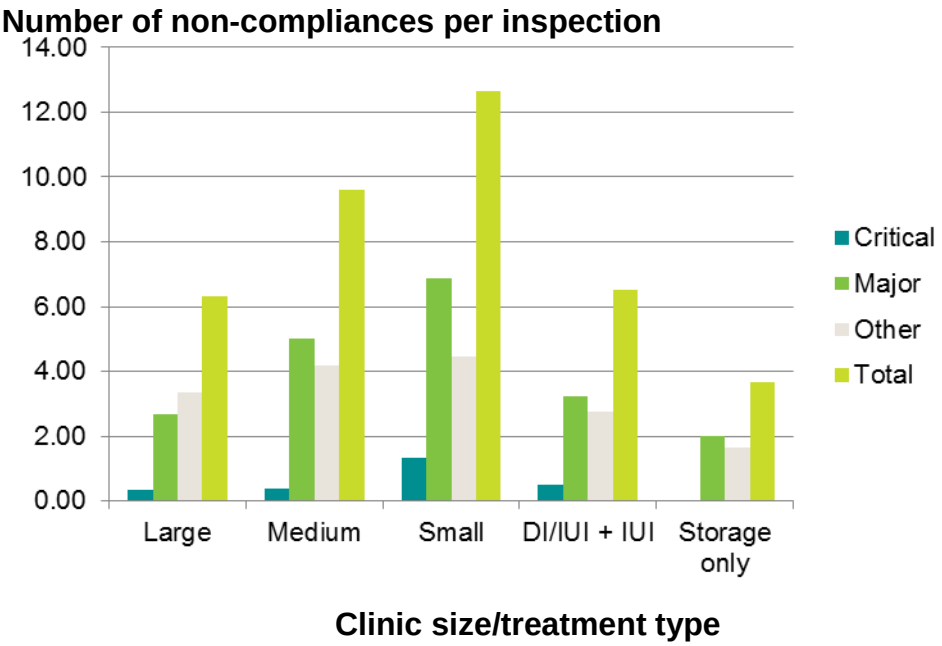


Figure 3: Five most frequently observed non-compliances by clinic size and type

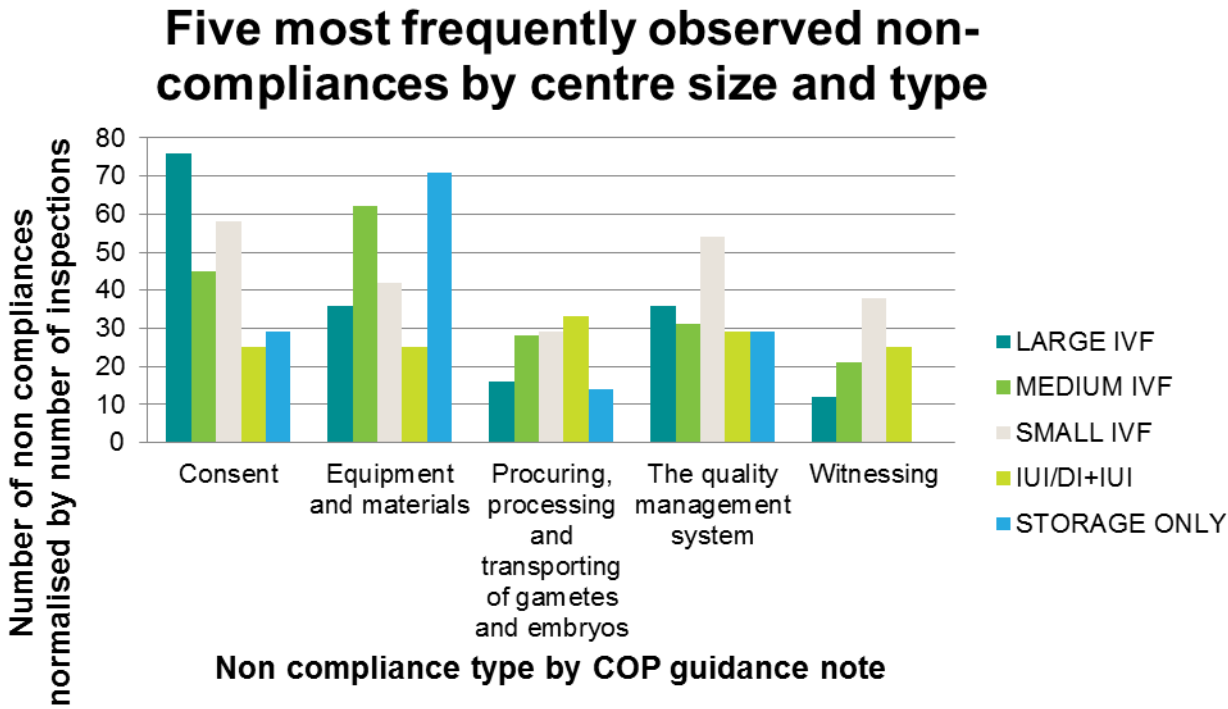


Table C: The detection prevalence per 100 inspections in 2013/15 of all non-compliances, by type, as a function of inspection type (All; renewal; interim) and clinic size and activities (Large IVF clinic; medium size IVF clinic; small IVF clinic; IUI/DI+IUI; storage only). The top six non-compliance types in each class are highlighted in pink.

	Detection rate/100 inspections in 2013-15							
Non-compliance type	**ALL**	**RENEWAL**	**INTERIM**	**LARGE IVF**	**MEDIUM IVF**	**SMALL IVF**	**IUI/DI+IUI**	**STORAGE ONLY**
Confidentiality and privacy	19	20	18	32	14	25	13	0
Consent	84	77	92	112	93	108	38	29
Counselling	12	20	2	12	7	33	0	0
Data submission	36	39	31	56	55	29	8	0
Donor payment	6	10	0	0	14	8	0	0
Donor selection	30	43	14	32	38	54	0	14
Egg sharing	6	10	0	4	14	4	0	0
Embryo testing	3	5	0	12	0	0	0	0
Equipment and materials	62	93	22	56	86	63	38	71
ICSI	2	2	2	0	3	4	0	0
Import and export	9	15	2	12	7	21	0	0
Incidents and complaints	6	11	0	8	3	13	4	0
Information provision	26	39	8	20	38	33	17	0
Multiple births	18	21	14	20	34	21	0	0
Payment of HFEA fees	4	3	4	0	14	0	0	0
Premises and facilities	31	43	16	32	31	54	13	14
Procuring, processing and transporting of gametes and embryos	53	85	12	48	45	71	63	14
Record keeping and document control	22	34	6	28	17	25	25	0
Research and training	11	18	2	20	17	8	0	0
Staff	30	38	20	16	28	54	33	0
Storage of gametes and embryos	14	18	8	12	17	21	4	14
Suitable practices	20	30	8	16	28	29	4	29
The quality management system	86	126	35	88	76	92	96	71
Third party agreements	30	48	8	40	34	33	13	29
Traceability	45	59	27	52	62	50	21	14
Website	5	7	2	8	7	0	4	0

Welfare of the child	17	25	6	20	21	13	17	0
Witnessing	53	64	39	52	59	67	50	0

Table D: The detection prevalence per 100 inspections in 2013/15 of only critical and major non-compliances, by type, as a function of inspection type (All; renewal; interim) and clinic size and activities (Large IVF clinic; medium size IVF clinic; small IVF clinic; IUI/DI+IUI; storage only). The top six non-compliance types in each class are highlighted in pink.

Non-compliance type	ALL	RENEWAL	INTERIMS	LARGE IVF	MEDIUM IVF	SMALL IVF	IUI/DI+IUI	STORAGE ONLY
Confidentiality and privacy	7	8	6	8	10	13	0	0
Consent	50	34	67	76	45	58	25	29
Counselling	8	15	0	0	7	29	0	0
Data submission	17	13	20	28	17	17	8	0
Donor payment	0	0	0	0	0	0	0	0
Donor selection	9	13	4	8	7	25	0	0
Egg sharing	5	8	0	4	10	4	0	0
Embryo testing	0	0	0	0	0	0	0	0
Equipment and materials	44	64	18	36	62	42	25	71
ICSI	1	2	0	0	0	4	0	0
Import and export	3	5	0	4	3	4	0	0
Incidents and complaints	4	7	0	4	3	8	0	0
Information provision	7	13	0	4	14	8	4	0
Multiple births	9	7	12	4	24	8	0	0
Payment of HFEA fees	1	2	0	0	3	0	0	0
Premises and facilities	18	25	10	16	17	38	8	0
Procuring, processing and transporting of gametes and embryos	26	41	6	16	28	29	33	14
Record keeping and document control	9	15	2	12	3	17	8	0
Research and training	3	5	0	4	3	4	0	0
Staff	14	15	12	4	10	29	17	0
Storage of gametes and embryos	9	13	4	12	14	13	0	0
Suitable practices	8	8	8	0	10	21	0	14
The quality management system	37	48	22	36	31	54	29	29
Third party agreements	11	18	2	20	7	13	4	14
Traceability	8	13	2	4	17	4	8	0
Website	0	0	0	0	0	0	0	0

Welfare of the child	8	11	4	8	10	8	8	0
Witnessing	22	25	18	12	21	38	25	0

Figure 4: Number of non-compliances observed in 2014/15 by guidance note and severity.

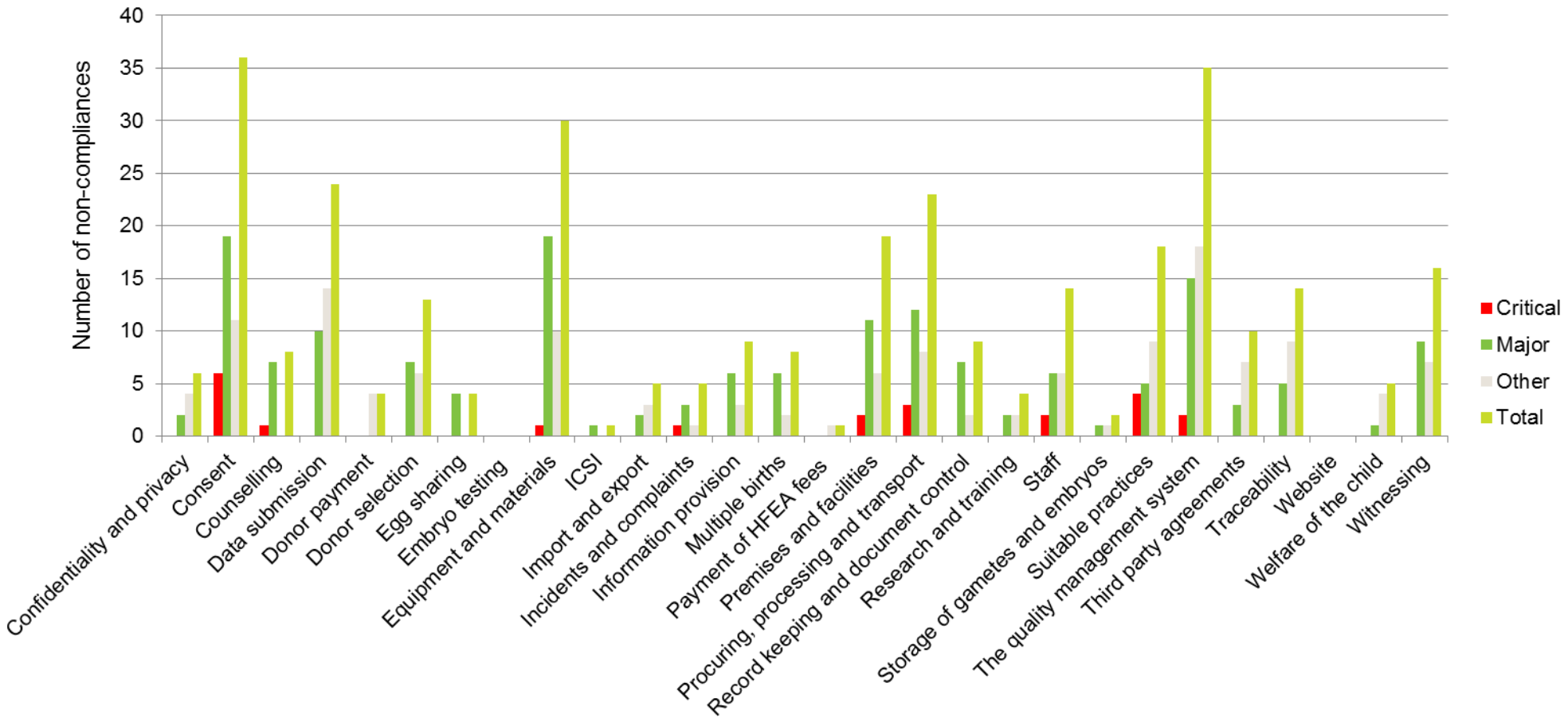


Table E: The percentage change in the prevalence of critical and major non-compliance types between 2013/14 and 2014/15, as a function of inspection type (All; renewal; interim) and clinic size and activities (Large IVF clinic; medium size IVF clinic; small IVF clinic; IUI/DI+IUI; storage only). Prevalence rate changes are proportionately colour coded from dark green at -100% (i.e. a decline to zero), to clear at 33%, to dark red at 300% and above. The prevalence rate of all non-compliance types in all inspections in 2014/15 (top 10 marked in pink) is included to show where prevalence increases may be relevant.

		As %increase between 2013/14 and 2014/15 IN RATE/100 inspections							
	Prevalence rate 2014/15	**ALL**	**RENEWAL**	**INTERIM**	**LARGE IVF**	**MEDIUM IVF**	**SMALL IVF**	**IUI/DI+IUI**	**STORAGE ONLY**
Confidentiality and privacy	16	-38	3	-100	-100	280	-100		
Consent	95	61	16	129	86	19	67	0	-100
Counselling	21	1395	1133			90			
Data submission	63	134	-8	467	171	-53	400	400	
Donor payment	11	No entries because no critical or major non-compliances were recorded in 2014/15							
Donor selection	34	336	363	143	8		233		
Egg sharing	11	647	517			280			
Embryo testing	0								
Equipment and materials	79	33	7	94	-46	138	-29	0	100
ICSI	3	No entries because no critical or major non-compliances were recorded in 2013/14							
Import and export	13	274	208				-100		
Incidents and complaints	13	No entries because no critical or major non-compliances were recorded in 2013/14							
Information provision	24	461	363				67	-100	
Multiple births	21	180		21		43			
Payment of HFEA fees	3	-100	-100			-100			
Premises and facilities	50	247	131	871	225	185	483	-100	
Procuring, processing and transporting of gametes and embryos	61	116	96	21	-64	90	900	200	
Record keeping and document control	24	336	440	-100	117		400	400	
Research and training	11	274	208		-100				
Staff	37	114	93	143	-100	-100	900	400	

Storage of gametes and embryos	5	-79	-78	-100	-100	-100	-17		
Suitable practices	47	No entries because no non-compliances were recorded in 2013/14							
The quality management system	92	38	9	102	-46	52	94	100	33
Third party agreements	26	-38	-42	-100	-100	90	233	-100	-100
Traceability	37	134	157	-100	-100	185		400	
Website	0	All non-compliances in 2014/15 were included in information provision							
Welfare of the child	13	-77	-74	-100	-100	-100	-100	400	
Witnessing	42	12	76	-70	-46	-5	33	150	

Table F: Critical, major and other non-compliances and the implementation of recommendations to address them, at clinics of varying size and activities in 2013/14 and 2014/15. The corresponding percentage of recommendations implemented is also shown.

clinic size/activity	Non-compliances found/recommendations implemented (as %)			
	Critical	Major	Other	All
2013-15				
All clinics	30/25 (83%)	338/283 (84%)	439/379 (86%)	**807/687 (85%)**
2013/14				
Large	5/5 (100%)	39/38 (97%)	82/81 (99%)	126/124 (98%)
Medium	2/2 (100%)	54/53 (98%)	98/81 (83%)	154/136 (88%)
Small	0	43/38 (88%)	67/53 (79%)	110/91 (83%)
DI/IUI + IUI	0	34/30 (88%)	50/46 (92%)	84/76 (90%)
Storage only	1/0 (0%)	5/5 (100%)	4/4 (100%)	10/9 (90%)
Grand Total	8/7 (88%)	175/164 (94%)	301/265 (88%)	**484/436 (90%)**
2014/15				
Large	4/4 (100%)	32/29 (91%)	40/36 (90%)	76/69 (91%)
Medium	4/2 (50%)	50/36 (72%)	42/39 (93%)	96/77 (80%)
Small	12/10 (83%)	62/38 (61%)	40/26 (65%)	114/74 (65%)
DI/IUI + IUI	2/2 (100%)	13/11 (85%)	11/8 (73%)	26/21 (81%)
Storage only	0	6/5 (83%)	5/5 (100%)	11/10 (91)
Grand Total	22/18 (82%)	163/119 (73%)	138/114 (83%)	**323/251 (78%)**

Compliance activities 2014/15: clinical governance learning

Strategic delivery:	☒ Setting standards	☐ Increasing and informing choice	☐ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	13		
Paper number	HFEA (16/09/2015) 770		
Meeting date	16 September 2015		
Author	Paula Nolan, Clinical governance lead/Inspector		
Output:			
For information or decision?	For information		
Recommendation	N/A		
Resource implications	In budget		
Implementation date	Through ongoing compliance activities		
Communication(s)	Through the annual incidents report.		
Organisational risk	☐ Low	☒ Medium	☐ High
Annexes	Annex 1: Clinic Focus articles Annex 2: Learning disseminated by other professional bodies Annex 3: Review of patient complaints Annex 4: Adverse incidents in fertility clinics: lessons to learn		

1. Background

1.1. An estimated 1% of the 60,000 cycles of IVF treatment that are carried out in the UK each year are affected by some sort of adverse incident.

1.2. The Person Responsible (PR) for an HFEA licensed clinic has a statutory duty to report and analyse the causes of incidents[1]. Similarly, the Authority has a duty[2] to investigate and take appropriate control measures in relation to reported incidents[3].

1.3. The primary reason for reporting and investigating incidents is to improve safety for patients, embryos and clinic staff. Reporting an incident is not enough on its own: to be most effective, learning should be extracted from each and every incident to minimise the risk of it happening again.

1.4. The HFEA has a national role in gathering information on incidents, identifying patterns and disseminating learning across the sector so that clinics can learn from the mistakes of others.

1.5. The PR also has a duty to implement and adhere to a complaints procedure. Every year, in addition to investigating incidents, the HFEA investigates a small number of complaints from patients unhappy about some aspect of their treatment. In 2014, for the first time we shared a summary of learning from patient complaints with the sector. As with incidents, there were common threads in the complaints made to the HFEA and the analysis was shared to help clinics deal with and learn from complaints more effectively.

2. Clinical governance developments in 2014/15

2.1. In 2013 the Authority published contextual information about incidents to promote shared learning across the sector. In July 2014, we published a summary of incidents reported by clinics between 1 January 2010 and 31 December 2012[4]. This report outlined the key features of the incidents reported by clinics and made recommendations to help clinics avoid having similar incidents. In December 2014, we published our first annual report, looking at incidents reported by clinics between 1 January 2013 and 31 December 2013[5]. The second annual report for incidents reported in 2014 (see annex 4) will be published today.

2.2. In the last year, to promote transparency and information sharing we developed a dedicated governance section on the HFEA website. This section includes links to all published A grade incident investigation reports and the

[1] An incident is a serious adverse event or reaction as defined at 27.2 and 27.3 of the Code of Practice.
[2] S.15A of the Act.
[3] Further information on our approach to incident handling can be found at http://www.hfea.gov.uk/6678.html
[4] http://www.hfea.gov.uk/docs/Adverse_incidents_in_fertility_clinics_2010-2012_-_lessons_to_learn.pdf
[5] http://www.hfea.gov.uk/docs/INCIDENTS_REPORT.pdf

accompanying Licence Committee minutes; the risk grading matrix; relevant definitions; and descriptions of the types of incidents that fall into the different incident categories[6].

2.3. Our inspectors have adjusted the focus of inspection to look for evidence that clinics have learnt from incidents rather than focussing on clinics' processes for incident reporting. Moreover, where clinics seem to be struggling to recognise when an incident should be reported to the HFEA the Clinical Governance Lead now provides bespoke incident training sessions to individual clinics.

2.4. Clinics reporting a high number of administration incidents[7] have also been offered further focused assistance by the Clinical Governance Lead. This support has encouraged clinics to carry out in-depth analysis of the causes of incidents (root cause analysis using the "five-why" technique – the subject of a well-attended session at the 2014 HFEA annual conference). This work is in the early stages however one clinic has managed to reduce their administration incidents from nine in 2014 to two this year following a focussed site visit.

2.5. Clinic Focus (the HFEA's monthly e-mail for licensed clinics) is being used as a platform to share ad hoc lessons from incidents (see annex 1) and also to disseminate good practice advice on handling complaints (see annex 3) and learning disseminated by other professional bodies (see annex 2).

2.6. We have also re-developed the patient complaint section of the HFEA website. This section now includes advice on how to make a complaint[8].

3. What we have learnt

3.1. The number of incidents reported in 2014 is not significantly different from previous years. "A" grade incidents usually happen as the result of a unique set of circumstances and are not usually foreseeable but where apparently avoidable low risk incidents (particularly administration incidents leading to breaches in confidentiality) continue to recur we are concerned that clinics' root cause analysis may not be sufficiently robust to identify effective corrective actions. This means that some avoidable incidents may continue to recur.

3.2. The recommendations and "lessons learnt" included in the previously published incident reports may need more time to be absorbed by clinics but one explanation may be that clinics are failing to embed learning as quickly or effectively as we would like.

3.3. Recent discussions with the Patient Safety Investigation Unit at NHS England suggest that this may be reflected across the healthcare sector in general. It is a common observation that corrective actions following incidents tend to impose additional administrative burdens (checking, documenting, double and triple checking) which may be impractical to adhere to and ineffective in

[6] http://www.hfea.gov.uk/6678.html
[7] especially breaches in patient confidentiality
[8] http://www.hfea.gov.uk/1072.html

preventing reoccurrence of incidents. To combat this, we are aiming to encourage clinics to fully engage with incident investigations to identify the root causes and opportunities for improvement rather than blaming "human error". This change in focus aims to encourage and promote the continued establishment of an open and learning culture in HFEA licensed clinics.

3.4. We also aim to keep our own processes under constant review and will aim to establish collaborative working relationships with NHS Improvement[9] to ensure that wider learning from colleagues working in patient safety in a healthcare setting feeds into our own ways of working.

3.5. The Authority is asked to note this report. In summary:

- We are seeking to influence the culture in licensed clinics so they develop an embedded learning and safety culture.
- We are aiming to ensure that our work on incident oversight reads across to our inspection activities.
- We are publishing a national report on incidents in 2014[10] today.

[9] The new jointly-led Monitor and NHS Trust Development Authority will be setting up a new Independent Patient Safety Investigation Service.
[10] See annex 4

Annex 1

Incidents case study: A cautionary tale on the use of benchtop incubators

Our recently published incidents report showed that equipment failure was the most commonly reported type of incident in the 'laboratory incidents' category. In the following case study, a clinic reflects on a major incident that occurred on their premises involving benchtop incubators.

"As embryologists working in the UK, we are lucky to have a legal framework and comprehensive sets of guidelines, regulations and professional standards around which to build our practice. Working in such a carefully controlled environment significantly reduces the risk of incidents, so it is always a major shock when a serious incident occurs. However, as part of the investigative process, it is also important to share any learning points identified.

Our unit has been using a combination of large front loading and benchtop mini-incubators for several years, without any previous significant issues. The benchtop incubators were introduced into practice in 2009 as part of a drive to introduce new technology to improve embryo implantation rates, following publication of the HFEA multiple births minimisation strategy. Benchtop incubators with a minimal chamber volume reportedly allowed better control of temperature (Cook et al, 2002) and better recovery of gas concentration after opening. This was said to lead to an improved and optimal culture environment (Fujiwara et al, 2007) as well as taking a mixed gas feed, enabling the use of low oxygen, which is potentially beneficial during extended culture to the blastocyst stage (Catt et al 2000; Meintjes et al 2009).

An extensive Installation Operational Qualification (IOQ) was carried out in our laboratory and a validation over several months provided confirmatory evidence of potential improved performance compared to the traditional large incubator. The IOQ, however, identified a potential issue with independent monitoring. In the large incubators, because of large chamber size, it was possible to monitor both CO2 and temperature independently, on a 24-hour basis, with an appropriate alarm system to alert on-call staff if either factor strayed outside set limits. In the bench top incubators, it was only possible to monitor temperature, as accurate CO2 probes were too large to fit inside the chamber.

A risk assessment was carried out and as a result, extra checks put in place to counteract this potential risk, such as regular measurement of pH, daily visual checks on the gas supply and the use of pH reference dishes following services and any prolonged period of inactivity.

However, such measures cannot identify problems with CO2 levels which occur outside normal working hours and recently, following a change of the humidification set, the gas supply to the culture chambers failed overnight after two days of working adequately. There had been a leak between the filter set and the gas inlet, probably due to a misthread the connector. As the gas supply to the gas inlet had not failed, the incubator did not go into system alarm and the fault went undetected overnight, causing irreparable damage to the embryos being cultured within. This represented a major incident for the unit and the patients involved.

Small chamber incubators, with or without time lapse, are in very common use throughout the UK and worldwide, but several currently have no capability for independent monitoring, particularly of CO2. Although providing improved overall performance over a number of years, this potential design flaw also poses a risk of which all embryologists should be aware. Due to this incident we have stopped using these particular benchtop incubators for overnight culture of embryos in our unit."

Contingency planning

As part of our commitment to share learning amongst clinics based on actual experience, this month we are looking at an incident around contingency planning. We have asked two centres to offer advice on their learning based on an actual incident and what a good contingency plan should consist of.

The scenario

In this case study ongoing building works at centre A meant that the contingency arrangement with centre B was activated. It became apparent after the arrangement was activated that centre B did not have the same licence as centre A. This effectively meant that centre B was carrying out an activity that they were not licenced to perform.

The learning outcomes

Regularly review arrangements

Contingency planning is normally set out in general terms to ensure that it covers all potential emergencies, in this case, citing the reasons for invoking the contingency arrangement. There may never be a need to invoke the arrangements and therefore they may remain relatively untested until they are required.

It is therefore important to **regularly check and review the contingency plan** for any changes within the clinics which may impact the effectiveness implementing the plan. For example, changes may include modifications to the clinics' licensed activities, changes in embryology methods or changes in capacity.

Have a shared checklist

A clear, shared checklist can help both parties to review the required contingency arrangements and to identify any major differences which would prevent the transfer of some or all patients. Pre-planning and working to a checklist will ensure that the plans can be completed smoothly and efficiently for all parties involved.

In this case where patient transfer was required, speed of response is essential and the checklist can be used to allow the transferring and receiving clinic to review both short and long term requirements.

After an incident the checklist can also assist in the post-transfer review to identify any areas for improvement.

What to include in a checklist

The checklist should be tailored to the specific needs of your clinic. However the following items should be considered:

- Communications with the HFEA informing the respective Inspectors for both clinics. This will ensure that specific guidance can be provided as required.
- Review the treatment licence for both clinics to ensure that there are no gaps.
- Review capacity in both clinics to ensure that the treatments can be safely transferred and accommodated.
- How information will be communicated to patients to minimise any concerns.
- Review if any equipment, consumables or staff to be transferred to receiving clinic.
- Discuss protocols to be followed.

The suggestions listed are intended to act as a guide to help improve or refine your current and we welcome your views in on ways of working that would help your peers.

Annex 2

Off-label use of intralipid infusions

Following concerns from the President of the RCOG about the administration of intralipid infusion to women undergoing IVF and those with a history of recurrent miscarriage, you should pay particular attention to the risks when prescribing the use of medicines off label.

The use of intralipid infusion for these indications represent off-label use of the medicine. Healthcare professionals' responsibilities when prescribing a medicine off-label may be greater than when prescribing a medicine for use within the terms of its licence. If you are prescribing the use of medicines off label you should pay particular attention to the risks which may include: adverse reactions; product quality; discrepant product information or labelling (eg, the patient information leaflet may be inconsistent with the medicine's off-label use). The MHRA provides guidance on off-label use of medicines on its website.

What you should do now

If you are prescribing the use of intralipid infusion off-label you should consider the advice of the President of the RCOG in relation to the evidence base for the use of the medicine in terms of its safety and efficacy.

- Take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up.
- Record the reasons for prescribing this medicine in the patient's records.
- Review the information that you provide to patients to make sure that you explain the reasons for prescribing this medicine off-label where there is little evidence to support its use.
- Document what information has been provided to your patients in the patient's records.

The documentation of your rationale for prescribing intralipid infusion off-label and of the information provide to patients receiving this treatment may be reviewed in the course of your HFEA inspection. This advice should be followed in all cases where you prescribe the use of medicines off-label.

Annex 3

HFEA report on patient complaints

We have carried out a review of patient complaints made to the HFEA about clinics.

Most people undergoing treatment have a positive experience. However when things do go wrong, it is important to deal with such issues in the right way so that the individual can receive justice and the organisation can learn from what went wrong.

We can only consider a complaint that indicates a potential breach of the Act, licence conditions or directions. We expect clinics to take complaints seriously, carry out an investigation into the issues raised, explain what went wrong and offer an apology (when appropriate). We also expect clinics to explain what measures have been taken to put matters right. If you do this well then patients feel they have been listened to and that their concerns have been acknowledged and taken seriously.

During calendar years 2011, 2012 and 2013, the HFEA received 133 queries from patients regarding complaints about clinics. Most complainants had not accessed the clinic's grievance procedure and simply wanted advice on whether or not they had grounds to make a complaint and if so, how to do so.

During the same three-year period, nine queries were investigated further. In seven of these the intervention was minimal and required no further action other than contacting the clinic to chase up the response or to ask the clinic to re-review their complaint response to make it clearer. One complaint resulted in a further investigation by the HFEA and one complaint resulted in a site visit and further investigation.

What bad looks like according to those surveyed:

- No formal acknowledgement of the complaint
- A lack of accuracy in the clinic's response (for example, a letter that contains wrong names or incorrect treatment dates, indicating to the complainant that the clinic has not investigated their complaint seriously).
- Apologies that feel insincere or part of a generic corporate template (for example, a complaint response that begins with "I am sorry that you felt you have cause to complain").
- Responses that ignore specific concerns or do not fully engage with the concerns raised by the complainant.
- A response that contains defensive or legalistic language.
- Late responses or no response at all.

What good looks like according to those surveyed:

- Having access to an 'intermediate' contact – perhaps a general manager – to discuss a concern before submitting a formal complaint.
- A response that addresses the initial complaint directly and accurately.
- A personalised apology.

- The offer of face-to-face meetings with plenty of time to talk through the complaint response in detail.
- A single point of contact to support the complainant and help them understand what they want to achieve through their complaint.
- Clarity at every stage of the complaint process. If a complaint is complex in nature and may take longer than usual to investigate, complainants should be kept up to date with their case.
- A final response that includes the lessons that have been learnt and what steps the clinic will take.
- Staff training on how the complaints system works and how to help patients access it.
- Training and support for staff that have had a complaint upheld about them.

You may want to review your own complaint handling procedures to make sure that this aspect of the service is as good as it can be.

Annex 4

Adverse incidents in fertility clinics: lessons to learn

To follow

Compliance and enforcement policy

Strategic delivery:	☐ Setting standards	☐ Increasing and informing choice	☒ Demonstrating efficiency economy and value

Details:	
Meeting	Authority
Agenda item	14
Paper number	HFEA (16/09/2015) 771
Meeting date	16 September 2015
Author	Debra Bloor, Chief Inspector
Output:	
For information or decision?	For decision
Recommendation	It is recommended that the Authority agrees the revisions proposed in this paper and its annexes.
Resource implications	In budget
Implementation date	Draft policy to be published on website and publicised in a Clinic Focus article. September to December 2015: focussed consultation and piloting of policy. Implementation of final revisions: December 2015. Final revisions referred to Authority early 2016.
Communication(s)	Policy to be published in final form April 2016.

Organisational risk	☐ Low	☐ Medium	☒ High

Annexes	Annex 1: A review of matters to be considered on renewal or grant of a licence as referenced in indicative applications guidance Annex 2: Advantages and disadvantages of licences of different lengths Annex 3: Factors which a Licensing Committee may consider to be aggravating features when considering whether to impose regulatory sanctions Annex 4: Compliance and Enforcement Policy showing proposed track changes

1. Background

1.1. The HFEA's Compliance and Enforcement (C&E) policy (http://www.hfea.gov.uk/docs/Compliance_and_Enforcement_Policy_(2011).pdf) sets out our approach on the escalation and management of concerns about regulatory compliance. This policy is part of a suite of documents that also includes the Indicative Sanctions Guidance (http://www.hfea.gov.uk/docs/Indicative_Sanctions_Guidance.PDF) and the Indicative Applications Guidance (http://www.hfea.gov.uk/docs/2009-08-21_Indicative_applications_guidance.pdf).

1.2. This paper sets out draft proposals and recommendations for the update of this suite of documents based on learning from recent experiences and feedback from Authority members and committee Chairs on the factors that should be taken into account when considering regulatory sanctions. This paper is one of a series that sets out the proposed future direction of the regulatory regime based on previous findings and experience and in consideration of the goals of the HFEA's strategy.

1.3. This revised policy will be subject to a focused consultation and will be piloted in the next three months. Final recommendations and proposals will be referred to the Authority early in 2016 prior to implementation in April 2016.

2. The C&E policy: review and recommendations

2.1. The C&E policy is a living document that guides the compliance team when there are difficult decisions to be made. The biggest challenges arise when decisions are made about whether regulatory non compliance poses such a significant risk that suspension or revocation of a licence may be warranted. Experience suggests that the principles and application of the current policy are broadly effective in guiding the compliance team's activities in a considerate and proportionate way.

2.2. Routine inspection findings are based on a snapshot of evidence and observations but are effective in highlighting where improvements are required. In the majority of cases non compliances observed on inspection do not pose an immediate and/or direct risk to patients, their gametes or embryos and effective recommendations for improvement can be framed and implemented. In this respect the levels of scrutiny applied in the course of routine regulatory activity appears appropriately calibrated.

2.3. Learning from a recent case suggests that where serious regulatory sanctions may be warranted then consideration should be given to the conduct of a more forensic review of a clinic's practices: to determine whether the critical non-compliance(s) prompting action represent one off anomalies, a practice, or are indicative of other serious failings.

2.4. When a decision not to recommend grant of a licence is being considered this may be at a time when the relations between the HFEA and the licensed clinic are strained. In such circumstances, there can be a reluctance to conduct further investigations for fear of accusations of harassment. Clinic staff may feel or allege they are being treated differently and or disproportionately. To provide clarity and ensure transparency, it is recommended that the current policy is updated to explain that informal action may include further, potentially forensic scrutiny of a clinic's practices where there have been observations of non-compliance that have posed or may pose a future risk to the safety of patients or to their gametes or embryos, or where a serious breach of the Act is observed or suspected. In enshrining this in the policy this should ensure clinics are only subject to such scrutiny if concerns are suitably serious while empowering the compliance team in what may otherwise be challenging circumstances.

2.5. The current C&E policy does not set out the circumstances in which a report of the findings of any investigation will be drafted and referred to a licensing committee. It is recommended that a report should be drafted whenever improvements are required and that the report should be referred to a licensing committee and be published on the HFEA's website. It is recommended that where an investigation concludes that concerns have no foundation and that there are no recommendations for improvement then no further action beyond documenting this finding in the management review records will be taken.

2.6. Amendments to the current policy are also proposed to rationalise the practical sequence of events. The compliance team's current practice is to hold a management review meeting when a concern is identified to decide whether a concern is sufficiently serious to warrant further investigation and to decide and document the agreed course of action. It is recommended that the policy is updated to reflect this current practice.

2.7. Proposed changes (including additional minor changes to those outlined above) are tracked in the copy of the C&E policy at annex 4.

3. The indicative applications guidance: review and recommendations

3.1. The indicative applications guidance sets out the matters to be considered on renewal or grant of a licence and provides a framework for deciding the length of licence to grant.

3.2. A review of the current guidance is included at annexes 1 and 2. As a result of the review it is recommended that consideration be given to fairly substantive changes to the guidance.

3.3. It is recommended that the guidance is amended to reference matters outlined below.

- Consideration of the clinic history should routinely include (but not be restricted to) consideration of the committee minutes from the time of the clinic's last renewal or four years (if the licence was renewed less than four years prior to the application under consideration); implementation of recommendations made at the time of the last inspection; and co-operation with any alerts, advice and/or recommendations made in the intervening time;
- When considering the duration of a licence the committee should consider the scale of non-compliance; the PR's apparent understanding of the impact of the non-compliance; the PRs commitment (or otherwise) to implement corrective actions within agreed timescales; and most importantly, the risks of non-compliance to safety of patients, their embryos or gametes and or the quality of service at the time that the decision is being made.
- When considering the duration of a licence the committee should also consider the quality of service provided by the clinic. To assure consistency and proportionality consideration of quality should be based on observation of the clinics long term trends in success rates, and; feedback provided by patients.

3.4. In relation to the length of licence to be granted it is recommended that four year licences remain the norm for treatment clinics; three year licences are considered where there are concerns that warrant further focused inspection after one year; two year licences are not routinely issued; one year licences are issued where there are wide ranging concerns that mean a full inspection within one year is indicated; consideration is given to the issue of Special Directions in exceptional circumstances where a clinic's licence is likely to expire before it can be demonstrated that substantive improvements have been effective.

4. Indicative sanctions guidance: review and recommendations

4.1. Experience suggests that the principles and application of the current policy are broadly effective, ensuring the proportionality and consistency in relation to regulatory sanctions.

4.2. A review of the current guidance is included at annex 3. As a result of the review it is recommended that consideration be given to changes to the guidance with respect to factors listed as aggravating. The recommendations for change aim to align the guidance with the sections of the Act that outline when the Authority may revoke vary or suspend a licence.

4.3. In summary it is recommended the guidance is revised to list the following as aggravating factors:

- Failure by the PR to ensure that suitable practices are used to ensure the safety of patients their gametes or embryos and or the quality of service provided and or the quality of service (option two at point 1 of annex 3).

- Failure by the PR to ensure compliance with the conditions of the licence where this may carry a risk to the safety of patients their gametes or embryos and or the quality of service.
- The PR ceases to be considered a suitable person by virtue of dishonesty and or failure to cooperate with investigations particularly where this may have compromised the safety of patients their gametes or embryos and or the quality of service.
- Failure by the PR to ensure suitability of staff; that proper equipment is used or that premises are suitable particularly where this has or may impact on the safety of patients their gametes or embryos and or the quality of service.

Annex 1: A review of matters to be considered on renewal or grant of a licence as referenced in indicative applications guidance

The current indicative applications guidance sets out the matters that a Licensing Committee (LC) (either a Licence Committee of the Authority or the Executive Licensing Panel) will normally take into account when deciding the duration of a licence. The following annex records whether information on these matters is currently made available to these committees and makes suggestions for revising the guidance. The recommendations for revision are informed by feedback from Committee Chair's, Authority members (in the course of a workshop), and on the basis of current decision making practices of the Executive.

Matters to be considered on renewal or grant of a licence	**Reporting of these matters**	**Comment and suggestion on the continuing reference to this requirement in the guidance**
1. Adherence to the regulatory principles published by the Authority	• Reports are currently structured to report inspection findings with reference to regulatory principles. However, the report does not specifically comment on compliance with principles.	• As reference to regulatory principles is inherent in compliance with statutory requirements then it is not considered likely to be an advantage for LC or ELP to be guided to consider these matters specifically when considering the duration of a licence. • It is recommended that the guidance to consider regulatory principles is removed from the applications guidance
2. History of compliance with statutory requirements; Directions issued by the Authority; Licence Conditions; and the Code of Practice issued by the Authority	• A clinic's "history of compliance" in terms of the implementation of recommendations made in previous reports is commented on explicitly in inspection reports. Reports also document co-operation with any guidance, alerts, advice and/or recommendations made in the time between inspections. • Information about a clinic's history is also	• Making an assessment of the "history" of non-compliance is a very significant factor in informing the Executive's recommendation relating to the duration of any licence to be granted. • To maintain consistency**, it is recommended that guidance clarifies that consideration of the clinic history should routinely include**

	contained in minutes made available to the LC.	**(but not be restricted to) consideration of the committee minutes from the time of the clinic's last renewal or four years (if the licence was renewed less than four years prior to the application under consideration); implementation of recommendations made at the time of the last inspection; and co-operation with any alerts, advice and/or recommendations made in the intervening time**. It is recommended that the committee papers should therefore include four years of licensing history in the form of committee minutes to show a picture of compliance over the entire time period since the last grant of the licence. • As noted below where there is a previous occurrence of failure to implement recommendations for improvement and/or take appropriate action with respect to alerts, advice or guidance then there may be justifiable reason to return to a clinic earlier than the two year norm so that evidence of the implementation of effective corrective action can be reviewed in the course of a focused site visit. This is not meant to be punitive but is intended to encourage and ensure regulatory compliance.
3. Compliance with recommendations made by Licence Committee/Executive Licensing Panel/Compliance Department	• See above – this is captured in consideration of a clinic's history	• It is recommended that this is removed from the applications guidance

4. Status of the quality management systems in place at the premises to be licensed Status of the premises and facilities at the premises to be licensed Timely provision of accurate Register data to the Authority	• All non-compliance with statutory requirements – including these aspects of practice - is commented on in reports.	• In the absence of assurance that the PR has or will ensure compliance with statutory requirements then the statutory test for issue of a licence (as outlined in decision trees) cannot be met and a licence cannot be recommended or granted. • These three aspects of compliance (the requirement to have a QMS, suitable premises and to submit data to the HFEA) have no unique role in ensuring the safety of gametes, embryos or patients however and it is recommended that this is removed from the applications guidance**.** • **It is recommended that the guidance is revised to note that the when considering the duration of a licence the committee should consider the scale of non-compliance; the PR's apparent understanding of the impact of the non-compliance; the PRs commitment (or otherwise) to implement corrective actions within agreed timescales; and most importantly, the risks to safety of patients, their embryos or gametes and or the quality of service of non-compliances as they remain at the time that the decision is being made.** • This recommendation aims to ensure proportionality - so even if a report documents a large number of non-compliances, where there has been a prompt and effective response it is recognised that the risks associated with non-

		compliance have been mitigated. Where the PRs response indicates failure to commit to make improvements or even failure to appreciate the seriousness of non-compliance then there may be reduced confidence that compliance can be assured going forward and therefore there may be justifiable reason to return to a clinic earlier than the two year norm so that evidence of the implementation of effective corrective action can be reviewed in the course of a focused site visit. As above this is not meant to be punitive but is intended to encourage and ensure regulatory compliance.
5. Number of incidents reported by the clinic in comparison to the average number of incidents reported per clinic	• The Executive does not compare the number of incidents reported by clinics. Serious incidents (grade A and some grade B incidents) are the subject of reports to LC	• Any reference to specific incidents in routine inspection reports could have the effect of deterring open and transparent incident reporting and this in turn could impact on opportunities for learning from incidents. • It is recommended that the guidance is revised to remove reference to these matters. • It is noted that in considering an incident investigation report a LC would take into account the risks of any non-compliance or failure identified in the investigation and the clinic's history and this should provide assurance that due consideration is given to incidents in matters of licensing.
6. Number of complaints made to the Authority against the Clinic in comparison to the average number of complaints per clinic	• The Executive does not compare the number of complaints made against clinics and this is not referenced in inspection reports. The number of complaints reported is small and	• It is recommended that the guidance is revised to remove reference to these matters.

	often beyond the remit of the HFEA (being in relation to costs, funding, waiting times etc.).	• Should a complaint investigation identify serious concerns that warrant recommendations for improvement or even regulatory sanction then this would be escalated to LC in a separate report so, as with incidents, there is assurance that where relevant, due consideration is given to complaints in matters of licensing.
7. Number of multiple embryo transfers in comparison to the annual range set by the Authority	• The number of multiple embryo transfers is not a proxy for multiple live birth rates or multiple clinical pregnancy rates. • Data on the number of multiple embryo transfers are not available to the inspection team and are not therefore included in reports. • Clinics receive alerts from the HFEA's risk based assessment tool where there is a upward trend in their clinical multiple pregnancy rate. Clinics are expected to investigate the reasons for the trend and where appropriate to implement improvements. monitoring of clinics' clinical multiple pregnancy rate is continuous.	• It is recommended that the guidance is revised to remove reference to these matters in acknowledgement that compliance with the multiple births target is captured in general consideration of regulatory compliance.
8. Number of live births in comparison to the national average	• These data are available to the inspection team and are commented on in all reports. • Clinics receive alerts from the HFEA's risk based assessment tool where there is a downward trend in their success rates. Clinics are expected to investigate the reasons for the trend and where appropriate to implement improvements. Monitoring of clinics' success	• It should be noted that a clinic's response to performance alerts is commented on in reports and so issues of persistent poor performance play a part in the decision on the duration of licence to be recommended. However, this matter goes to the quality of service provided rather than regulatory compliance. Like regulatory compliance the quality of service is a significant factor in determining the recommendation about the duration of a licence.

	rates is continuous.	It is noted however that success rates form only a part of the assessment of quality of service. • **In consideration of this it is recommended that the guidance is revised to note that when considering the duration of a licence the committee should also consider the quality of service provided. To assure consistency and proportionality consideration of quality should be based on observation of the clinics long term trends in success rates, clinical multiple pregnancy rates; and feedback provided by patients**.

Annex 2 – Advantages and disadvantages of licences of different lengths

Length of Licence	Anticipated circumstances of issue	Advantages and disadvantages
4 years	It is suggested that consideration is given to the issue of a 4 year licence where: • a clinic has taken appropriate action in relation to any non-compliances identified as posing a risk to patients, their gametes or embryos; • where the Person Responsible has given a commitment to the implementation of all the required recommendations in relation to critical and major non compliances • the clinic's history suggests that the PR has previously implemented recommendations for improvement and or advice and guidance. • there are no serious concerns about the quality of service based on observation of success rates; multiple birth rates; and patient feedback.	A four year licence minimises the regulatory burden for clinics with an unannounced observation based interim inspection occurring at year two.
3 years	Licences could be issued for 3 years where a clinic has: • a history that indicates a previous failure to implement recommendations for improvement in the time since the last licence renewal; • no history (as with a new clinic – particularly one with no previous history of HFEA requirements)	A three year licence would allow a clinic to be subject to an interim inspection within one year (rather than the usual two) to review evidence of implementation of recommendations and/ or to review quality of service. Depending on the issues for review this inspection is likely to be announced. The clinic would perceive an increased regulatory burden in the first year but if the interim inspection

	• there are concerns related to quality of service.	findings were to demonstrate compliance then the clinic could revert to the usual cycle with renewal after a further two years. If the interim inspection failed to find evidence of compliance with recommendations then a committee would have an opportunity to consider regulatory sanctions within one year of the grant of the licence rather than the usual two. The imposition of an interim inspection within one year (rather than a renewal which would be needed if a one year licence were to be granted) would allow the compliance team to conduct a targeted inspection: this would have the effect of minimising the impact on compliance resources while providing a clear signal to the clinic that the Authority requires improvement. The added advantage of a targeted inspection is that the clinic and the compliance team would not focus on activities that were considered fully compliant at the previous inspection. It is noted that should the interim inspection highlight ongoing concerns procedures for imposition of additional licence conditions or for revocation are more complex mid licence but a licence can be varied to impose conditions or a notice of proposal to revoke a licence can be issued at any time. It is rare however for a clinic to fail to implement recommendations for improvement within prescribed timescales. **It is recommended that three year licences are**

		adopted as the norm in the circumstances described and for new clinics without any significant experience of HFEA regulatory requirements.
2 years	Licences could be issued for 2 years in the circumstances described above	The options in this case are • targeted interim at year one followed by renewal at year two, This would send a signal to the clinic that improvement is required but in the absence of an opportunity to revert to the usual two year inspection cycle in the event of satisfactory compliance at year one could impose a disproportionate regulatory burden on the clinic and impact on compliance team resources; • renewal at year two only. This could permit persistence of non-compliance, followed by a non-focussed renewal review of all activities including those considered compliant at the time of original renewal. **It is not recommended that two year licences are usually issued.**
1 year	Licences could be issued for 1 year in the circumstances described above or where concerns are particularly serious.	This would increase the burden of regulation but would have the effect of giving the compliance team a clear opportunity to review improvements made after one year. There would also be opportunity for imposition of additional conditions should non-compliance persist at the time of the one year renewal. This would impact negatively on compliance resources

		with the conduct of a renewal inspection after one year requiring re review of all activities as opposed to those requiring improvement. This would be warranted should concerns be wide ranging. **It is recommended that this option is considered where there are serious wide ranging concerns and there is either a poor history of compliance or insufficient information to assure a committee that the required improvements will be made.**
Adjournment and/or issue of Special Directions	Where there is a history that suggests serious concerns about a PR's ability to ensure regulatory compliance then a LC could give consideration to adjourning a decision (perhaps requiring issue of Special Directions) pending the submission of further evidence.	This would have the benefit of allowing grant of a licence only after the PR was able to demonstrate – through the submission of audits or even following a further inspection – not only that recommendations for improvement have been implemented but also that they have been **effective** in preventing recurrence of non-compliance. Demonstration of the effectiveness of corrective actions requires a clinic to be operational and then to conduct an audit of relevant practices to provide assurance of their compliance with requirements This option may be most effective where there are very serious concerns about the PRs understanding of the need for improvement and/or in the case of serious concerns about performance at a newly licensed clinic where there is inevitably limited information to support a conclusion that a PR is likely to meet requirements.

Annex 3: factors which a Licensing Committee may consider to be aggravating features when considering whether to impose regulatory sanctions

Aggravating features as currently referenced in the indicative sanctions guidance	**Comments on these features**	**Suggested amendment to indicative sanctions guidance**
1. Failure to obtain required consents relating to use/storage of gametes and embryos and/or to keep proper records of such consents Failure to comply with consents relating to use/storage of gametes and embryos Failure to comply with witnessing protocols and procedures Failure to comply with multiple birth minimisation strategy without good reason Failure to provide Authority with information required to be included in the Statutory Register under Section 31 of	The HFEA's risk based assessment tool (RBAT) recognises • Consent failures • Incorrect identification of gametes/embryos • Multiple Pregnancy • Incorrect or incomplete information on donors as four of the six most significant risks associated with IVF treatment. RBAT also considers the following as significant risks of IVF: • Cross infection of gametes, embryos or patients • Damage or Loss of gametes or embryos Where a clinic fails to ensure suitable practices are in place to mitigate these key risks then regulatory sanctions may clearly be warranted. It should be acknowledged however that non-compliances with respect to these areas of	Option 1 Failure of the PR to mitigate the risks of the following to be referenced as aggravating features in the indicative sanctions guidance: • Consent failures • Incorrect identification of gametes/embryos • Multiple pregnancy rate • Cross infection of gametes, embryos or patients • Incorrect or incomplete information on donors • Damage or loss of gametes or embryos In recognition however that this list is not and cannot be exhaustive and that there may be other factors which could pose risks to the safety of patients and or their gametes or embryos it is proposed that the indicative sanctions guidance could be significantly simplified as suggested below. Option 2 **Failure by the PR to ensure that suitable practices are used to ensure the safety of patients their gametes or embryos and or the quality of service provided and or the quality of service provided to be referenced as an aggravating feature in the**

the Act (critical information about donors for example)	practice are common and regulatory sanctions would not usually be considered necessary unless a clinic failed to act on recommendations for improvement.	**indicative sanctions guidance.** While this option is broader, it does reflect actual practice and by referencing the requirement for suitable practices this also aligns the guidance to the circumstances described in the Act[1] when a licence may be revoked, varied or suspended.

[1] **Section 18 (Revocation of licence) of the 1990 Human Fertilisation and Embryology Act (as amended) (the Act)**
(2) The Authority may revoke a licence otherwise than on application under subsection (1) if--
(a) it is satisfied that any information given for the purposes of the application for the licence was in any material respect false or misleading,
(b) it is satisfied that the person responsible has failed to discharge, or is unable because of incapacity to discharge, the duty under section 17,
(c) it is satisfied that the person responsible has failed to comply with directions given in connection with any licence,
(d) it ceases to be satisfied that the premises specified in the licence are suitable for the licensed activity,
(g) it ceases to be satisfied that the person responsible is a suitable person to supervise the licensed activity,
(i) it is satisfied that there has been any other material change of circumstances since the licence was granted.
Section 17 of the Act
(1) It shall be the duty of the individual under whose supervision the activities authorised by a licence are carried on (referred to in this Act as the "person responsible") to secure--
(a) that the other persons to whom the licence applies are of such character, and are so qualified by training and experience, as to be suitable persons to participate in the activities authorised by the licence,
(b) that proper equipment is used,
(d) that suitable practices are used in the course of the activities, . . .
(e) that the conditions of the licence are complied with,
(g) that the Authority is notified and provided with a report analysing the cause and the ensuing outcome of any serious adverse event or serious adverse reaction.
19C Power to suspend licence
(1) Where the Authority--
(a) has reasonable grounds to suspect that there are grounds for revoking a licence, and
(b) is of the opinion that the licence should immediately be suspended,

2. Breach of patient confidentiality Breach of statutory storage periods for storage of gametes/embryos Failure to notify Authority of incidents Failure to properly investigate complaints from users of, or persons affected by, the service offered by the clinic	As described in annex 1, non-compliance with statutory requirements – including these aspects of practice - is commented on in reports and influences any recommendations on the grant or otherwise of a licence. Where failure to ensure compliance with these (or any statutory requirements) has implications for the safety of patients, their gametes or embryos then this might lead to a conclusion that the PR has failed to ensure the use of suitable practices and, therefore, to discharge their duty.	It is recommended that specific reference to these features is removed from the indicative sanctions guidance. **It is recommended that failure by the PR to ensure compliance with the conditions of the licence where this may carry a risk to the safety of patients their gametes or embryos and or the quality of service provided should be referenced as an aggravating feature in the indicative sanctions guidance.**
3. Repeated breaches of licence conditions or failure to comply with Directions issued by the Authority Failure to comply with recommendations or warnings made by Inspector/Compliance Department Failure to comply with recommendations or warnings	As noted in paragraph 2 of annex 1, the history of compliance is commented on in reports and influences any recommendations on the grant or otherwise of a licence.	It is recommended that specific reference to these features is removed from the indicative sanctions guidance. These matters are captured in the recommendations suggested above.

issued by Licence Committee		
Dishonesty Failure to co-operate with investigation or inspection Failure to notify Authority of material change in circumstances	These matters go to the suitability of the PR.	**It is recommended that the guidance be revised to reflect that it will be considered an aggravating factor where the person responsible ceases to be considered a suitable person to supervise the licensed activity by virtue of dishonesty and or failure to cooperate with investigations particularly where this may compromise the safety of patients their gametes or embryos and or the quality of service provided.**
Abuse of trust/position Disregard for system of regulation Disregard of generally accepted/established guidelines or Code of Practice Failure to respond to correspondence from Authority	Assessment of these matters is considered likely to be subjective	It is recommended that specific reference to these features is removed from the indicative sanctions guidance in acknowledgement.
	The indicative sanctions guidance does not currently reference that failure to ensure the suitability of staff; that proper equipment is used, and; the suitability of premises may be grounds for revocation or suspension of a licence.	**It is recommended that the guidance be revised to reflect that it will be considered an aggravating factor where the person responsible fails to ensure suitability of staff; that proper equipment is used and that premises are suitable particularly where this may impact on the safety of patients their gametes or embryos and or the quality of service provided.**

Annex 4: Compliance and Enforcement Policy showing proposed track changes

Purpose of this policy

1.1 This document and appendices set out the Authority's policy on the approach to be adopted, and the measures taken, by the Authority's Compliance Department in order to promote and maintain compliance by licensed centres with:

a) all relevant statutory provisions;~~the provisions of the Human Fertilisation and Embryology Act 1990 ("the Act");~~
b) licence conditions;
c) directions issued by the Authority; and
d) the Code of Practice issued by the Authority under Section 25 of the Act.

1.2 This policy replaces all previous policies relating to these matters.

When to apply this procedure

2.1. The planned inspection process

2.2 The escalation and management of concerns regarding the compliance and or the quality of service provided by a centre

The enforcement policy

3. THE INSPECTION PROCESS

3.1 The purpose of an inspection is to:

a) assess the extent to which centres comply with the Act; licence conditions; directions and the provisions of the Code of Practice;
b) provide an independent and professional perspective on the running of the centre;
c) promote good practice so that centres can improve the quality of service they provide to patients and donors;
d) provide centres with a positive learning experience;
e) provide centres with the opportunity to feed back on their experience of the inspection process, in order to assist the Authority to continually improve its procedures;
f) give patients reliable information about a centre's compliance with statutory and other obligations and about the quality and safety of licensed activities undertaken at that centre.

3.2 All inspections will be:

a) evidence based, consistent, proportionate and open to scrutiny;
b) undertaken in a professional and courteous manner;

c) be focused on risk;
d) aim to add value for centres and service users.

3.3 ~~The core assumption will be that centres wish to demonstrate compliance with the Act; licence conditions; directions and the Code of Practice. The onus is on centres to demonstrate compliance not on inspectors to find fault.~~

3.4 During the course of an inspection of a licensed centre, the inspection team may identify and require improvements to be made. The inspection team will explain to the Person Responsible ~~for the centre~~ why any improvement needs to be made and the ~~legal~~ basis for requiring it. The team will take account mitigating factors (those being the factors set out in the Indicative Sanctions Guidance) when considering what recommendations to make. ~~of the challenges a centre might face in meeting a requirement (but must always be mindful of the health, safety and well-being of people who use the service)~~.

3.5 A report ~~of every inspection~~ will be drafted following every inspection. The Persons Responsible ~~for licensed centre~~ will be shown the report in draft and will be provided with a reasonable opportunity to comment on the findings and recommendations of the draft report.

3.6 The ~~final~~ report will be sent to the Executive Licensing Panel or Licence Committee. The Executive Licensing Panel or Licence Committee make the final decision as to whether a licence should be granted, renewed, allowed to continue, varied, revoked or suspended. The Executive Licensing Panel or Licence Committee also make the final decision as to the actions a centre should take in relation to any area(s) of non-compliance identified as part of the inspection visit.

3.7 After consideration by the Executive Licensing Panel or Licence Committee, ~~routine li~~nspection ~~R~~reports will normally be published on the Authority's website. ~~Reports will be produced and published in a style and format which is accessible to all our stakeholders, particularly patients~~.

4. THE ESCALATION AND MANAGEMENT OF CONCERNS REGARDING THE COMPLIANCE OF A CENTRE

4.1 Where the ~~Authority~~ executive becomes aware ~~that a licensed centre has failed to comply with the provisions of the Act; the conditions attached to its licence; relevant directions issued by the Authority; or the Code of Practice issued by the Authority~~of concerns about a centre's compliance or performance, a management review meeting will be held to evaluate the risk and determine a proportionate course of action. ~~as outlined below~~. ~~Minutes~~A record of the management review meeting will be kept. ~~.it will normally first seek to encourage the centre to undertake any necessary remedial action and improvements. Where a centre persistently fails to comply, the Authority will seek to achieve compliance via an escalating scale of informal measures to~~

~~formal enforcement action. The diagram at Appendix 1 demonstrates this approach.~~

4.2 Following an evaluation of the actual or potential risks to the safety of patients, gametes and or embryos arising as a consequence of the concerns under investigation, consideration will be given to the most appropriate action. Informal action, including any or all of the following, may be taken ~~Informal action may including any or all of the following actions~~:

a) implementation of a period of performance monitoring

b) contacting and/or meeting with the Person Responsible and/or other key staff members to discuss concerns

c) an investigation into the foundation, scope and /or scale of concerns. This may include commissioning a review by an expert advisor.

d) an unannounced or scheduled inspection visit (depending on the nature of the concerns under investigation). Where there have been observations of non-compliance that have or may pose a risk to the safety of patients, their gametes or embryos or where a serious breach of the Act is suspected the inspection may include potentially forensic scrutiny of some or all of a centre's practices. Where it is necessary to protect the identity of a whistle-blower or information source the investigation or inspection may be initiated before the full details of any concerns or allegations are provided to the PR;

e) ~~contacting the Person Responsible to discuss area(s) of non-compliance and remedial action identified that that the Person Responsible must undertake and the timescales for doing so if formal enforcement is to be avoided;~~

f) where investigation identifies areas for improvement, completion of a report of the findings of the investigation informing the Person Responsible ~~in writing of the minimum levels~~ of the required improvements ~~identified that that the Person Responsible must undertake~~ and the timescales their implementation~~if formal enforcement is to be avoided~~;

~~g) meeting with the Person Responsible to discuss requirements and improvement options (including formulating an improvement plan);~~

~~h)~~g) sending a warning letter to the Person Responsible, informing him that formal enforcement will be undertaken if the identified improvements are not completed within a given time scale;

~~i)~~h) referring a report of the findings of an investigation to the Executive Licensing Panel or Licence Committee documenting recommendations.

4.3 Where actual risks to the safety of patients, gametes and or embryos are identified then the following actions may be taken without recourse to the actions descrivbed above ~~Formal action may include any or all of the following actions:~~

a) referring ~~the case~~a report for consideration by the Executive Licensing Panel / Licence Committee with a recommendation that the licence should be varied (including by imposing additional conditions);

~~referring the case for consideration by the Executive Licensing Panel / Licence Committee with a recommendation that an additional inspection be scheduled in order to monitor compliance~~

~~b) referring the case~~a report ~~for consideration by the Executive Licensing Panel/Licence Committee with a recommendation for that a shortened term licence should be granted;~~

~~c)~~b) referring ~~the case~~the a report for consideration by the Licence Committee with a recommendation that the licence should be revoked (or suspended);

~~d)~~c) exercising powers under Section 39 of the Act (taking possession of material from licensed centres during an inspection)

~~e)~~d) applying for a warrant in accordance with 40 of the Act;

~~f)~~e) where a criminal offence may have been committed, referring the matter to the police for criminal investigation; or

f) where professional codes of conduct may have been breached, referring the professional concerned to the relevant professional body;

g) where concerns may be relevant to another regulator, informing the relevant regulatory body.

4.4 The Authority's compliance department may take formal action if:-

a) there are concerns about the ability of the Person Responsible to discharge his duties under Section 17 of the Act;

b) the centre has not completed or does not appear likely to complete any necessary recommendations for improvement within the stipulated time frame;

c) the centre has a previous history of non-compliance or failure to ~~undertake remedial actions~~implement recommendations for improvement promptly or within required timeframes;

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d) there is a risk to patients or service users, or to gametes and embryos; or

e) there is evidence that a criminal offence may have been, or is being, committed.

4.5 In deciding whether to take formal or informal action, the Authority's compliance department will use professional judgement, may take legal advice; and will act proportionately. The compliance department will not make a recommendation for the revocation (or suspension) of the Licence unless one or more of the requirements of Section 18(1) or (2) of the Act are met.

4.6 ~~The key mechanism in deciding what action (if any) to take, will be the Management Review. Where the compliance department becomes aware that a centre may not be complying with the Act; licence conditions; directions; or the Code of Practice, a management review meeting will held in relation to that centre. Subsequent review meetings may be held to monitor the situation~~.

4.7 ~~The conduct of the Management Review meeting will be in accordance with the department's protocol and the review meetings will be minuted to provide an audit trail of the consideration of the case and to demonstrate compliance with the principles set out in this policy.~~

4.8 The initial management review will include the centre inspector and at least one ~~Head of Department~~senior member of the compliance team and such other persons considered appropriate. Those conducting the review will at all times, seek to act in a way which is:

- fair and non-discriminatory;
- targeted;
- efficient and effective;
- transparent;
- focused on patients;
- proportionate;
- risk focussed;
- timely;
- co-ordinated;
- consistent.

4.9 ~~In taking action or making recommendations to the Licence Committee, the Authority's compliance department will take account of the **attitude** of the PR and the centre's compliance history, the **risk** to patients and the **impact** on people using the service.~~

4.10 ~~Any recommendations made in respect of proposed conditions should be "SMART" (Specific, Measurable, Achievable, Realistic and Time-bound)~~

4.11 ~~The~~ Informal action and or recommendations will be formulated by the management review team. Formal action will be agreed with the Chief Inspector and/or the Director of Compliance ~~shall formulate any~~

~~recommendations to be made at the conclusion of the Management Review~~. Where there is a recommendation ~~is that the matter should be referred~~to refer a concern to the police or that a warrant should be obtained, the recommendation will be brought to the attention of the Chief Executive.

4.12 Where the Authority has reasonable grounds for suspecting that an offence under the 1990 Act is being or has been committed on any premises, it may apply to a Justice of the Peace for a warrant to enter, search and seize materials from those premises.

4.13 Where the Chief Executive has been informed that the recommendation of the Management Review is that a warrant should be applied for, they ~~shall~~ will inform the Chair of the Authority of the recommendation and the reasons for it.

4.14 The Chair may consult the Deputy Chair and the Chair of the Audit and Governance Committee about the recommendation.

4.15 In the event of a disagreement amongst those consulted, the Chair may veto the recommendation. The decision to apply for the warrant shall otherwise be made by the Chief Executive.

Appendix 1

~~Fig. 1: An illustration of the escalating scale of informal measures to formal enforcement action~~