Human Fertilisation & Embryology Authority

# Authority meeting

## Date: 19 July 2022 – 10.45am to 2.35pm

## Venue: HFEA Office, 2nd Floor 2 Redman Place, London E20 1JQ

| Agenda item | Time |
|---|---|
| 1. Welcome, apologies and declarations of interest | 10.45am |
| 2. Minutes of the meeting held on 18 May and matters arising<br>For decision | 10.50am |
| 3. Chair and Chief Executive's Report – to note<br>For information | 11.00am |
| 4. Committee Chairs' Reports<br>For information | 11.15am |
| 5. Performance Report<br>For information | 11.30am |
| Lunch break | 12.00pm |
| 6. Treatment add-ons: updating the rating system and evidence base<br>For decision | 12.30pm |
| 7. Modernising Fertility Regulation - update<br>For information | 1.30pm |
| 8. Any Other Business | 2.30pm |
| 9. Close | 2.35pm |

# Minutes of Authority meeting held on 18 May 2022

| Details: | | | |
|---|---|---|---|
| Area(s) of strategy this paper relates to: | The best care – effective and ethical care for everyone<br>The right information – to ensure that people can access the right information at the right time<br>Shaping the future – to embrace and engage with changes in the law, science and society | | |
| Agenda item | 2 | | |
| Meeting date | 19 July 2022 | | |
| Author | Debbie Okutubo, Governance Manager | | |
| **Output:** | | | |
| For information or decision? | For decision | | |
| Recommendation | Members are asked to confirm the minutes of the Authority meeting held on 18 May 2022 as a true record of the meeting | | |
| Resource implications | | | |
| Implementation date | | | |
| Communication(s) | | | |
| Organisational risk | ☐ Low | ☒ Medium | ☐ High |
| Annexes | | | |

# Minutes of the Authority meeting on 18 May 2022 held at the HFEA Office, 2nd Floor 2 Redman Place, London E20 1JQ

| | | |
|---|---|---|
| Members present | Julia Chain<br>Catharine Seddon<br>Jason Kasraie<br>Tim Child<br>Frances Flinter<br>Graham James<br>Geeta Nargund | Jonathan Herring<br>Gudrun Moore<br>Alison Marsden<br>Alex Kafetz<br>Zeynep Gurtin<br>Alison McTavish |
| Apologies | Frances Ashcroft | |
| Observers | Amy Parsons (Department of Health and Social Care - DHSC) | |
| Staff in attendance | Peter Thompson<br>Richard Sydee<br>Clare Ettinghausen<br>Rachel Cutting | Paula Robinson<br>Debbie Okutubo<br>Joanne Anton<br>Catherine Drennan |

### Members

There were 13 members at the meeting – eight lay and five professional members.

## 1. Welcome and declarations of interest

**1.1.** The Chair opened the meeting by welcoming Authority members and staff. The Chair stated that the meeting was audio recorded in line with previous meetings and for transparency reasons, and that the recording would be made available on our website to allow members of the public hear it.

**1.2.** Members were advised that Catharine Seddon was now on the board of Children and Family Court Advisory and Support Service (Cafcass).

**1.3.** Declarations of interest were made by:

- Tim Child (PR at a licensed clinic)
- Jason Kasraie (PR at a licensed clinic)
- Geeta Nargund (Clinician at a licensed clinic)
- Alison McTavish (Professional at a licensed clinic).

## 2. Minutes of the last meeting

**2.1.** Members agreed that the minutes of the meeting held on 23 March 2022 were a true record of the meeting and could be signed by the Chair.

**2.2.** The status of all matters arising was noted.

## 3. Chair and Chief Executive's report

**3.1.** The Chair gave an overview of her engagement with key stakeholders and the decision-making committees of the Authority. The Chair commented that she spoke at the British Infertility Counselling Association (BICA) conference last week giving an update on the HFEA's preparation for modernising the Act, including the establishment of the Legal Advisory Reform Group (LRAG). It was noted that the Chair of BICA had joined LRAG. The Chair further commented that even though we did not currently have a counsellor sitting as an Authority member, the involvement of BICA in the work of LRAG was very much valued.

**3.2.** Regarding filling vacancies to the Scientific and Clinical Advances Advisory Committee (SCAAC), members were advised that following an open process of selection and interviewing, two new members had been appointed.

**3.3.** The appraisals for longer standing Authority members took place in the last fortnight and the Chair's appraisal will take place next week. Following the Chair's appraisal, objective setting will occur with all Authority members.

**3.4.** The annual accountability meeting with the Department of Health and Social Care (DHSC) was scheduled for the week commencing 23 May and the Chief Executive had written a letter summarising our work during the past year to the department, which would form part of the discussion at the meeting. It was noted that the letter will be circulated to Authority members.

**3.5.** The Chair further commented on the induction session for new members that took place recently and that she had joined for part of it. She expressed her thanks to the Chief Executive and the Senior Management Team (SMT) for putting the programme together. Members commented that they felt it was a very good induction and thanked SMT for giving up their time to do this. Members also commented that the training with the Legal Advisor for Licence Committee and Statutory Approvals Committee members was very useful.

**3.6.** The Chair commented that some members were yet to complete their online cyber security training.

**3.7.** The Chief Executive provided an update on the key external activities that he has been involved in since the last Authority meeting.

**3.8.** In response to a question, it was noted that there were no enquiries or updates on the import or export of gametes or any news relating to surrogates from Ukraine.

**3.9.** In terms of the effects of inflation on staff recruitment, the Chief Executive commented that recruitment was holding up, but some roles were more difficult than others to fill as the labour market remained competitive. He further commented that the longer this current situation continued, the higher the risk of it having an adverse effect on the HFEA.

### Standing orders

**3.10.** The Chief Executive presented the update to Standing Orders to enable the Scientific and Clinical Advances Advisory Committee (SCAAC) to have an additional Authority member to sit on the committee.

**3.11.** All members voted in favour of the change.

Decision

**3.12.** Members noted the Chair and Chief Executive's report and that the accountability letter to the department will be circulated to members.

## 4. Committee Chairs' reports

**4.1.** The Chair invited Committee Chairs to add any other comments to the presented reports.

**4.2.** The Licence Committee Chair (Alison Marsden) gave an update on the meeting held on 5 May 2022 and welcomed the new members that had joined the committee.

**4.3.** The Statutory Approvals Committee (SAC) Chair (Jonathan Herring) commented that they had met three times since the last Authority meeting and that similar to the Licence Committee, there was now a change in membership, and welcomed all the new members.

**4.4.** The Chair commented that members on SAC operated from a pool and that as long as members could attend six to seven meetings a year the committee's monthly meetings would remain quorate.

Decision

**4.5.** Members noted the Committee Chairs' updates.

## 5. Performance report

**5.1.** The Chief Executive commented that by the next meeting, there will be an updated version of the key performance indicators report, following development work on several indicators.

**5.2.** Members were advised that performance in March was generally good but that there were four red indicators:

- HR1: Sickness
- HR2: Turnover
- C1: Efficiency of the end-to-end inspection and licensing process
- C3 PGT-M average processing.

**5.3.** It was noted that the staff sickness indicator had remained red over the last two months, partly as a result of two staff members being on long term sick leave.

**5.4.** During March, staff turnover remained high. It was noted that an all-staff event was held in May and a third of the staff members were new since the last such opportunity, before the Covid pandemic. The Chief Executive commented that such a level of turnover put a considerable strain on our work and that there was an expectation that this would continue to be a challenge.

**5.5.** An update was given on the status of PRISM. The Chief Executive stated that progress with PRISM was positive. Members were advised that clinics that were using PRISM directly had an average error rate of less than 1% but those clinics using third party solutions (API) had an average error rate of between 6 to 8%. We therefore needed to work with the latter group to get every clinic up to the same level of performance on error rates. There were six clinics left to deploy and this should happen over the next few weeks.

**5.6.** Members asked about the PGT-M average processing time and where the bottlenecks were. The Chief Executive responded that there was some variability in the factors causing delays from month to month. Part of the issue was the unpredictability of when applications would be made, and in what numbers; and securing a peer reviewer who could perform their part of the process in time for an application to progress to a monthly meeting meant that some items would take longer to reach the committee. On the part of members, it was felt that attending SAC meetings once a month was all we could ask members to accommodate. Lastly, it was difficult to predict how complicated an application will be until we received it.

**5.7.** Members commented that we needed to become more pragmatic about peer reviewers, and that from the patient's point of view the wait was probably twice as long, and therefore turnaround time needed to be improved where possible.

**5.8.** The SAC Chair also agreed that it was difficult to predict the number and end to end length of applications since all agendas were application led. The committee often considered similar conditions alongside the condition applied for, and it was suggested that one possibility might be to consider whether this was always the right course of action.

**5.9.** Regarding the key performance indicator scorecard, the Chief Executive commented that the new report format would address some of the concerns that members might have and provide better insight into the data.

**5.10.** Members asked what was being done about the PRISM outliers. The Chief Executive responded that clinics that had PRISM could see their input errors immediately, since it was visible to them on their systems. With API clinics, the errors were not so apparent to users, however, it is possible for API users to log on to PRISM to see errors.

**5.11.** The Chief Executive commented that we were trying to build a culture among clinics of getting it right first time and that training would continue to be rolled out for PRISM and API users so they can deliver the best care for patients and make accurate data returns to the HFEA.

**5.12.** Members asked if the Authority could work with third party suppliers (APIs) to eliminate errors. The Chief Executive responded that these were commercial companies that we do not regulate. We engaged with them on developing their API solution for PRISM but they were now responsible for ensuring their customer clinics was able to provide accurate data to the register.

**5.13.** On staff turnover, members asked what were the common themes from exit interviews, so that lessons learned could be implemented to retain staff. The Chief Executive responded that the general theme was that in a small organisation like the HFEA there were few opportunities for promotion and that in some roles, public sector salaries were not competitive compared to the private sector. The Chief Executive commented that unfortunately there was little or nothing the HFEA could do about either.

### Strategy and Corporate Affairs

**5.14.** The Director of Strategy and Corporate Affairs presented this item. She informed members that the Fertility Show took place in London as a face-to-face event for patients to meet with clinics and this year the HFEA took the decision not to have a stand. However, various staff and Authority members had taken part in sessions on specific topics for patients.

**5.15.** It was noted that the Director of Strategy and Corporate Affairs was in conversation with the British Fertility Society about further follow-on actions from the ethnic diversity in fertility treatment report. A second clinic workshop following the actions in this report would be held in June.

**5.16.** The report on the HFEA patient survey has been published in April and was covered in the media and social media. Our report on Covid-19 and fertility treatment in 2020 had been published in May and also received widespread coverage.

**5.17.** The Planning and Governance team were working on an updated set of Key Performance Indicators for the report to be presented at the July Authority.

**5.18.** SCAAC's next meeting would be in June and they will be looking at whether the evidence base used to review treatment add-ons should be expanded. A patient and clinic staff survey on the HFEA add-ons information was currently being undertaken and we had received a very good response. The results of the survey on what information we presented on the HFEA website on add-ons, as well as the SCAAC recommendation on the evidence base would be brought back to Authority for decision in due course.

## Compliance and Information

**5.19.** The Director of Compliance and Information presented to the Authority. There was good progress being made against the backlog on the Opening the Register (OTR) service. The team closed 147 cases in March and received 70. In April, 67 cases were closed and 58 were received, the lower number processed was due to staff annual leave and other project work. In May, to date they had closed 62 cases with another 72 ready for second checking and 97 were being worked on. In this calendar year the team had responded to 403 requests for information.

**5.20.** Members were advised that they had received positive feedback from service users and the Director thanked the OTR team.

**5.21.** Members were advised that in April, four planned and one additional inspections were carried out. In May there are eight planned and four additional inspections. There are 70 planned inspections scheduled for the remaining months of this year.

**5.22.** The new Head of IT is now in post with a handover period with the current Head of IT who is retiring at the end of May. Members were advised that much focus was on cyber security in response to the increased global threat. A penetration test has been carried out on PRISM and the Register and a further test is planned for IT infrastructure in July. Other control measures have been put in place and we will continue to monitor our systems.

**5.23.** The Chair commented that she was pleased to see that the OTR backlog was being cleared as this would put us in good stead for 2023.

## Finance and Resources

**5.24.** The Director of Finance and Resources presented this item. Members were advised that the figures were not actuals as the billing of clinics was based upon assumptions from the 2019/2020 figures. It was noted that until a full reconciliation was done, we would not know the actual income. It was further noted that the clinics that were not yet on PRISM would continue to have estimates which would be reconciled once they were fully reporting through PRISM.

**5.25.** For the underspend, that will be reconciled once the proper data has been inputted.

**5.26.** Members were advised that the budget for this financial year had been delegated and that the Chief Executive had signed it off.

**5.27.** Members asked about our policy on reserves. The Director of Finance and Resources responded that we could only spend money that we had generated in that financial year.

Decision

**5.28.** Members noted the performance report.

## 6. Covid-19 update

**6.1.** The Director of Strategy and Corporate Affairs commented that the decision regarding whether to revoke GD0014 v2 was deferred from the last meeting. Members were advised that to help understand the impact of Covid-19 on fertility treatment, a report was published on 17 May 2022. The Authority noted the hard work from clinic staff to ensure safe services could resume during the pandemic.

**6.2.** Members were advised that from March 2020 until April 2022 information for patients and clinic staff related to Covid-19 was prioritised on our website. Going forward these pages will no longer be updated but the information will be retained on the website for reference and will be revised if the pandemic situation changes in the future.

**6.3.** At the March 2022 Authority meeting, members considered whether it was the right time to revoke GD0014v2 as legal restrictions had now eased across the UK and it was good regulatory practice to remove unnecessary rules.

**6.4.** In response to a question the Director of Compliance and Information reassured members that there was flexibility to quickly reintroduce GD0014 v2 should a significant wave occur in the future.

**6.5.** The Chair commented that there was anecdotal evidence that many patients suffered delays in accessing tests or procedures before having fertility treatment due to the effect of the pandemic and asked the professional members what their experiences were.

**6.6.** Members commented that delays were seen in services (both in women and men services) and this adversely affected patients, in particular older women. Some members commented that in terms of diagnostics, they were no longer seeing any delays in semen analysis although in some areas such as general gynaecology there were still delays.

**6.7.** Members asked how staff planned on using and learning from the report, especially in the primary care setting and in communities where they already were experiencing delays in accessing services.

**6.8.** The Director of Strategy and Corporate Affairs commented that GPs could be both an enabler and a blocker to accessing treatment and that there was anecdotal evidence that some patients from Black and Minority Ethnic communities sometimes delayed accessing GP services. It was noted that there were originally plans for working with GPs to be part of the business plan but owing to pressures on primary care due to Covid it had been necessary to delay this work.

**6.9.** In response to a question, it was noted that if there was a regional lockdown, it may not be necessary to reintroduce GD0014 v2 since clinics had developed their protocols for the first wave which they could reintroduce.

**6.10.** Members commented that the vaccination programme in the UK had helped us in terms of Covid and therefore, while caution was appropriate, we did not need to be overcautious as we were not in the same place as some other countries. It was also noted that in the National Health Service (NHS) they planned six months ahead and that learning had occurred through working and living with Covid.

**6.11.** A member asked if the Authority received feedback from patients about their experience of announcements from the HFEA and agreed to discuss with the Director of Strategy and Corporate Affairs outside of the meeting and share the feedback that they had received in their organisation.

**6.12.** Some members commented that they were comfortable with the way the Authority navigated the Covid-19 situation and asked about the psychological impact and the live birth rate as there was some evidence that this had fallen globally over the last two years.

**6.13.** The Director of Compliance and Information responded that there was no data that we could use to verify this, because not all clinics had caught up with data submission following PRISM launch. There was therefore no way of measuring the effects of the pandemic on live births but that this would be updated in the future fertility trends data report in 2023.

**6.14.** Members commented that there was huge demand for translation services in some clinics and asked if the HFEA experienced the same. The Director of Strategy and Corporate Affairs responded that we had very few, if any, direct requests to translate our information.

**6.15.** The Chair commented that we would continue to keep an eye on this situation and that once PRISM was fully implemented across all the clinics, we should analyse the data we held.

### Decision

**6.16.** Members agreed to revoke GD 0014v2 since almost all legal restrictions had been lifted by the Westminster and devolved governments.

**6.17.** Members noted the Covid-19 and fertility treatment report published in May 2022.

**6.18.** Members noted that patient and professional information relating to Covid-19 would no longer be updated on our website unless the situation with the pandemic changed again.

**6.19.** Members noted the preparation that had taken place as required for the Covid-19 Public Inquiry.

## 7. Gamete and embryo storage

**7.1.** The Head of Policy presented this item. The current legal regime was outlined and members were advised that following a consultation on gamete and embryo storage, the Government introduced changes to the HFE Act 1990 in the Health and Care Act 2022.

**7.2.** The key storage changes were discussed. Members were told that:

- patients wishing to store gametes or embryos for their own treatment would be able to store for up to a maximum of 55 years, provided that they renewed their consent every 10 years
- Donors would be able to store for up to 55 years and did not need to renew their consent
- Transitional provisions would enable patients who already had gametes or embryos in storage to benefit from the extended storage period provided certain steps were taken within prescribed timeframes

- The 2009 regulations were being revoked. All patients would need to move to the new regime. Patients using extended storage for premature infertility would need to be contacted by their clinic
- Patients could consent to the use and storage of their gametes or embryos in the event of their death for 10 years from their date of death, or 10 years from when they were certified as having lost capacity.

**7.3.** The risks associated with these changes were also explained to members, which included:

- The complexity of the new rules
- Provisions on posthumous use would negatively impact some patients
- Significant changes required clinic staff to understand them, which would take time
- There was a short time frame for implementation.

**7.4.** Members were advised that the starting date for the new law was 1 July 2022 and the transitional period would start on that date and end on 30 June 2024.

**7.5.** The Head of Policy went on to explain the HFEA's next steps which were:

- To publish the new Clinic guide, along with new and revised consent forms, (including renewal of consent forms) and the revised General Directions on the Clinic Portal by the end of May/early June.
- The new standard licence conditions and General Directions which would come into force on 1 July 2022 would be signed off by the Chair who had delegated authority from the Board.
- There would be a strikethrough of out-of-date Code of Practice guidance on storage and clinics would be directed to the Clinic Portal storage information, with an update to the Code of Practice to follow in due course.
- To use the transitional period to continue to work with clinics to develop further guidance and training material, including hosting a number of training events and webinars to help clinics understand and implement the new changes.

**7.6.** In response to a question from members, it was noted that the Chair of the Association of Reproductive and Clinical Scientists (ARCS) was engaged on the storage changes. Members further commented that ARCS should have a role to play in providing best practice guidelines on contacting patients for renewal of consent.

**7.7.** Regarding the website, members requested that the website should be updated and that there should be explanations on cost.

**7.8.** On the 10-year renewal of consent, members asked who had the responsibility for keeping patient contact details up to date – the clinic or the patient. Staff explained that there was no legal duty on either and so there would therefore need to be co-operation between both parties.

**7.9.** Also, the guidance to clinics on the renewal of the consent process would include an explanation of the actions they needed to take. The Head of Legal explained that pro-forma notices were being developed to reduce the burden on clinics. Members commented that templates will be very useful as the language used in the regulations says 'reasonable steps' should be taken, which could have a number of definitions.

**7.10.** The Director of Compliance and Information commented that short videos or other tools would be put together as part of the training for clinic staff.

**7.11.** Members commented that GPs usually had up to date addresses for patients, therefore clinics should be encouraged to work with GP surgeries to contact patients who might inadvertently not update their addresses.

**7.12.** In response to a question, the Chief Executive clarified that our role as the regulator was to provide all the necessary advice and guidance to clinics to support them in managing the changes, but that ultimately it is the clinics' responsibility to ensure that they comply with the new storage rules and that they obtain the necessary consents from their patients.

**7.13.** Members commented that careful communication with patient groups and patients should also be considered.

**7.14.** The Director of Strategy and Corporate Affairs stated that there was an agenda item on the stakeholder group meeting later this month and in June to discuss the storage changes.

**7.15.** The Chair thanked the team for all the work they were doing.

Decision

**7.16.** Members noted the gamete and embryo storage changes and the next steps for the HFEA.

## 8. Modernising Fertility Regulation - update

**8.1.** The Director of Strategy and Corporate Affairs presented this item. Members were reminded that the aim of this work was to deliver an outline proposal on the modernisation of the HFE Act to the DHSC at around the end of the year.

**8.2.** Members were advised that a group had been established to advise the Authority on some of the issues. The Legislative Reform Advisory Group (LRAG) would be meeting periodically and the papers would be circulated to members and posted on the HFEA website.

**8.3.** It was noted that all suggestions that came out of the group would be shared with the Authority.

**8.4.** Members commented that it was interesting to see views on the power to levy financial penalties and commented that they were in support of that area being pursued.

**8.5.** A question was raised about whether the roles and responsibilities of Persons Responsible (PRs) and Licence Holders should be reviewed, with a view to incorporating wider board responsibility for the way clinics function. In response, Members commented that PRs set the culture in clinics and there may be an issue if more than one person held this responsibility, since it might render the role less effective. It was noted that the idea of having a nominated deputy for a PR could perhaps be explored further but in terms of the governance structure and ensuring compliance, licence holders and PRs should be the ones taking on that responsibility.

**8.6.** The Director of Strategy and Corporate Affairs commented that some of the points raised by members were brought up during the deliberations at the last LRAG meeting and that the responses from LRAG will be shared with the Authority.

**8.7.** It was noted that in proposing ways of modernising the Act, we were hoping to have powers which would give us greater flexibility to improve patient protection.

**8.8.** The Chair commented that papers would come to the Authority in early autumn and members would have the opportunity to get together and have a detailed discussion at that stage.

Decision

**8.9.** Members noted the issues raised and the next steps in relation to modernising the Act.

**8.10.** Members were advised that LRAG minutes will be sent to them.

## 9. Any other business

**9.1.** There was no other business.

## Chair's signature

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

Signature

Chair: Julia Chain

Date: 19 July 2022

# Authority meeting

# Matters Arising

## Details about this paper

| | | | |
|---|---|---|---|
| Area(s) of strategy this paper relates to: | The best care – effective and ethical care for everyone<br>The right information – to ensure that people can access the right information at the right time<br>Shaping the future – to embrace and engage with changes in the law, science, and society | | |
| Meeting | Authority meeting | | |
| Agenda item | 2 | | |
| Meeting date | 19 July 2022 | | |
| Author | Debbie Okutubo, Governance Manager | | |
| **Output:** | | | |
| For information or decision? | For information | | |
| Recommendation | To note and comment on the updates shown for each item and agree that items can be removed once the action has been completed. | | |
| Resource implications | To be updated and reviewed at each Authority meeting | | |
| Implementation date | 2022/23 business year | | |
| Communication(s) | | | |
| Organisational risk | **X** Low | ☐ Medium | ☐ High |

| ACTION | RESPONSIBILITY | DUE DATE | PROGRESS TO DATE |
|---|---|---|---|
| **Matters arising from the Authority meeting – actions from 18 May 2022** | | | |
| **3.6** Some members that are yet to complete their cyber security training. | Governance Manager | May 2022 | Seven members are yet to let the Governance Manager know if they have completed their Security & Data Protection online training. |
| **5.1** The updated key performance indicator report to be presented at the July Authority meeting. | Head of Planning and Governance | July 2022 | **Completed** – see paper set. |
| **Matters arising from the Authority meeting – actions from 23 March 2022** | | | |
| **7.8** The Audit and Governance Committee to review the HFEA's financial performance for 2021/22 | Director of Finance | June 22 | It was discussed at the 28 June AGC meeting.<br><br>**Completed** |
| **8.6** Next steps in relation to HFEA response to Covid-19 to be discussed at the May 22 Authority meeting. | Director of Compliance and Information | May 2022 | **Completed** |
| **Matters arising from the Authority meeting – actions from 9 February 2022** | | | |
| **7.11** The Executive to consult with members for input on gamete and embryo storage until May 2022. | Director of Strategy and Corporate Affairs | May 2022 | It was an agenda item at the May Authority meeting.<br><br>**Completed** |
| **Matters arising from the Authority meeting – actions from 24 November 2021** | | | |
| **11.10** Options on how compliance information including inspection reports and licensing decisions could be made | Director of Strategy and Corporate Affairs | November 2022 | No further progress. Legislative changes relating to storage and other key areas have taken priority at this point. |

| ACTION | RESPONSIBILITY | DUE DATE | PROGRESS TO DATE |
|---|---|---|---|
| more visible and easier to find on the website. | | | **Recommendation that it be delayed for 12 months.** |
| **Matters arising from the Authority meeting – actions from 23 September 2021** | | | |
| **5.18** Backlog on OTR | Director of Compliance and Information | March 22 | Staff are gaining competence and there is a significant increase in the amount of OTRs being processed. An improved way of reporting the performance indicator is being discussed and will be introduced as an increased amount of applications in the backlog are now being worked on.<br>This remains a standing agenda item under Director's performance report. |
| **9.15** Discussion to be held with multiple birth outliers | Director of Compliance and Information | September 22 | To be raised at inspections. |
| **Matters arising from the Authority – actions from 7 July 2021** | | | |
| **5.7** PGT-M being out of target of the 75 working days | Director of Compliance and Information | July 22 | This will be kept under review and will be reported to a future Authority meeting. |
| **8.14** Fertility trends - Multiple birth – A report publishing our data on multiple births. | Head of Research and Intelligence | July 22 | A paper on multiple births was published on 8 February 2022.<br><br>**Completed** |
| | | | |

# Chair and Chief Executive's report

## Details about this paper

| | |
|---|---|
| Area(s) of strategy this paper relates to: | Whole strategy |
| Meeting: | Authority |
| Agenda item: | 3 |
| Meeting date: | 19 July 2022 |
| Author: | Julia Chain, Chair and Peter Thompson, Chief Executive |
| Annexes | N/a |

## Output from this paper

| | |
|---|---|
| For information or decision? | For information |
| Recommendation: | The Authority is asked to note the activities undertaken since the last meeting. |
| Resource implications: | N/a |
| Implementation date: | N/a |
| Communication(s): | N/a |
| Organisational risk: | N/a |

## 1. Introduction

**1.1.** The paper sets out the range of meetings and activities undertaken since the last Authority meeting in May 2022.

**1.2.** Although the paper is primarily intended to be a public record, members are of course welcome to ask questions.

## 2. Activities

**2.1.** The Chair has continued to engage with the decision-making functions of the Authority and with key external stakeholders:

- 23 May – Annual Accountability meeting with the Department for Health and Social Care followed by my annual appraisal meeting
- 24 May – Public Chairs Forum meeting on diversity in public appointments
- 27 May – Chaired Legislative Reform Advisory Group
- 7 June – Participated in Nuffield Council on Bioethics / HFEA workshop on donor anonymity
- 22 June – Attended Progress Educational Trust event celebrating 30 years
- 27 June – Chaired Legislative Reform Advisory Group
- 28 June – Observed Audit & Governance Committee meeting and the same day gave an interview to the British Medical Journal on proposed law reform changes
- 11 July – Attended the Horizon scanning meeting for 2022

**2.2.** The Chief Executive has continued to support the Chair and taken part in the following externally facing activities:

- 19 May – Interview with Hannah Devlin (The Guardian)
- 23 May – Annual Accountability meeting with the DHSC (with Julia)
- 27 May – Attended Legislative Reform Advisory Group
- 27 May – Interview with Wall Street Journal
- 6 June – Attended SCAAC meeting
- 7 June – Participated in Nuffield Council on Bioethics / HFEA workshop on donor anonymity
- 8 June – CEO roundtable regulatory/assurance discussion with Second Permanent Secretary DHSC
- 14 June – Chaired MRC / HFEA roundtable on research and legislative reform
- 15 June – Participated in Standards in Public Life seminar with Lord Evans
- 16 June – Chaired CRICK / HFEA roundtable on research and legislative reform
- 22 June - Attended Progress Educational Trust event celebrating 30 years
- 27 June – Attended Legislative Reform Advisory Group
- 28 June – Attended Audit and Governance Committee
- 11 July – Attended the Horizon scanning meeting for 2022

# Committee Chairs' reports

## Details about this paper

| | |
|---|---|
| Area(s) of strategy this paper relates to: | The best care/The right information |
| Meeting: | Authority |
| Item number: | 4 |
| Meeting date: | 19 July 2022 |
| Author: | Paula Robinson, Head of Planning and Governance |
| Annexes | - |

## Output from this paper

| | |
|---|---|
| For information or decision? | For information |
| Recommendation: | The Authority is invited to note this report, and Chairs are invited to comment on their Committees. |
| Resource implications: | In budget |
| Implementation date: | Ongoing |
| Communication(s): | None |
| Organisational risk: | Low |

# 1. Committee reports

**1.1** The information presented below summarises Committees' work since the last report.

# 2. Recent committee items considered

**2.1** The table below sets out the recent items to each committee:

| Meetings held | Items considered | Outcomes |
|---|---|---|
| **Licence Committee:** | | |
| 7 May 2022 | 1 Initial Research Licence (resumed)<br>1 Renewal Treatment Licence<br>1 Special Direction (continuation of licence) | All granted/approved |
| 1 July 2022 | 2 Renewal Treatment Licences | The minutes from this meeting have not yet been finalised |
| Other comments: | Licensing items to meetings from 1 July onwards will have a new licence issued, with revised standard licensing conditions reflecting the storage changes. This will apply to renewals, interims and variations. | |
| **Executive Licensing Panel:** | | |
| 17 May 2022 | 1 Initial<br>2 Renewals<br>3 Interims<br>1 Special Direction (continuation of licence) | All granted/approved |
| 1 June 2022 | 4 Renewals<br>1 Interim<br>1 Change of Person Responsible<br>1 Change of Licence Holder<br>1 Focused Inspection Summary | All granted/approved |
| 9 June 2022 | Additional meeting to issue amended special directions for licence continuation to 4 clinics from 1 July 2022, in connection with changes to storage limits. | All granted/approved. |
| 14 June 2022 | 1 Initial<br>2 Renewals<br>1 Interim<br>2 Change of Person Responsible | All granted/approved |
| 29 June 2022 | 3 Renewals | All granted/approved |
| Other comments: | The volume of items continues to be high at most meetings. | |

| Meetings held | Items considered | Outcomes |
|---|---|---|
| | Licensing items to meetings from 1 July onwards will have a new licence issued, with revised standard licensing conditions reflecting the storage changes. This will apply to renewals, interims and variations. | |
| **Licensing Officer decisions:** | | |
| | ITE Certificates - 22<br>Change of Centre Name - 0<br>Change of Licence Holder – 4<br>Voluntary Revocations – 0<br>Amendment to Centre Address - 0 | All granted/approved |
| Other comments: | None. | |
| **Statutory Approvals Committee:** | | |
| 28 April 2022 | 2 Mitochondrial Donation applications<br>2 PGT-M applications<br>2 Special Direction applications | All granted/approved |
| 26 May 2022 | 2 PGT-M applications<br>2 Special Direction applications | All granted/approved with the exception of 1 Special Direction which was refused. |
| 30 June 2022 | 2 Mitochondrial Donation applications<br>5 PGT-M applications | The minutes from this meeting have not yet been finalised. |
| Other comments: | None. | |
| **Audit and Governance Committee:** | | |
| 28 June 2022 | Annual Report and Accounts approval<br>External Audit annual opinion<br>Internal Audit annual opinion and recommendations<br>Update on digital projects<br>HR bi-annual report<br>Counter-fraud Strategy and Action Plan | - |
| Other comments: | None. | |
| **Scientific and Clinical Advances Advisory Committee:** | | |
| 6 June 2022 | Monitoring COVID-19 research | Committee expanded this standing agenda item to monitoring relevant public heath developments. |

| Meetings held | Items considered | Outcomes |
|---|---|---|
| | Literature review - impact of stress on fertility treatment outcomes | Committee to continue monitoring research on this priority topic. |
| | Treatment add-ons application form – androgen supplementation | Application rejected, does not meet current definition of an add-on. Decision tree to be reviewed in line with evolution of treatment add-ons information. Application to be re-reviewed in future as the definition of an add-on develops. |
| | Treatment add-ons – expansion of the evidence base | Committee gave a recommendation to the Authority on the expansion evidence used to review add-on traffic light ratings. To be considered as part of agenda item six of this meeting. |
| Other comments: | None. | |

## 3. Recommendation

**3.1** The Authority is invited to note this report. Comments are invited, particularly from the committee Chairs.

# Performance report

## Details about this paper

| | |
|---|---|
| Area(s) of strategy this paper relates to: | Whole strategy |
| Meeting: | Authority |
| Agenda item: | 5 |
| Meeting date: | 19 July 2022 |
| Author: | Shabbir Qureshi, Risk and Business Planning Manager |
| Annexes | Annex 1: Performance scorecard<br>Annex 2: Financial management information<br>Annex 3: High level KPIs |

## Output from this paper

| | |
|---|---|
| For information or decision? | For information |
| Recommendation: | The Authority is asked to note and comment on the latest performance report. |
| Resource implications: | In budget |
| Implementation date: | Ongoing |
| Communication(s): | The Senior Management Team (SMT) reviews performance in advance of each Authority meeting, and their comments are incorporated into this Authority paper.<br><br>The Authority receives this summary paper at each meeting, enhanced by additional reporting from Directors. Authority's views are discussed in the subsequent SMT meeting.<br><br>The Department of Health and Social Care reviews our performance at each DHSC quarterly accountability meeting (based on the SMT paper). |
| Organisational risk: | Medium |

# 1. Latest review

**1.1.** The attached report is for performance up to and including May 2022.

**1.2.** Performance was reviewed by SMT in June 2022.

**1.3.** The financial information was not available in time for this report and a verbal update will be provided

# 2. Key trends

**2.1.** Performance was generally good in May.

### Red indicators in May (3)

- HR2: Turnover
- C1: Efficiency of the end-to-end inspection and licensing process
- C4: Mito application average processing

**2.2.** The annexes to this paper provide a scorecard giving a performance overview, high-level financial information and the monthly management accounts and more detailed information on KPIs.

# 3. Follow up from previous Authority performance discussion

**3.1.** Members commented about PGT-M processing time. An update to the reporting system for PGT-M applications is underway and this will be available for the next Authority meeting which will provide more detailed information about the stages in the process.

# 4. IT and Register performance reporting

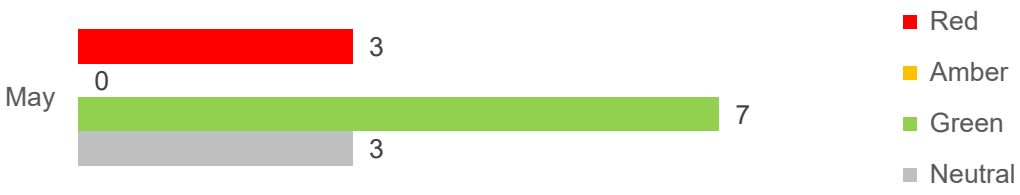
**4.1.** Three Meditex clinics are still to be deployed and may not be online until September as they are a small company and have developers on leave for the summer. They provide less than 3% of the overall volume.

**4.2.** Performance is good. The current error rate is 0.8% for direct clinics and the API rate has continued to reduce and is now at 6.5%.

**4.3.** We are continuing to actively engage with clinics to support them in improving submission rate quality to PRISM.

# Annex 1 HFEA Performance scorecard and management commentary – May data

**Breakdown of total Red, Amber, Green and Neutral Indicators (please note Finance data is not available)**




| RAG | Area | Trend and key data |
|---|---|---|
| **Red – not at target** | **People -** Employee turnover<br>Target: between 5%-15% | 24.4% Turnover<br>Two leavers this month, although one was a retirement. |
| **Red – not at target** | **Regulatory efficiency -** Time for end-to-end inspection and licensing process<br>Target: 100% in 70 working days or less | 67% within target. Average of 75 wds (items beginning with an inspection) |
| **Red – not at target** | **PGT-M –** average processing time<br>Target: 75 working days or less | 20% within target<br>86 average days taken |
| **No target** | **Engagement -** HFEA website sessions | 82,033 sessions<br>(86,920 in same month last year) |

**Management commentary**

During May, staff turnover has remained high. We had two leavers in May and one new starter. Sickness has reduced significantly with three members of staff returning from long term sick.

The end-to-end inspection and licensing process has remained in red in May with several inspections above the 70 working day target. A review of this KPI has been completed and we are dividing the existing 70-day KPI between the compliance and licencing teams to better identify where the shortfalls in performance are occurring. New tracking data has been collected since April, however, due to the inspection period being spread over three months, full performance figures will not be available until July information has been added. Two new RAG ratings have been created; one to track inspection delivery and another to track the first 55 working days since inspection date.

The OTR backlog is now reducing with the highest number being sent back in May. The number of new OTR requests have also increased significantly.

We are in the process of updating the KPIs used within the Comms team, with updated reports for our social media channels. Technical issues with Google Analytics and the software used to track social media have impacted our ability to provide new data. We expect to resolve these issues shortly.

**Red indicators in May:**

**HR:**

- **HR2 Turnover:** turnover is slightly higher this month, we have two leavers and one new starter.

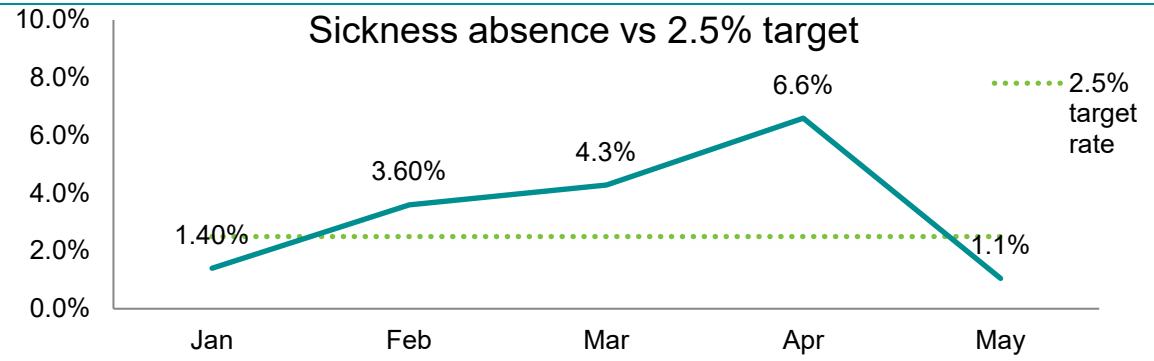
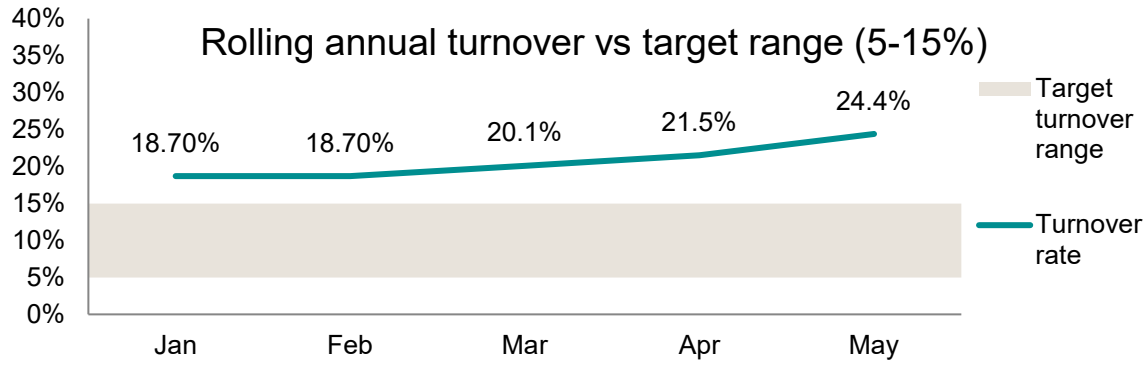
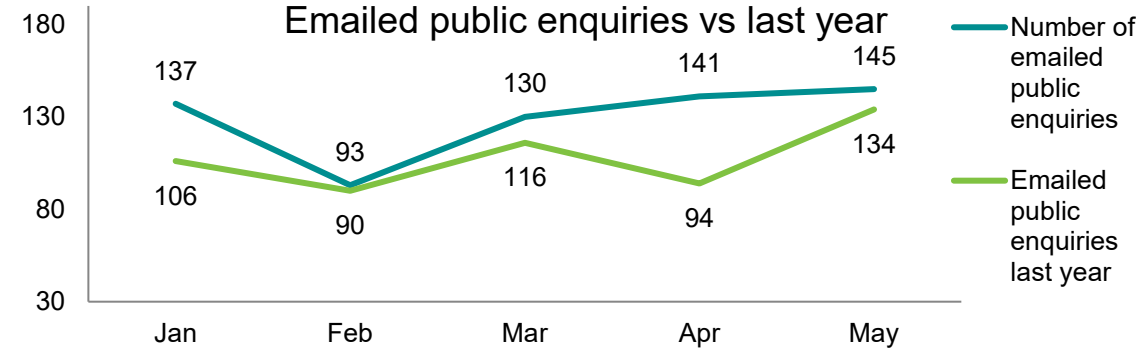
**Compliance & licensing:**

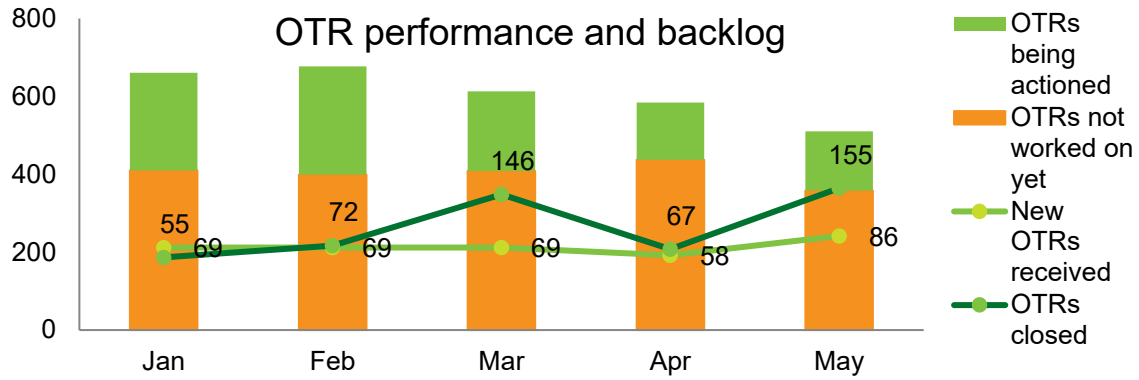
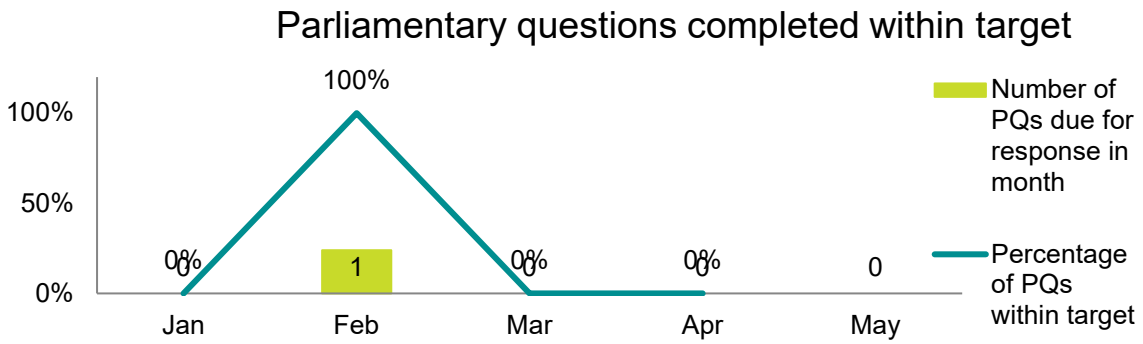
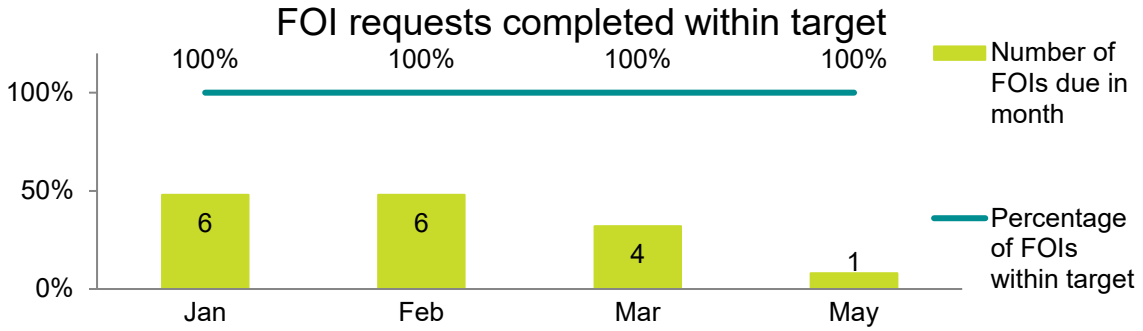
- **C1 Efficiency of the end-to-end inspection and licensing process:** five inspections were over the 70 working day target. One took 154 days due to inspector commitments, the other four narrowly missed the KPI; one was due to a PR challenging a non-compliance.
- **C4 Mito average processing time:** both of the applications due in the month were above the 90 working day target by four days.

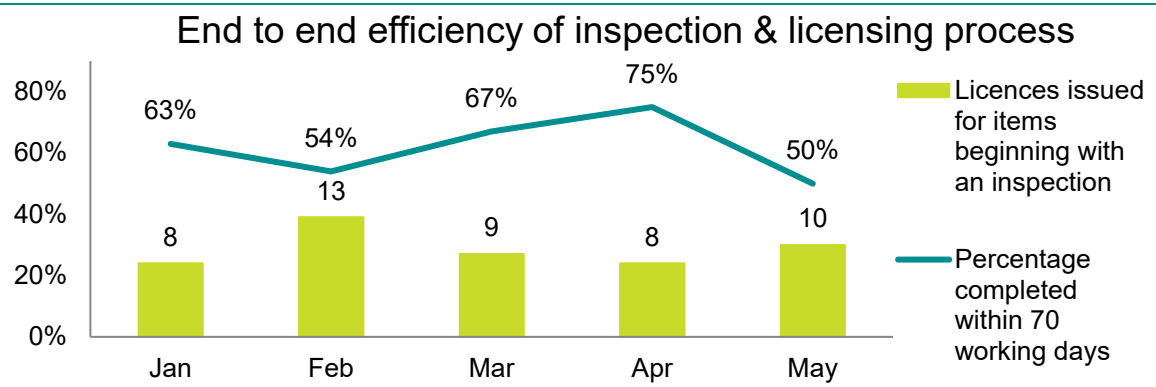
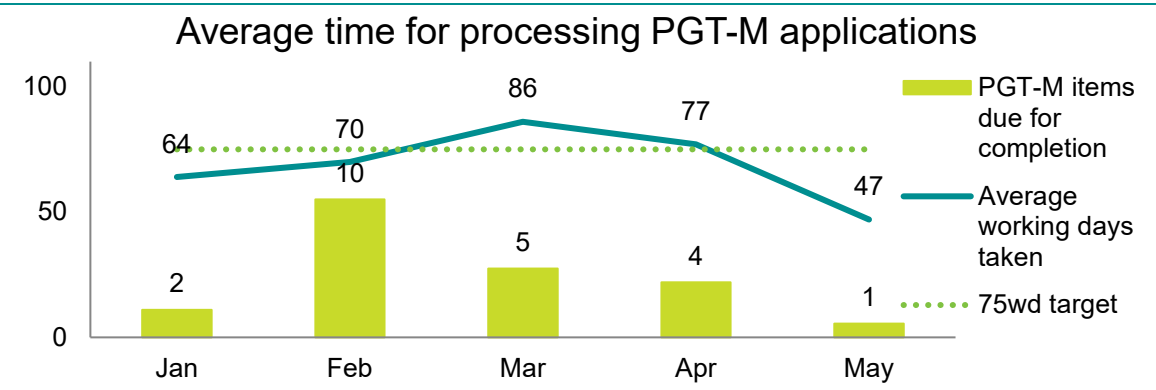
## Annex 2 Financial management information

A verbal update will be provided.

## Annex 3 – Key performance indicators – Authority summary

| Key performance indicator name and description | Graph showing performance trend for last 5 months | Commentary (if any) | RAG rating |
|---|---|---|---|
| HR1 – Sickness<br><br>**Target**: less than or equal to 2.5%. Target is based upon ONS 2018 data (2.7% for the public sector) |  | Sickness has reduced significantly with 3 people returning to work | Green |
| HR2 – Turnover<br><br>**Target**: between 5 and 15% turnover for the rolling year. |  | 69 – Headcount<br>76 – Establishment (posts)<br><br>Turnover remains high with 2 leavers and 1 joiner | Red |
| Supplementary data - Public enquiries<br><br>No target. |  | 13 complaints, 9 complex and 57 straight forward enquiries. Themes included data terminology, complex surrogacy, testing, donor gametes, add-ons and NHS funding | No target |

| Key performance indicator name and description | Graph showing performance trend for last 5 months | Commentary (if any) | RAG rating |
|---|---|---|---|
| R1 – Percentage of Opening the Register requests completed within 30 working day target.<br>(excludes counselling time)<br><br>**Target:** changed from 100% in 20wd to 95% in 30wd from April 2020.<br>**Note: target not currently active.** |  | Highest month with OTRs sent out as 3 members of start are now checking OTRs. Higher number of new OTRs received as well. | Neutral |
| RI1 – PQs responded to within deadline set<br><br>(Based on deadlines agreed with DHSC)<br><br>**Target:** 100% within deadlines set. |  | None. | Neutral |
| RI2 - FOIs responded to within deadline<br><br>**Target:** 100% within statutory deadlines. |  | Enquiries also remain high with a wide spread of themes. Success rates have been a key area of interest from patients. | Green |

| Key performance indicator name and description | Graph showing performance trend for last 5 months | Commentary (if any) | RAG rating |
|---|---|---|---|
| C1 - Efficiency of end-to-end inspection and licensing process.<br><br>**Target:** 100% within 70 working days (wds).<br><br>% processed in 70 working days, for items where minutes were sent in month. Measured from inspection date to date minutes sent. |  | Average working days taken – 87.<br><br>Most days taken: 154 working days<br><br>Least days taken: 19 working days. | Red |
| C3 – Average PGT-M processing<br><br>**Target:** average processing time of 75 working days.<br><br>Average number of working days taken for those due in month.<br>Note: Target changed from 66 to 75 in April 2020. |  | Average working days taken – 47 | Green |

# Treatment add-ons: updating the rating system and evidence base

## Details about this paper

| | |
|---|---|
| Area(s) of strategy this paper relates to: | The best care – effective and ethical care for everyone<br>The right information – to ensure that people can access the right information at the right time. |
| Meeting: | Authority |
| Agenda item: | 6 |
| Meeting date: | 19 July 2022 |
| Author: | Sonia Macleod, Scientific Policy Manager |
| Annexes | Annex A Summary results from surveys and focus groups<br>Annex B Evidence base used by Cochrane, NICE & MHRA<br>Annex C Evidence base used by SCAAC to date |

## Output from this paper

| | |
|---|---|
| For information or decision? | For decision |

| | |
|---|---|
| Recommendation: | **Proposals for evolving the rating system**<br>The Authority is asked to approve the wording attached to each circle/symbol for developing the treatment add-ons rating system.<br>**Additional outcomes which could be added to the rating system**<br>The Authority is asked to recommend:<br>• which (if any) additional outcomes should be rated by HFEA, and<br>• which add-ons these additional outcomes should apply to.<br>**Potential changes to the evidence base used to generate ratings**<br>The Authority is asked:<br>• whether to expand the evidence base based on the SCAAC recommendation<br>• to agree the next steps for developing an algorithm/decision tree and for any other considerations to incorporate into that process.<br>**Consequential changes to the criteria used by the HFEA when deciding whether to rate an add-on**<br>The Authority is asked to agree the proposed changes to the criteria the HFEA use when rating add-ons |
| Resource implications: | Additional financial resources and draw on staff capacity will be required if additional outcomes are included, as set out in the paper. |
| Implementation date: | Depending on decisions then a roll out will begin, starting with a discussion on amending the Consensus Statement with the Treatment Add-ons Working Group, as well as preparatory work on the presentational aspects in advance of the user acceptance testing. |
| Communication(s): | A summary of the survey results will be published on the treatment add-ons webpage.<br>A full communications plan to publish and promote any changes to the treatment add-ons pages and evidence base to patients and clinic staff will be developed following decisions made at this meeting. This will include user testing of any proposed changes. |
| Organisational risk: | Medium |
| Relating papers | **March 2022 Authority Paper**<br>**November 2021 Authority Paper**<br>**September 2021 Authority Paper**<br>**September 2019 Authority Paper** |

# 1. Introduction and Background

**1.1.** At the Authority meeting in September 2021 it was agreed that work would be undertaken to evolve the presentation of the rating system for treatment add-ons and to consider whether the evidence base for those ratings should be broadened. The Authority reiterated that patients should remain the primary audience for any future system. It was also agreed that SCAAC (Scientific and Clinical Advances Advisory Committee) should review the evidence base it considered as part of their add-ons review.

**1.2.** Early scoping work is detailed in the **November 2021 Authority paper** and the **March 2022 Authority paper** on treatment add-ons.

**1.3.** Since March 2022 we have carried out further work on the presentation of the ratings system and the potential inclusion of additional outcomes. This comprised two surveys with patients/public and professionals' survey and discussion in two patient focus groups.

**1.4.** In parallel, work was undertaken to consider the evidence base used to generate add-ons ratings which was considered at the June 2022 SCAAC meeting.

**1.5.** This paper summarises

- Proposals for evolving the rating system (section 2)
- Additional outcomes which could be added to the rating system (section 3)
- Potential changes to the evidence base used to generate ratings (section 4)
- Consequential changes to the criteria the HFEA use when defining an add-on (section 5).

# 2. Proposals for evolving the treatment add-ons rating system

Background

**2.1.** The current traffic-light rating system consists of three colours (red, amber and green or RAG), that indicate whether the evidence, in the form of high-quality Randomised Control Trials (RCTs), show that a treatment add-on is effective at improving the chances of having a baby for someone undergoing fertility treatment.

**2.2.** Two options were tested in the patients/public and professional surveys and explored in the focus groups – both of which develop the current 'RAG' system.

- Option A - A three category option based on the current RAG rating system
- Option B - A five category option which kept the green and amber rating, but which added a new category where there is insufficient evidence to reach a view and split the existing red category into two to specify circumstances where the evidence suggests no effect from where there are potential safety concerns

**2.3.** Summary results from the surveys and focus groups are set out in Annex A.

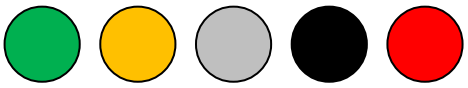
**Survey and focus groups results**

**2.4.** The scoping work carried out before the surveys suggested that either option could be a viable refinement of the current rating system. There is no absolute 'right' answer for all patients because views differ; throughout this scoping work diverse preferences were expressed, and these were not always mutually compatible. The survey results (see Annex A) indicate a tension between clarity that comes from simplicity and the desire for detail. **The survey results indicate a strong preference for five categories. The focus group participants also unanimously preferred Option B.**

**2.5.** If Option B is chosen then consideration will need to be given to the colours used for each category, as set out in Annex A. The red, grey and black colour choices are liked by the majority of patients/members of the public, who will be the primary users of this information. The black is the least well liked. Alternative colour choices could be trialled, but the survey results did not indicate a strong consensus on an alternative colour.

**2.6.** The respondents were asked whether they **preferred coloured circles or symbols**

## Circles or Symbols



or


**2.7.** There was a preference for circles from both patients/members of the public and professionals, but the difference was not particularly marked. The two focus groups preferred different options with one choosing symbols and the other opting for circles.

**2.8.** In the free text comments in the survey there were suggestions of a hybrid circles/symbol model with a warning triangle for the 'safety concerns and/or using this add-on may reduce treatment effectiveness' category and circles for other categories. In both the surveys and the focus groups it was mentioned that an exclamation might be a more appropriate symbol for the 'safety concerns and/or using this add-on may reduce treatment effectiveness' category. Taken together, there is therefore no one presentational option that all can agree on.

**For Decision**

**2.9.** After considering all these findings, a five category combined circles/symbols model has been developed as shown below. This approach retains the circles and the colours as the main visual element, but the addition of the symbols means that it is accessible to anyone who has impaired colour vision.

## Proposed new add-ons rating system

On balance, the evidence from high quality studies shows **this add-on is effective** at improving treatment outcomes for most fertility patients.

On balance, **it is not clear whether this add-on is effective** at improving treatment outcomes for most fertility patients. This is **because there are conflicting findings** between

different high quality studies – in some studies the add-on has been found to be effective, but in other studies it has not.

**We cannot rate the effectiveness of this add-on** at improving treatment outcomes for most fertility patients as there have been so few or no studies done.

On balance, the evidence from high quality studies shows that **this add-on has no effect on treatment outcomes** for most fertility patients.

**There are potential safety concerns** and/or, on balance, the evidence from high quality studies show that **this add-on may reduce treatment effectiveness for most fertility patients.**

**2.10.** **Authority is asked to approve the option above *and* the wording attached to each circle/symbol for developing the treatment add-ons ratings system.**

### Next steps

**2.11.** If Authority agree the proposed new rating system, then we will test this on our webpages before publishing. This will enable us to obtain feedback from end users to ensure the proposed presentation works well.

**2.12.** If required we will amend the consensus statement as it currently talks about red rated add-ons, which will need to be revised. This will be done in conjunction with the Treatment Add-ons Working Group (TAG).

## 3. Additional outcomes information which could be added to the add-ons rating system

### Background

**3.1.** As noted above, the current add-ons rating system only uses live birth rates when generating ratings. However, the external review of papers which is carried out to inform SCAAC's ratings has considered outcomes other than live births where that information is available.

**3.2.** All stages of the scoping work indicated a strong appetite for information on outcomes other than live births. The survey indicated that eight in ten professionals (79%) and patients/members of the public (79%) felt rating additional outcomes would be useful to patients. All participants in the focus groups felt information on additional outcomes would be beneficial for patients.

**3.3.** In considering this issue it is important to remember that different outcomes will be more or less relevant to different treatment add-ons. Survey respondents who answered that

additional outcomes should be rated by the HFEA were given a list of additional outcomes comprising:-

- Reducing the risk of miscarriage;
- Reducing the risk of OHSS;
- Reducing the risk of multiple births
- Outcomes specifically for women over 35
- Outcomes specifically for women over 40
- Other [free text box]

**Survey and focus groups results**

**3.4.** Reducing the risk of miscarriage was the outcome that was selected by the highest proportion of respondents, with 89% of professionals (who answered this question) and 93% of patients/members of the public (who answered this question) thinking the HFEA should provide information on this outcome.

**3.5.** The survey respondents who had selected additional outcomes were also asked to rank them in order of importance:

- Both professionals and the public rated reducing the risk of miscarriage as the most important outcome for the HFEA to produce information on.
- The 'other' category was ranked as highly important in both surveys. However, the 'other' category is heterogenous and most of the 'other' outcomes were only suggested by one individual. Time to pregnancy was flagged by professionals as particularly important for PGT-A. The heterogeneity of the 'other' category would make it difficult to draw meaningful conclusions from it, except for the indication of looking at time to pregnancy and/or time to live birth for PGT-A.

**Cost implications of including additional outcomes.**

**3.6.** Currently the independent reviewer studies only RCTs which report live birth rates. Under this approach the most recent review of treatment add-ons in 2021 involved the review of 55 publications in total at a cost of £11k (plus VAT). If additional outcomes were added the external reviewer would also need to review publications which report on these additional outcomes, which would have cost implications.

**3.7.** The additional cost will inevitably vary, depending on the number of additional outcomes requested and the number of available studies for each add-on. We have modelled the potential range of additional costs on the basis of a literature review, which suggests that were we to adopt the widest range of outcomes to the full range of reviewed add-ons, the costs of external review could increase sevenfold. The Authority will wish to take a view as to whether an increase in costs of that scale is justified and proportionate.

**For Decision**

**3.8.** Authority is asked to recommend:

- which (if any) additional outcomes should be rated by the HFEA, and
- which add-ons these additional outcomes should apply to.

**Next Steps**

If Authority decides to incorporate additional outcomes into the HFEA add-ons ratings, then they will need to be presented in an accessible format.

**3.9.** **Presenting information about additional outcomes.** Experts in communication who contributed to the early scoping work had said that tables are a good way to present such information, including to those with lower levels of literacy and/or learning disabilities such as dyslexia. Survey respondents found a table format clear.

**3.10.** If additional outcomes are to be included in the add-ons ratings then tables will be used to present this information and this approach will be reviewed during user acceptance testing.

## 4. Potential changes to the evidence base used to generate the add-ons ratings

### Background

**4.1.** As noted above, the current position is that only RCTs are used to generate ratings by SCAAC. However, there is a scarcity of RCTs on some of the add-ons - see Annex C

**4.2.** The evidence base used to generate add-ons ratings was previously considered by SCAAC in October 2019, with a specific focus on the potential of big data for informing outcomes. At that point SCAAC considered that retrospective studies of large data could not replace RCTs, but they may provide supporting evidence in some cases - for example identifying subgroup populations and evaluating long term patient safety outcomes.

**4.3.** At the 6 June 2022 SCAAC meeting the committee were asked to consider whether the HFEA should continue with an approach which uses RCTs as the sole determinate of any assessment, or if other types of evidence could be utilised. If a decision was taken to move beyond just RCTs then SCAAC were asked to recommend what types of evidence should be used and in what circumstances. The minutes of that meeting can be accessed here.

**4.4.** To facilitate the committee in their decision making a workshop was held on the morning of 6 June with invited expert speakers presenting the arguments for and against expanding the evidence base. At that workshop the HFEA Scientific Policy Manager also outlined the approach taken to evidence by Cochrane, the National Institute for Health and Care Excellence (NICE) and the Medicines and Healthcare Products Regulatory Agency (MHRA).

**4.5.** Cochrane, NICE and MHRA all use RCTs/meta-analysis of RCTs as their preferred evidence base. However, they all consider non-RCT evidence in specific circumstances. See Annex B for further details.

### SCAAC recommendation on expanding the evidence base

**4.6.** SCAAC were of the view that RCTs are the most appropriate type of evidence to assess the effectiveness of a given treatment intervention. And where there are RCTs of

sufficient quality then there was no need to look at other types of evidence. However, there was a majority view from SCAAC that where such RCTs were lacking it would be acceptable to widen the evidence base that is used to rate treatment add-ons. Any alternative evidence that is considered should be broadly aligned with methodology that is already used by Cochrane, NICE and the MHRA.

**4.7.** The quality of RCTs continues to be an important topic and therefore triangulation using non-RCT data could be considered even when there are meta-analyses and RCTs available.

**4.8.** SCAAC recommended to the Authority that in the absence of high-quality RCTs or meta-analyses, expanding the evidence base may be helpful when assigning treatment add-on ratings**.**

**Cost implications of expanding the evidence base**

**4.9.** The major financial cost associated with generating ratings is the cost of the independent review using 'GRADE methodology' of the evidence base for each add-on. The recommendation from SCAAC was to use non-RCT evidence only where there is an absence of good and robust RCTs or meta-analyses. The current HFEA definition of an add-on (see section 6 below) requires that there is at least one good published RCT in order for the HFEA to rate the add-on, so there would be no retrospective impact and associated costs of this change.

**4.10.** Any *new* add-on rating will require a review of the evidence base for that add-on. Should that review consider non-RCT evidence there would be an increase in costs and since non-RCT evidence is more heterogenous than RCT evidence, it is more difficult to predict the independent reviewer's cost per publication. However, non-RCT publications are likely to take longer to review than RCTs so will have a higher unit cost.

**4.11.** One potential mechanism to ensure that future workload and costs are more predictable is to adopt a similar approach as that used by NICE and to do a first sift of the literature and select only the top three publications to use as the evidence base for that rating that add-on. This approach could be applied either:-

- Selectively when there three or fewer RCTs available to limit to the independent reviewing to a maximum of three non-RCT publications, or
- to all new additions to the list of add-ons HFEA rating list, even if there are more than three published RCTs looking at that add-on.

**4.12.** SCAAC members felt it would be helpful for an algorithm or flow chart to be developed to assist them when expanding the evidence base and choosing what research to include. The HFEA uses flow charts or decision trees in a number of areas and they are also used by NICE and Cochrane.

**4.13.** At the June SCAAC meeting it was suggested that any algorithm or decision tree used to determine the further evidence base should be developed using the judgment of an expert statistician, SCAAC, and the Authority.

**For decision**

**4.14.** The Authority is asked:

- whether to expand the evidence base taking into account the SCAAC recommendation
- to agree the next steps for developing the algorithm/decision tree; and
- for any feedback to incorporate into the algorithm/decision tree development process

**Next Steps**

**4.15.** A decision tree/algorithm will be developed to determine how non-RCT evidence will be used by SCAAC when generating add-ons ratings. This will be taken to SCAAC for their consideration.

**4.16.** In addition, throughout our various discussions with experts and patients during the scoping work the importance of layering information to prevent viewer overload was stressed. Information on the evidence base should be presented in a layered way accessed from the add-on specific webpage. e.g. '*Evidence used'* should then click through to *'This rating is based on the following RCTs, Smith et al 2022, Jones et al 2021…'* There should also be a link to the papers/minutes from the SCAAC meeting(s) where each paper was discussed and the expert reviewer opinion of the paper. Our current add-on webpages do have the links to SCAAC minutes, but as we review the rating system, we will make this easier to navigate and more user-friendly.

## 5. Consequential changes to the criteria HFEA use when rating treatment add-ons

**Background**

**5.1.** There is no universally agreed definition of what constitutes a treatment add-on. At the September 2019 Authority meeting it was agreed that the HFEA would provide information on add-ons that met the following criteria:

- Additional treatments (to the core treatment e.g. IVF or IUI), that patients need unbiased information about effectiveness and risks, that are being offered in fertility clinics;
- where there is published scientific literature of a good RCT investigating the treatment's ability to improve the chances of having a baby; and
- where evidence on efficacy or safety for the use of the treatment in a clinical setting is lacking or absent.

**5.2.** As part of the changes to the add-ons rating, these criteria will also need to be updated as follows.

**5.3.** The HFEA will provide information on add-ons that met the following criteria:

- Additional treatments (to the core treatment e.g. IVF or IUI) that are being offered to the general patient population in licensed fertility clinics in the UK,

- Where there is published scientific literature which claims to demonstrate that the add-on improves live birth rates or other treatment outcomes rated by the HFEA; but
- where evidence of effectiveness for the use of the treatment in a clinical setting is lacking or absent; and
- where patients need unbiased information about the effectiveness and risks of this treatment.

**For Decision**

**5.4.** The Authority is asked to agree the proposed changes to the criteria the HFEA use when rating add-ons.

**Next Steps**

**5.5.** We will publish the amended criteria on the HFEA website, as appropriate, so that it is clear what we define as an add-on.

## 6. Recommendations

The sections above have outlined a number of issues and consequent recommendations which are now summarised here.

**Proposals for evolving the rating system**

**6.1.** The Authority is asked:

to approve the option C *and* the wording attached to each circle/symbol for developing the treatment add-ons ratings system.

**Additional outcomes which could be added to the rating system**

**6.2.** Authority is asked to recommend:

- Which (if any) additional outcomes should be rated by HFEA.
- Which add-ons these additional outcomes should apply to.

**Potential changes to the evidence base used to generate ratings**

**6.3.** Authority is asked:

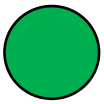
- whether to expand the evidence base taking into account the SCAAC recommendation
- to asked to agree the next steps for developing the algorithm/decision tree and for any feedback to incorporate into that process.

**Consequential changes to the criteria HFEA use when deciding whether to rate an add-on**

**6.4.** The Authority is asked to agree the proposed changes to the criteria the HFEA use when rating add-ons

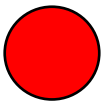
# Annex A – Patients/public & professionals surveys and the patient focus groups results

## Option A



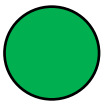
On balance, the evidence from high quality studies shows **this add-on is effective** at improving treatment outcomes for most fertility patients.

On balance, **it is not clear whether this add-on is effective** at improving treatment outcomes for most fertility patients. This is **because there are conflicting findings** between different high quality studies – in some studies the add-on has been found to be effective, but in other studies it has not.



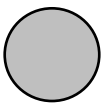
**We cannot rate the effectiveness of this add-on** at improving treatment outcomes for most fertility patients as there have been so few or no studies done.

## Option B



On balance, the evidence from high quality studies shows **this add-on is effective** at improving treatment outcomes for most fertility patients.

On balance, **it is not clear whether this add-on is effective** at improving treatment outcomes for most fertility patients. This is **because there are conflicting findings** between different high quality studies – in some studies the add-on has been found to be effective, but in other studies it has not.



**We cannot rate the effectiveness of this add-on** at improving treatment outcomes for most fertility patients as there have been so few or no studies done.

On balance, the evidence from high quality studies shows that **this add-on has no effect on treatment outcomes** for most fertility patients.

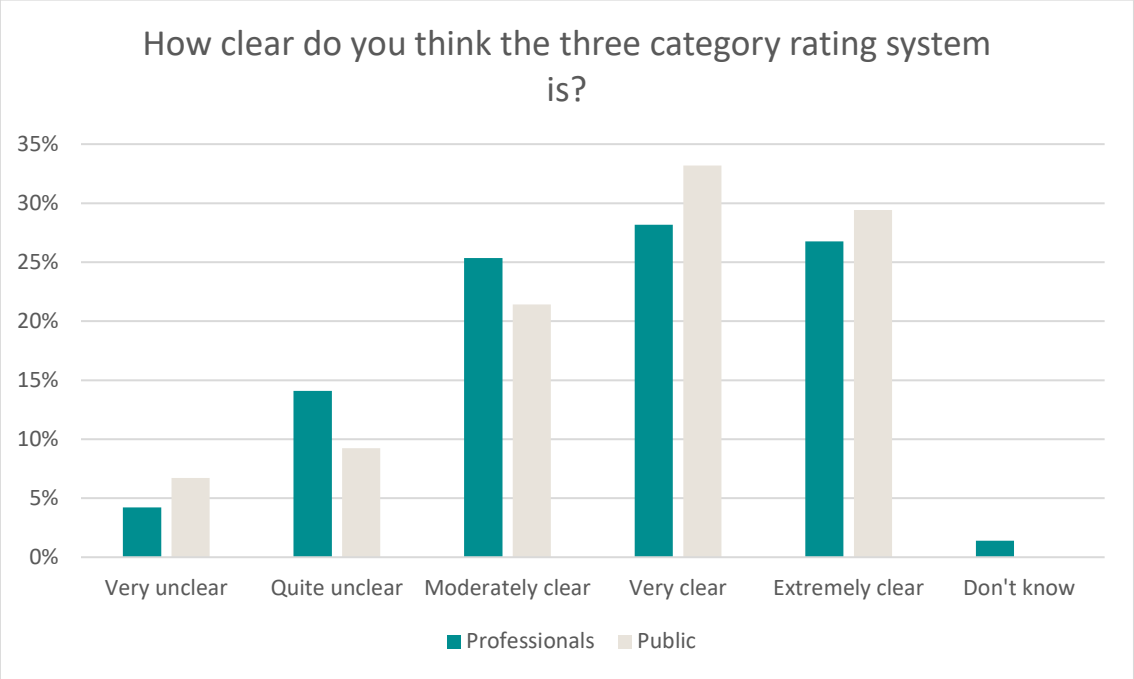
**There are potential safety concerns** and/or, on balance, the evidence from high quality studies show that **this add-on may reduce treatment effectiveness for most fertility patients.**

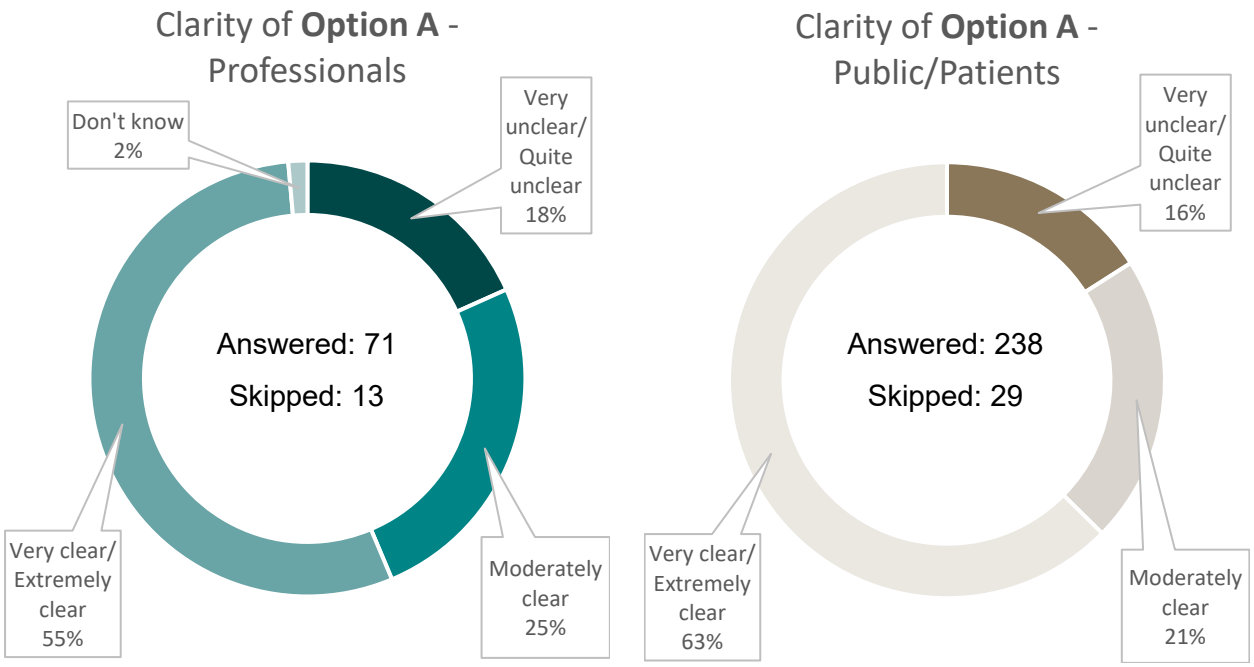
## Results from the Surveys

### 1. A variation of the current rating system with three categories

**Clarity of three categories** - The majority of respondents found this system clear,

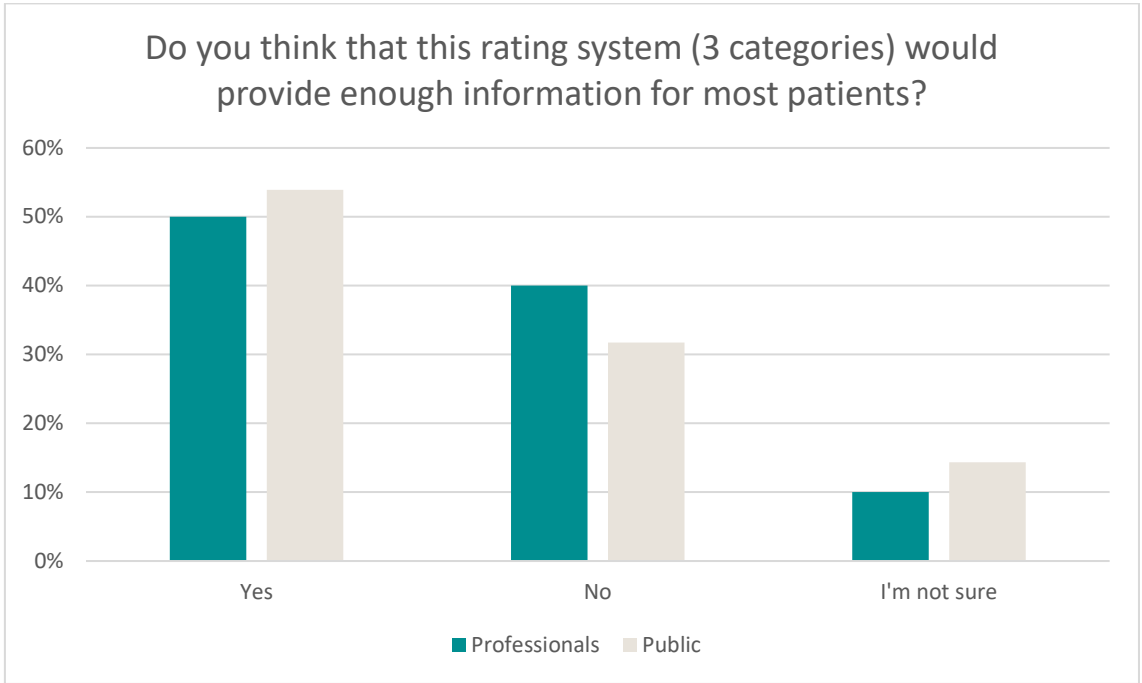
- 80% of professionals found it moderately, very or extremely clear (57/71)
- 89% of patients/members of the public found it moderately, very or extremely clear. (194/217)






**Detail level in three categories** - Respondents were asked if this system contained enough detail for most people

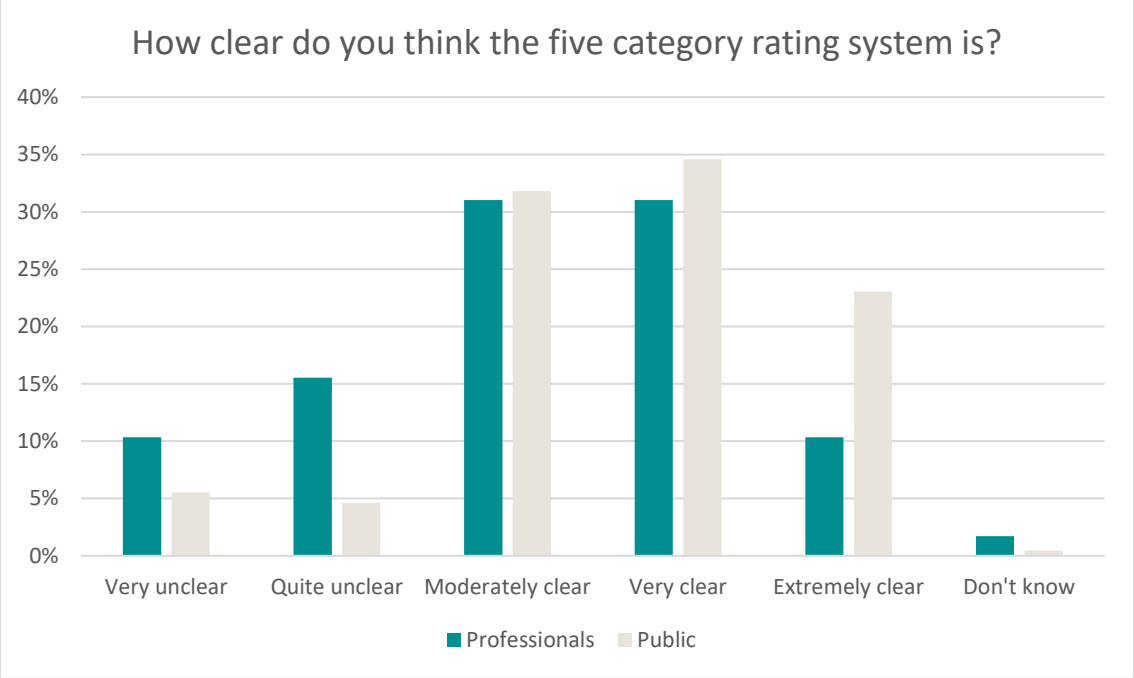
- 50% of professionals though it contained enough detail for most people (35/70)
- 54% of patients/members of the public though it contained enough detail for most people (124/230)

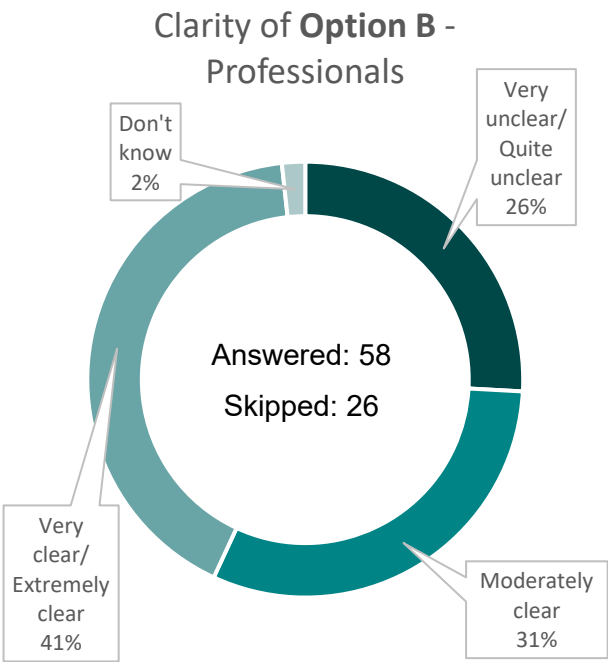


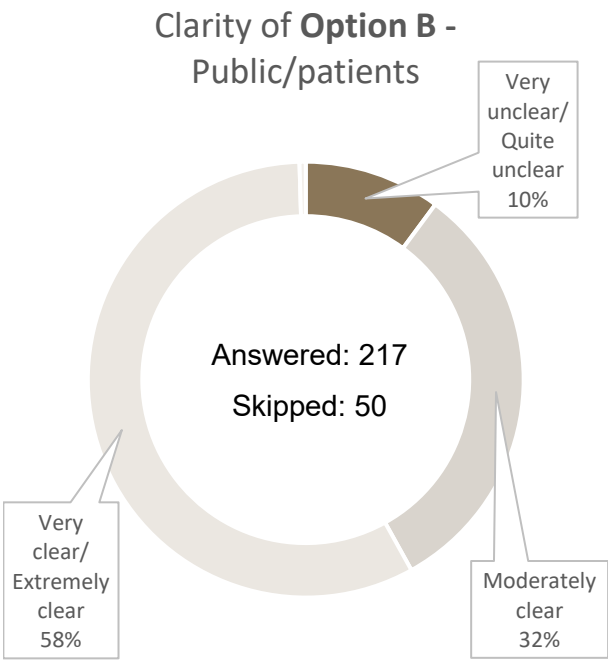
## 2. A variation of the current rating system with five categories

**Clarity of five categories-** The majority of respondents found this system clear,

- 72% of professionals found it moderately, very or extremely clear (42/58)
- 84% of patients/members of the public found it moderately, very or extremely clear. (200/238)

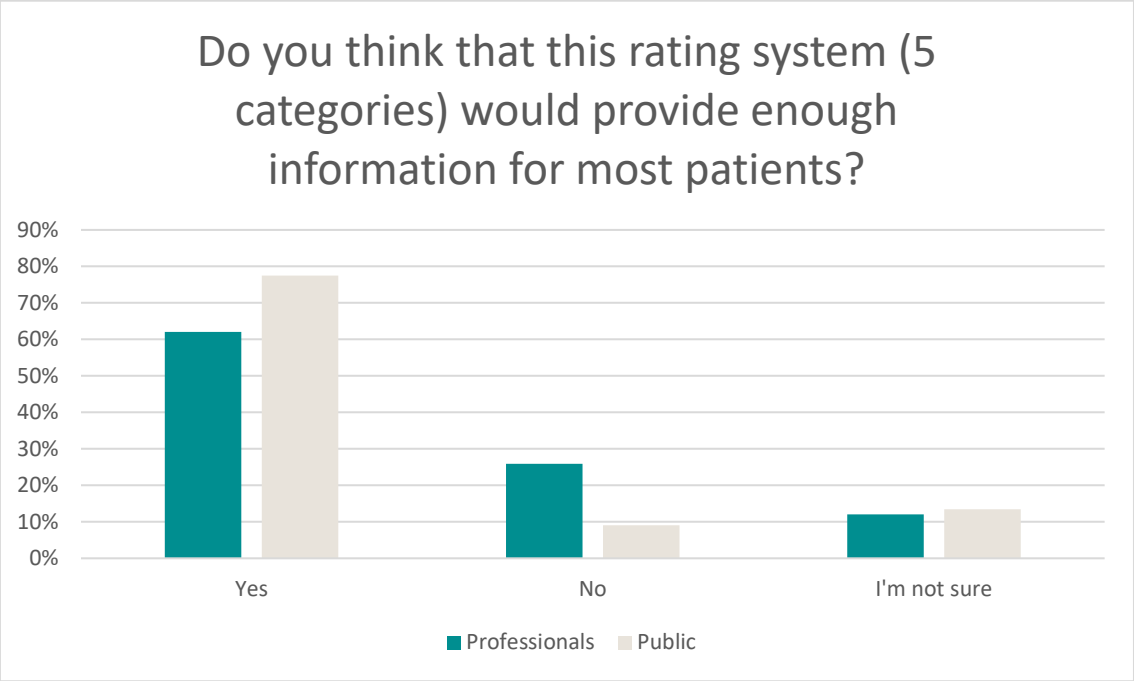


**Detail level in five categories** - Respondents were asked if this system contained enough detail for most people

- 62% of professionals though it contained enough detail for most people (36/58)
- 78% of patients/members of the public though it contained enough detail for most people (162/209)

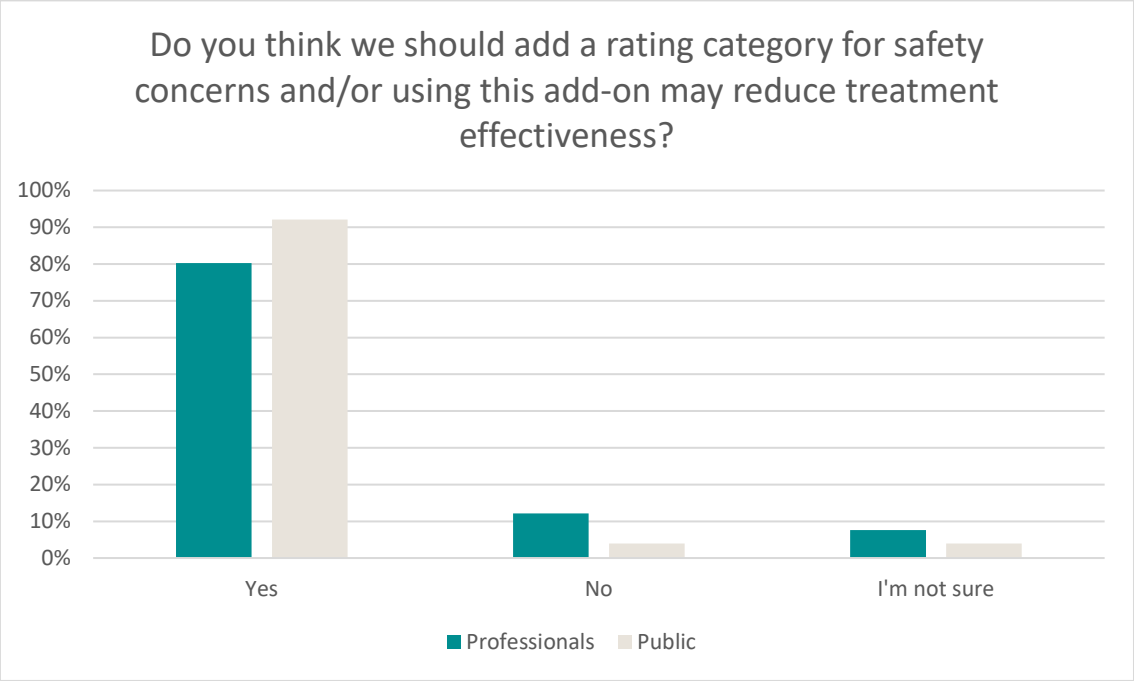


## 3. Increasing from three categories from to five

**Adding a category for safety concerns and/or reducing treatment effectiveness** -

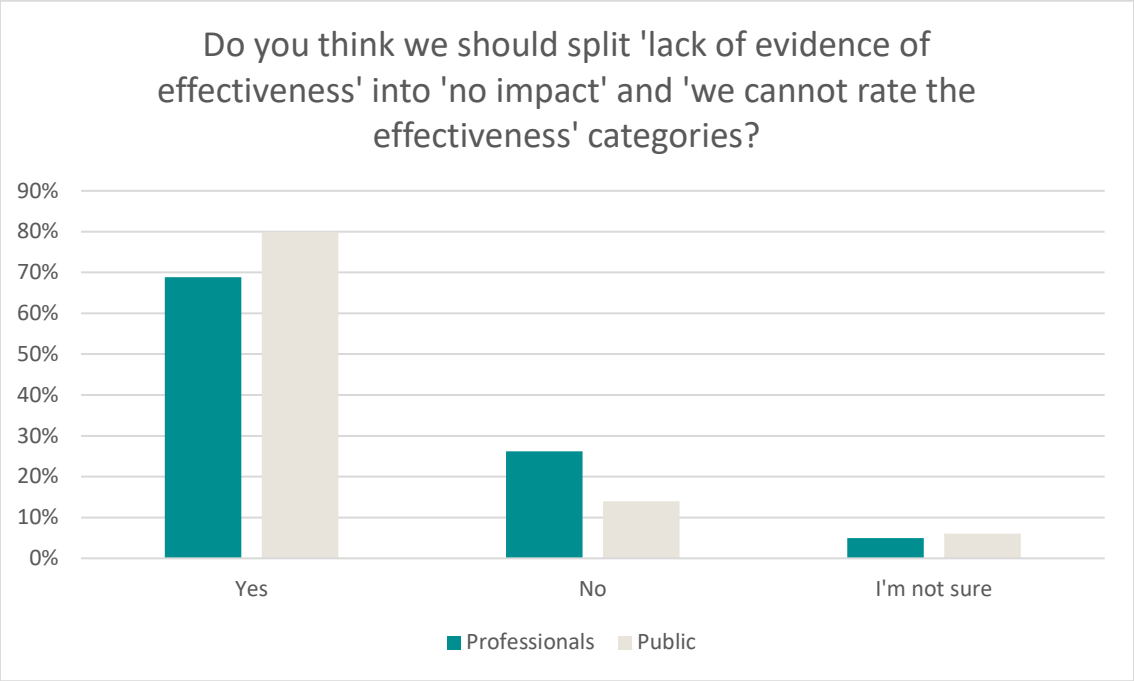
Respondents were asked for their views on adding a new category

- 80% of professionals thought this category should be added (53/66)
- 92% of patients/members of the public thought this category should be added (210/228)



**Splitting the 'lack of evidence' category** - Respondents were asked for their views on splitting categories on the 'lack of evidence' category into two categories

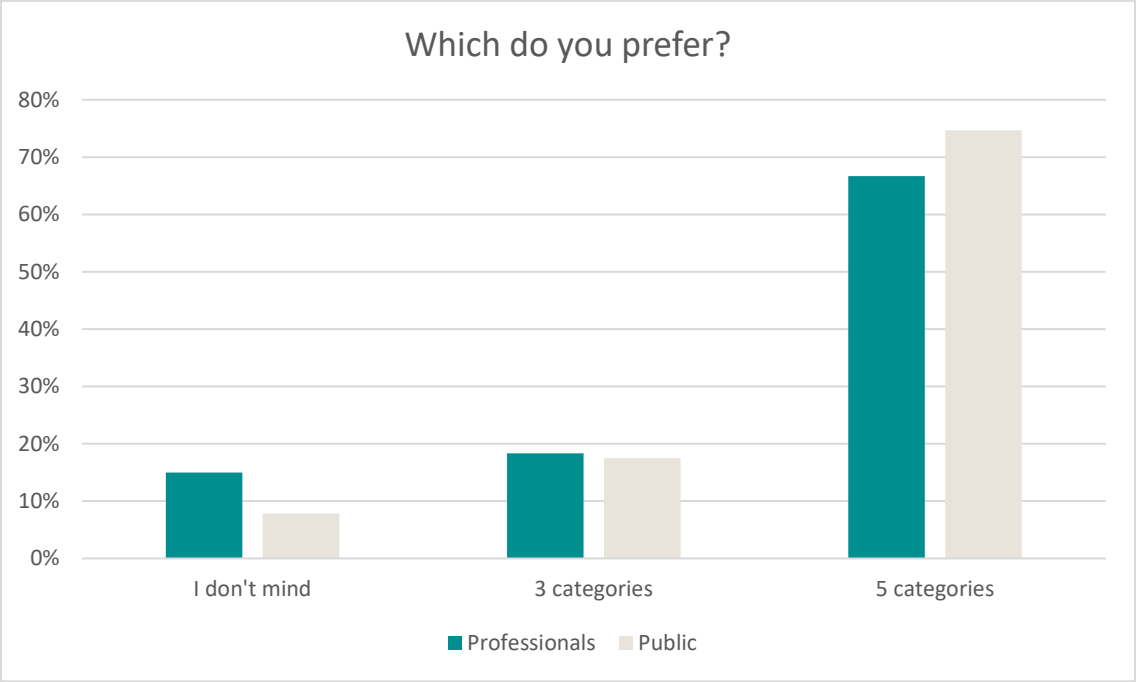
- 69% of professionals thought it should be split (42/61)
- 80% of patients/members of the public thought it should be split (172/215)

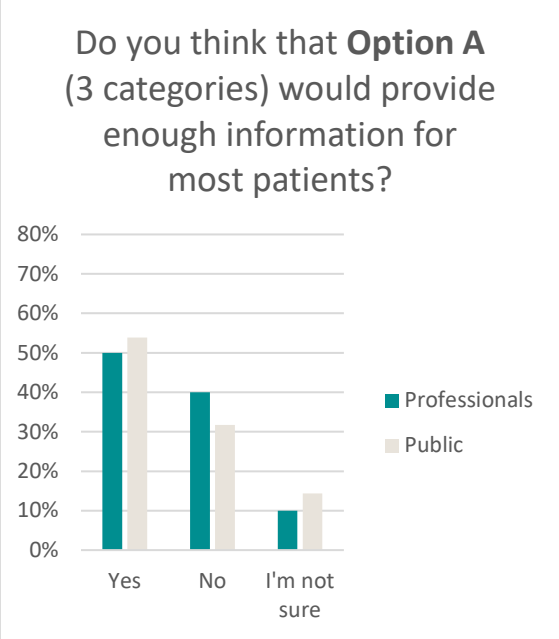


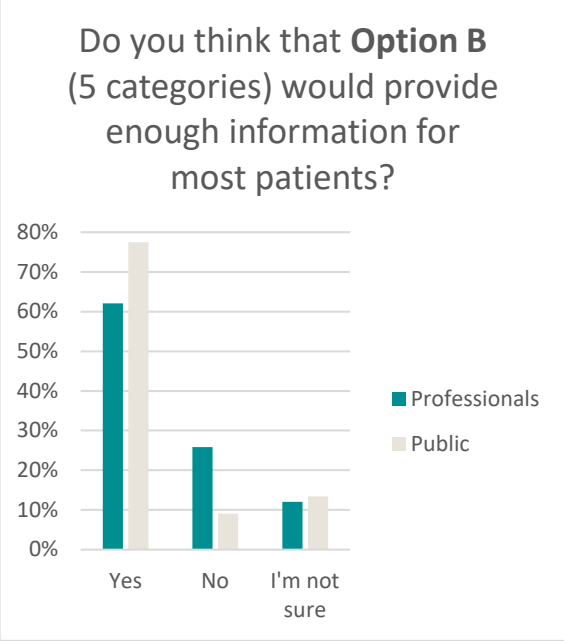
## 4. Three categories v Five categories

**Preference** - Respondents were asked for their preference between option A three categories and option B five categories

- 67% of professionals preferred five categories (40/60), 18% preferred three categories (11/60) and 15% didn't mind (9/60)
- 75% of patients/members of the public preferred five categories (162/217), 18% preferred three categories (38/217) and 8% didn't mind (17/217)



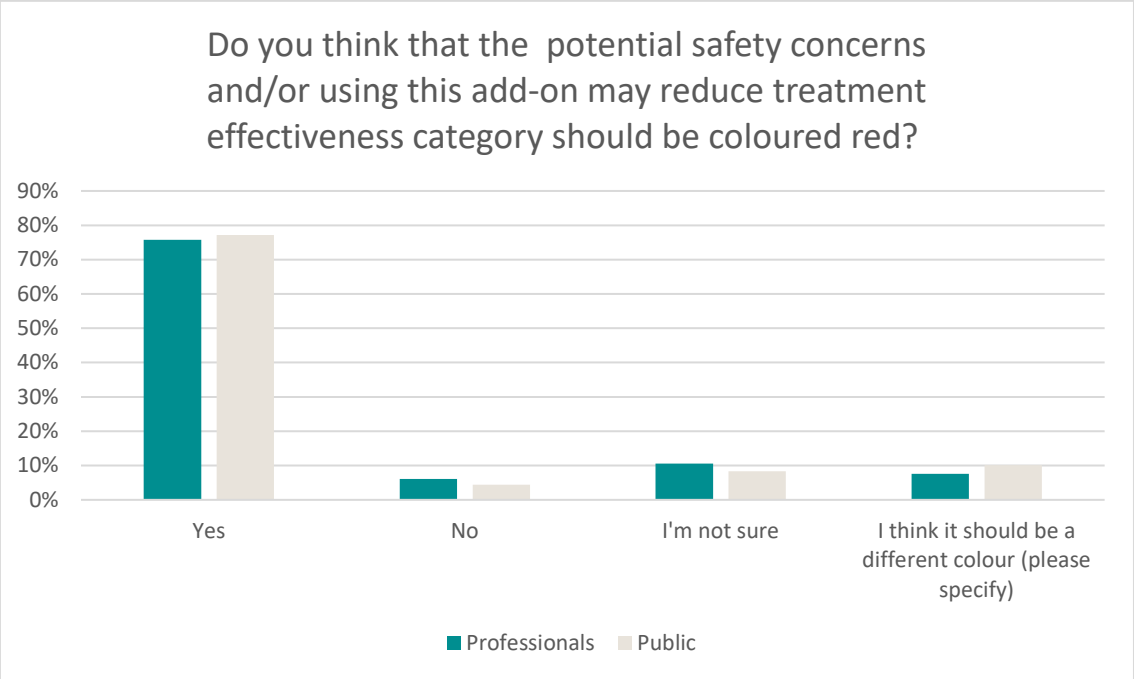



## 5. Potential colours for the new categories

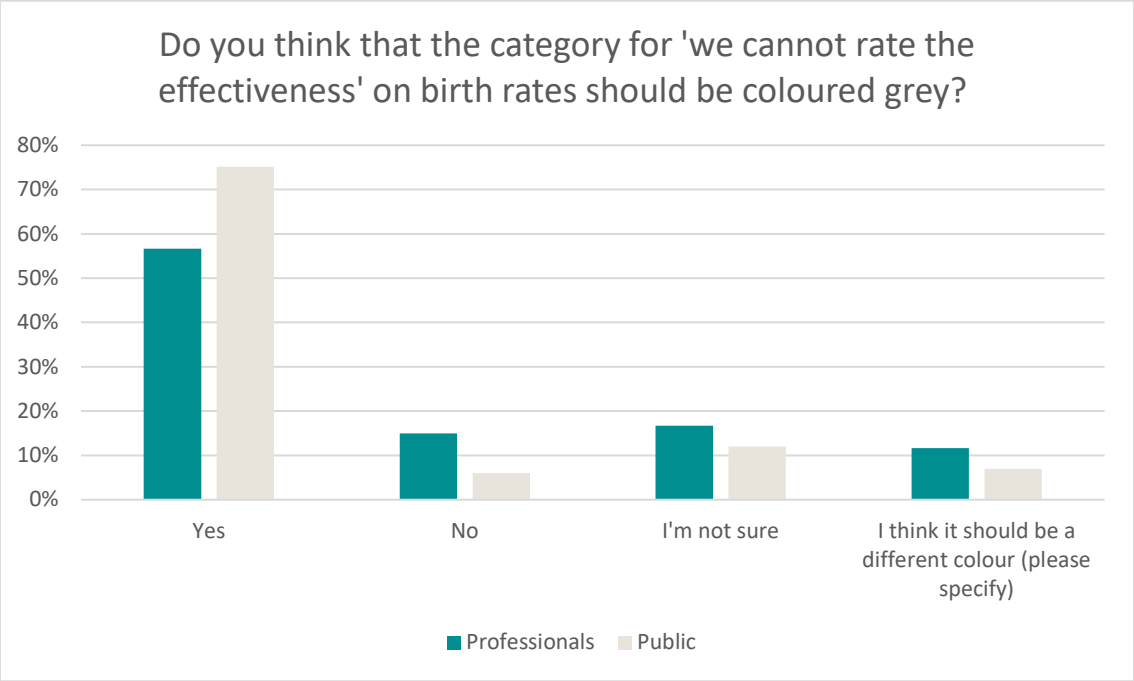
**Safety concerns and/or reducing treatment efficacy**- Respondents were asked if this category should be coloured red.

- 76% of professionals felt it should be red (50/66), 6% felt it should not be red (4/66), 10% were not sure (7/66) and 8% suggested a different colour (5/66)
- 77% of patients/members of the public felt it should be red (166/228), 4% felt it should not be red (10/228), 8% were not sure (19/228) and 10% suggested a different colour (23/228)



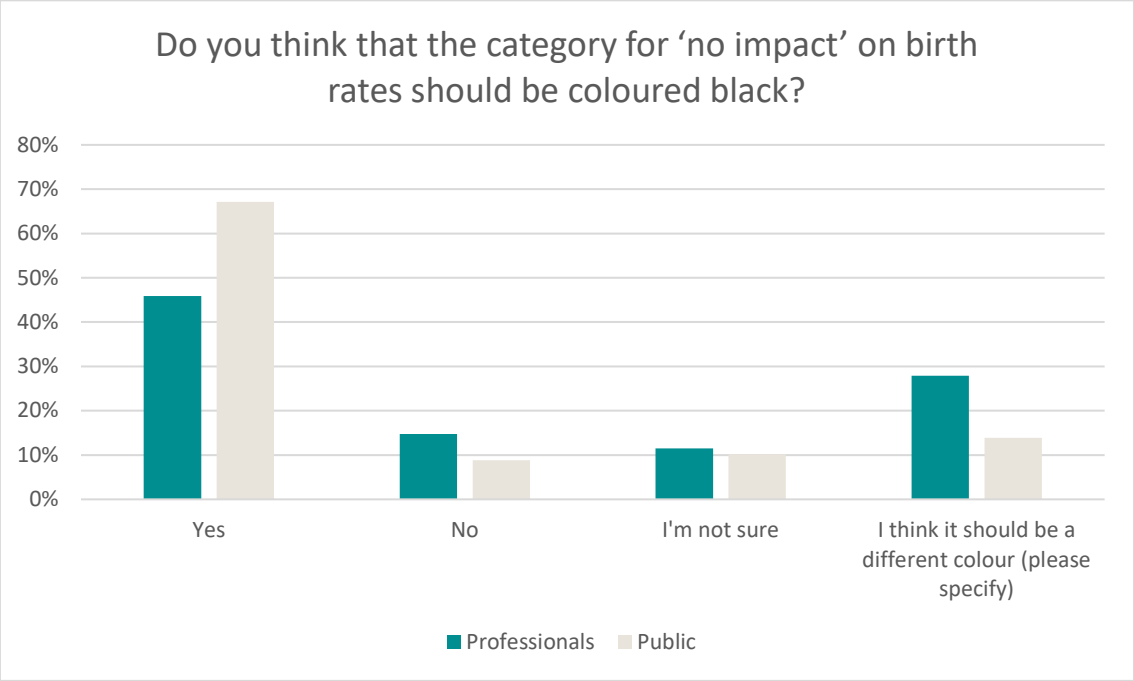
**We cannot rate the effectiveness**- Respondents were asked if this category should be coloured grey.

- 57% of professionals felt it should be grey (34/60), 15% felt it should not be grey (9/60), 17% were not sure (10/60) and 12% suggested a different colour (7/60)
- 75% of patients/members of the public felt it should be grey (163/217), 6% felt it should not be grey (13/217), 12% were not sure (26/217) and 7% suggested a different colour (15/217)



**This add-on has no effect on treatment outcomes**- Respondents were asked if this category should be coloured black.

- 48% of professionals felt it should be black (28/61); 15% of professionals felt it should not be black (9/61); and 28% of professionals felt it should be a different colour (17/61), 11% were not sure(7/61)
- 67% of patients/members of the public felt it should be black (145/216); 9% of patients/members of the public felt it should not be black (19/216); and 14% of patients/members of the public felt it should be a different colour (30/216), 10% were not sure (22/216)



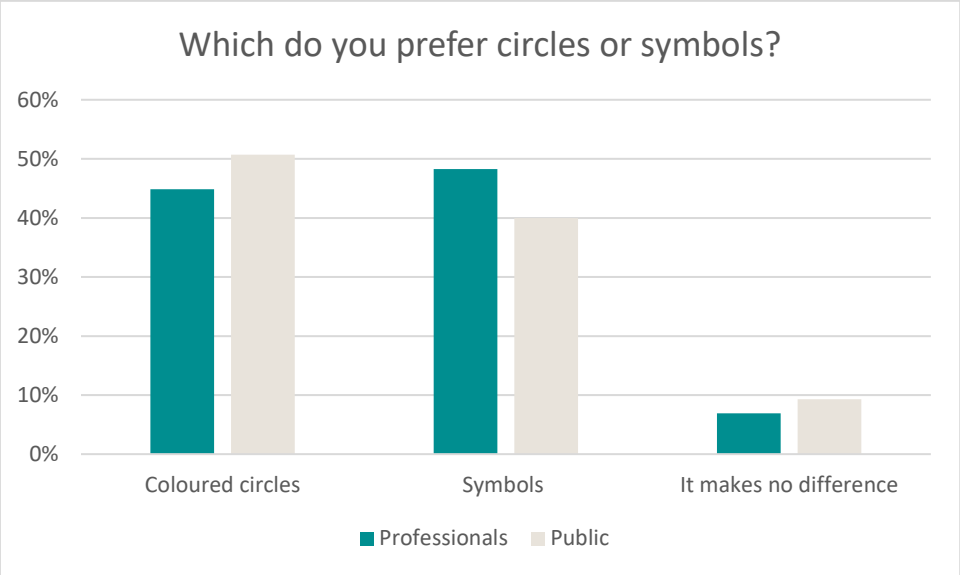

**Summary of colours**

- The choice of red for a category for 'safety concerns and/or using this add-on may reduce treatment effectiveness' was supported by three quarters of patients/members of the public (77%) and professionals (76%).
- The use of grey for the 'we cannot rate this add-on' category was supported by three quarters (75%) of patients/members of the public. However, fewer professionals felt it should be grey with just under six in ten (57%) of this view.
- There was less support for 'this add-on has no impact on treatment outcomes' being shaded black. Two thirds (67%) of patients/members of the public felt it should be black, whilst one in ten (10%) were not sure what colour it should be. One in ten (9%) thought it should not be black and one in seven (14%) suggested a different colour. Just under half (48%) of professionals felt it should be black; one in seven (15%) felt it should not be black, three in ten (28%) professionals felt it should be a different colour and the remaining one in ten (10%) were not sure.

## 6. Circles v Symbols

**Circles v Symbols** - Respondents were asked for their preference between circles and symbols

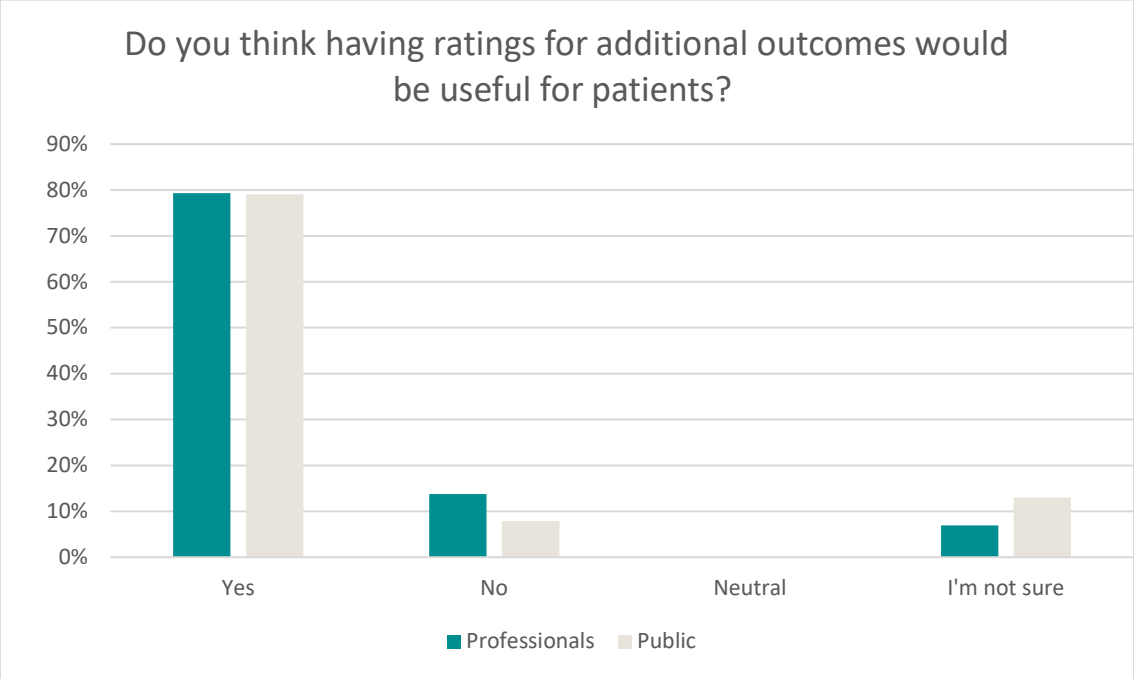
- 45% of professionals preferred circles (26/58); 48% of professionals preferred symbols (28/58); and 7% of professionals felt it did not make a difference (5/58)
- 51% of patients/members of the public preferred circles, (109/215); 40% of patients/members of the public preferred symbols, (86/215); and 9% of patients/members of the public felt it did not make a difference (20/215);



## 7. Additional outcomes

**Additional Outcomes** - Respondents were asked for their view on whether having ratings for additional outcomes would be useful for patients.

- 79% of professionals felt it would be useful to rate additional outcome (46/79)
- 79% of patients/members of the public felt it would be useful to rate additional outcomes, (170/215)




**Additional Outcomes** - Respondents selections of additional outcomes would be useful for patients.

| | Professionals who selected this option | % of respondents selecting this option |
|---|---|---|
| **Reducing the risk of miscarriage** | 42 | 89% |
| **Information for women age 40+** | 34 | 72% |
| **Reducing the risk of OHSS** | 28 | 60% |
| **Information for women age 35+** | 27 | 57% |
| **Reducing the multiple birth risk** | 24 | 51% |
| **Other [free text]** | 17 | 36% |
| **None of the above** | 1 | 2% |
| **Total who answered this question** | **47** | |

| | Patient/public who selected this option | % of respondents selecting this option |
|---|---|---|
| **Reducing the risk of miscarriage** | 177 | 93% |
| **Reducing the risk of OHSS** | 135 | 71% |
| **Information for women age 40+** | 128 | 67% |
| **Information for women age 35+** | 118 | 62% |
| **Reducing the multiple birth risk** | 79 | 41% |
| **Other [free text]** | 27 | 14% |
| **None of the above** | 3 | 2% |
| **Total who answered this question** | **191** | |

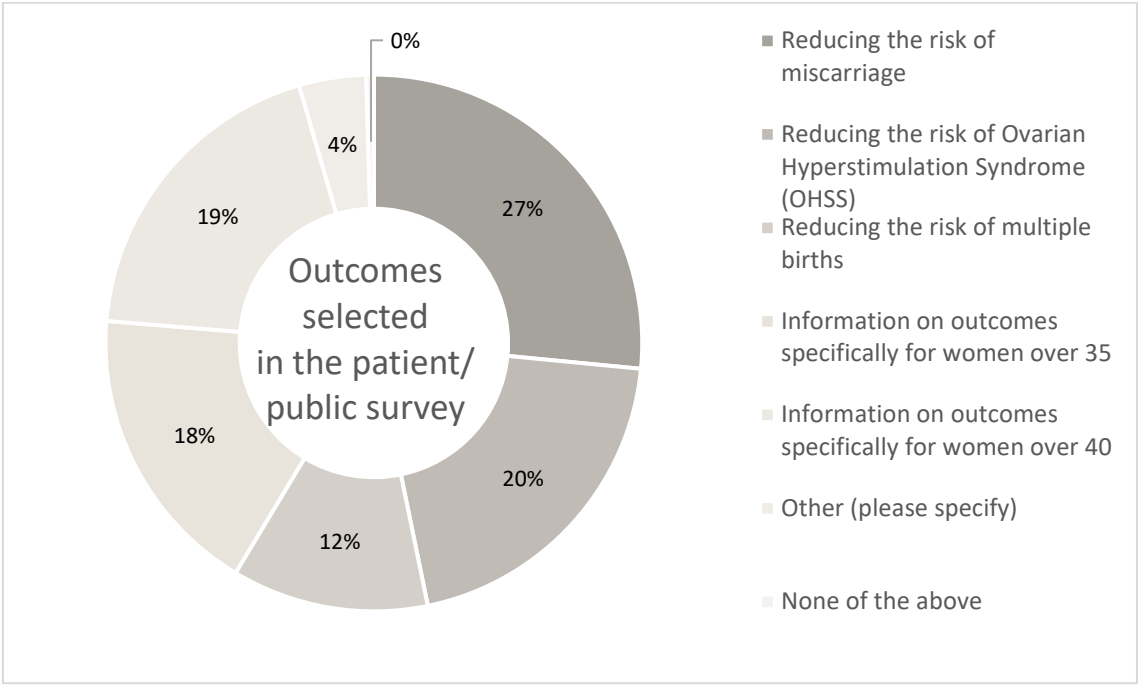
**Additional Outcomes** - Respondents were asked to select any of the following additional outcomes which they felt it would be useful for HFEA to include information on.

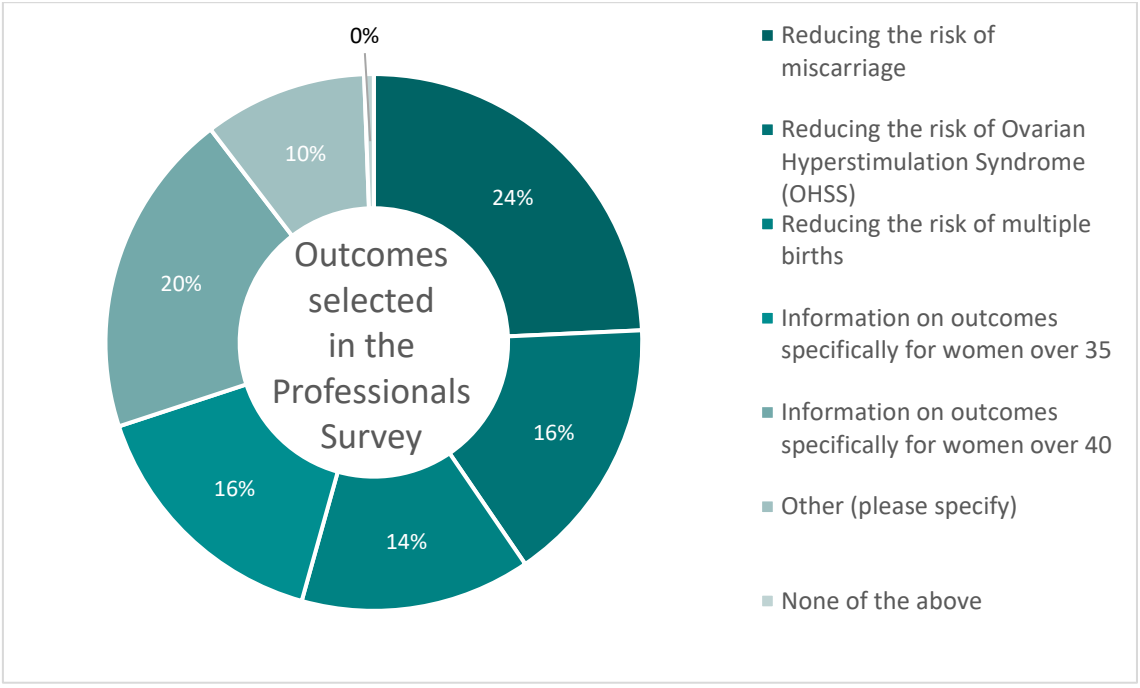
| | Professionals who selected this option | % of respondents selecting this option | Patient/public who selected this option | % of respondents selecting this option |
|---|---|---|---|---|
| **Reducing the risk of miscarriage** | 42 | 89% | 177 | 93% |
| **Reducing the risk of OHSS** | 28 | 60% | 135 | 71% |
| **Reducing the multiple birth risk** | 24 | 51% | 79 | 41% |
| **Information for women age 35+** | 27 | 57% | 118 | 62% |
| **Information for women age 40+** | 34 | 72% | 128 | 67% |
| **Other [free text]** | 17 | 36% | 27 | 14% |
| **None of the above** | 1 | 2% | 3 | 2% |
| **Total who answered this question** | **47** | | **191** | |

Reducing the risk of miscarriage was the outcome which was selected by the highest proportion of respondents across both surveys, with 89% of professionals and 93% of patients thinking HFEA should provide information on this outcome.

The outcome which was second in terms of selection by patients/the public was reducing the risk of OHSS; 71% of patient felt HFEA should rate add-ons on how they impact on this outcome. For professionals the outcome which was second with 72% was information for women age 40+.

In third place with patients/the public was information for women age 40+ at 67% Professionals had OHSS risk as the third most popular choice, with 60% of respondents selecting this option.



Ratings given to additional outcomes by professionals

| | 1 | | 2 | | 3 | | 4 | | 5 | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Reducing the risk of miscarriage** | **62%** | 24 | **15%** | 6 | **3%** | 1 | **18%** | 7 | **3%** | 1 | 39 |
| **Reducing the risk of OHSS** | **22%** | 6 | **22%** | 6 | **30%** | 8 | **19%** | 5 | **7%** | 2 | 27 |
| **Reducing the risk of multiple births** | **9%** | 2 | **30%** | 7 | **43%** | 10 | **9%** | 2 | **9%** | 2 | 23 |
| **Outcomes specifically for women over 35** | **8%** | 2 | **38%** | 10 | **8%** | 2 | **19%** | 5 | **27%** | 7 | 26 |
| **Outcomes specifically for women over 40** | **13%** | 4 | **19%** | 6 | **48%** | 15 | **16%** | 5 | **3%** | 1 | 31 |
| **[Insert text from Other]** | **33%** | 5 | **33%** | 5 | **13%** | 2 | **20%** | 3 | **0%** | 0 | 15 |

Ratings given to additional outcomes by patients/the public

| | 1 | | 2 | | 3 | | 4 | | 5 | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Reducing the risk of miscarriage** | **65%** | 106 | **23%** | 38 | **10%** | 17 | **2%** | 3 | **0.00%** | 0 | 164 |
| **Reducing the risk of OHSS** | **12%** | 15 | **45%** | 55 | **18%** | 22 | **19%** | 23 | **5%** | 6 | 121 |
| **Reducing the risk of multiple births** | **6%** | 4 | **17%** | 12 | **40%** | 29 | **8%** | 6 | **29%** | 21 | 72 |
| **Outcomes specifically for women over 35** | **21%** | 23 | **26%** | 28 | **32%** | 35 | **18%** | 19 | **3%** | 3 | 108 |
| **Outcomes specifically for women over 40** | **15%** | 18 | **26%** | 31 | **24%** | 28 | **19%** | 23 | **16%** | 19 | 119 |
| **[Insert text from Other]** | **30%** | 7 | **26%** | 6 | **26%** | 6 | **13%** | 3 | **4%** | 1 | 23 |

Ranking scores for additional outcomes

| | Professionals (43) | Public (173) |
|---|---|---|
| **Reducing the risk of miscarriage** | 4.15 | 4.51 |
| **Reducing the risk of OHSS** | 3.33 | 3.41 |
| **Reducing the risk of multiple births** | 3.22 | 2.61 |
| **Outcomes specifically for women over 35** | 2.81 | 3.45 |
| **Outcomes specifically for women over 40** | 3.23 | 3.05 |
| **[Insert text from Other]** | 3.8 | 3.65 |

| Importance | Patients/the Public | Professionals |
|---|---|---|
| 1st | Reducing the risk of miscarriage | Reducing the risk of miscarriage |
| 2nd | Other [specified previously] | Other [specified previously] |
| 3rd | Outcomes for women over 35 | Reducing the risk of OHSS |
| 4th | Reducing the risk of OHSS | Outcomes for women over 40 |
| 5th | Outcomes for women over 40 | Reducing the risk of multiple births |
| 6th | Reducing the risk of multiple births | Outcomes for women over 35 |

| Suggestion for 'other' additional information made by patients/the public | Frequency |
|---|---|
| Shortening time to pregnancy | 3 |
| Increase chance of pregnancy (as opposed to live birth) | 3 |
| Information on outcomes for women with repeated implant failure (3 or more failures) | 3 |
| Information for those using donor egg and donor sperm | 2 |
| Recurrent pregnancy loss or maybe recurrent early pregnancy loss (miscarriage) | 1 |
| More specific information be available for the BAME community if research indicates differing treatment outcomes | 1 |
| information on male fertility as well and not just outcomes. | 1 |
| Outcomes for women between 35 and 40 | 1 |
| Outcomes for women over 37 | |
| Information on outcomes for different age groups including under 30 | 1 |
| abnormalities in baby development | 1 |
| Type of infertility | 1 |
| Low ovarian reserve | 1 |
| Pain/discomfort (ie endometrial biopsy, LIT) | 1 |
| If the risk is connected to BMI this should be made clear | 1 |
| elapsed time to live birth (or clinical pregnancy) | 1 |
| average number of treatments to live birth (or clinical pregnancy) | 1 |
| Immune disorders | 1 |
| Information that indicated where an add-on tended to lead to more clinical pregnancies that didn't lead to live births | 1 |

| Suggestion for 'other' additional information made by professionals | Frequency |
|---|---|
| Time to pregnancy | 5 |
| Time to live birth | 2 |
| Information on outcomes for women with repeated implant failure (3 or more failures) | 1 |
| Endometrial thickness | 1 |
| Specific patient aetiologies | 1 |
| Information about fertilisation or embryos development | 1 |
| Information on outcome of severe male infertility | 1 |
| Information on outcome of poor ovarian response | 1 |
| Improving embryo quality and embryo utilisation | 1 |
| Lab performance | 1 |
| Prognostic and or diagnostic potential | 1 |
| Risk reduction (the nature of the risk was not specified) | 1 |
| stress reduction | 1 |
| Recognition of interventions being effective in specific patient populations, as well as the fact that treatments like ICSI and cryopreservation might not be beneficial in all patient groups. | 1 |
| Endometriosis/adenomyosis, | 1 |
| PCOS | 1 |
| Increasing chance of a healthy pregnancy rather than reducing chance of miscarriage | 1 |

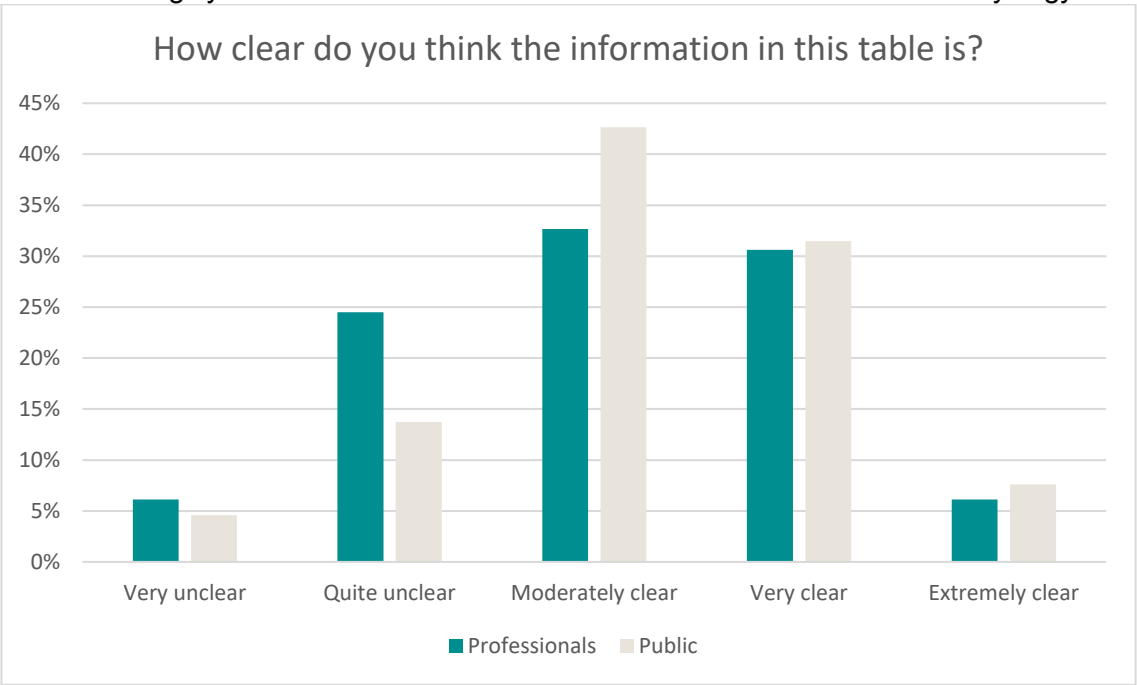
## 8. Tables as a way to present information on additional outcomes

**Use of Tables** - Respondents were asked for their view on how clear the following table with information in was.

| | **Live Birth Rate** | Reduced **miscarriage** risk | Reduced **OHSS** risk | Reduced **multiple births** |
|---|---|---|---|---|
| **Add-on 1** | 🟡 | 🟢 | N/A | N/A |
| **Add-on 2** | 🔴 | 🔴 | 🟢 | 🔴 |
| **Add-on 3** | 🟡 | N/A | N/A | 🟡 |

**Clarity of the table** - The majority of respondents found this system clear,

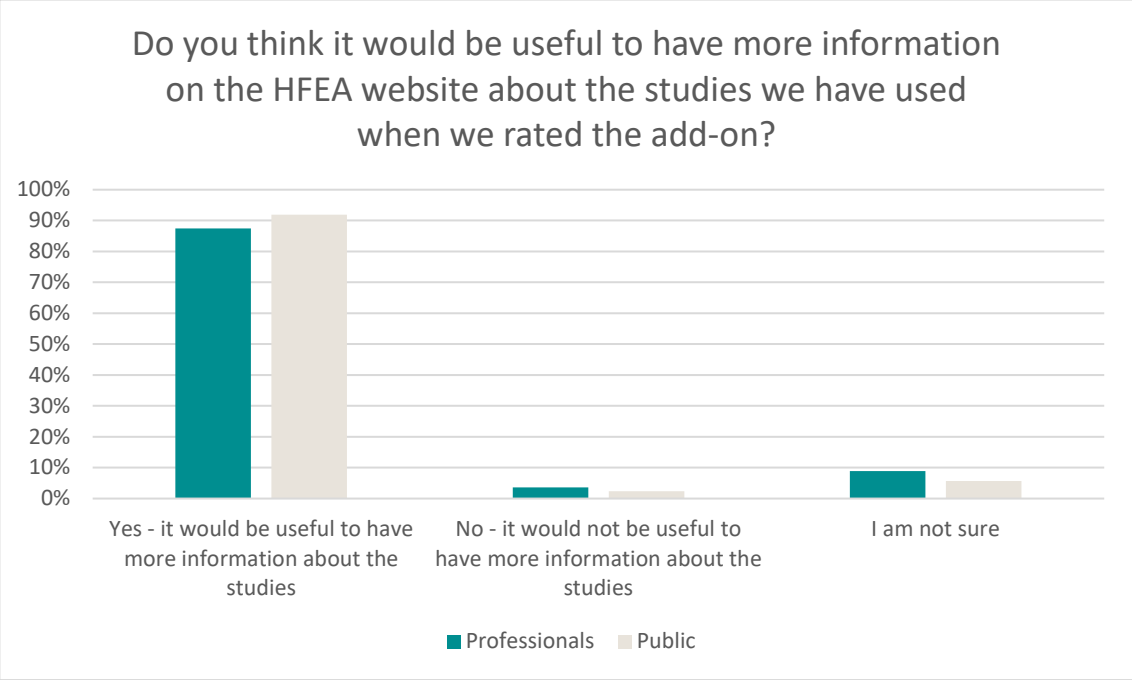
- 69% of professionals found it moderately, very or extremely clear (34/49)
- 82% of patients/members of the public found it moderately, very or extremely clear. (161/197)


How clear do you think the information in this table is?
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
Very unclear
Quite unclear
Moderately clear
Very clear
Extremely clear
Professionals
Public

# 9. Information on the evidence used to generate rankings

**Additional Outcomes** - Respondents were asked for their view on whether having more information on the evidence used to generate ratings would be useful.

- 88% of professionals (49/56) felt it would be useful for HFEA to provide more information
- 92% of patients/members of the public felt it would be useful for HFEA to provide more information (194/211)



## 10. Professional view of usefulness of rating systems

**Discussions with patients** – professionals were asked if they would find this rating system useful when discussing add-ons with patients

- 78% of professionals thought the three category would be somewhat useful, very useful or extremely useful (55/71) of these 37% felt it would be very useful or extremely useful (26/71)
- 79% of professionals thought the three category would be somewhat useful, very useful or extremely useful (46/58) of these 52% felt it would be very useful or extremely useful (30/58)

## Results from the Focus groups

Both focus groups were clear that fertility patients want information *'…one thing I would say is normally when you are communicating with patients and the public in general, I know there is a kind of you don't want to overload with information. I feel as if IVF patients are an exception to that. I feel as though they are information hungry. And they want to be informed.'* And that as the regulator HFEA have a responsibility to provide information *'If you do not provide it, it leaves a vacuum and then the information comes from other places. And those places may not be reliable.'*

### 1. Three categories v Five categories

Five categories were preferred over three categories, as one participant put it *'It is a complex area and I think it is very hard to give everyone enough information with just three.'* The addition of the we cannot rate the effectiveness of this add-on as so few studies have been done was particularly welcomed *'I definitely prefer the 'not being able to rate it', because I think that is more honest. I feel that as I come to look at that, I am not getting any false hope out of that. You are being dead honest about what that is about.'*

### 2. Potential colours for the new categories

### 3. Circles v Symbols

One group strongly preferred circles, with a recognition they might be less accessible*. 'I guess if people are colour blind, it actually then would help but I think for me, looking at that, the circles everyday of the week.'* The other group preferred symbols. There were suggestions for alternative symbols

- The use of an exclamation mark, !, for the potential safety concerns/reduction in treatment effectiveness was widely supported.

- Using a U for unrated, a ~, or a ? was suggested where there was not sufficient evidence to reach a rating

There was a concern that the – on the 'we cannot rate this category could be read as a minus.

Some comments in the survey had suggested having a system where the safety concerns/reduction in treatment effectiveness was represented by a warning triangle and the other categories had coloured circles. One group was against this approach, the other group was more accepting.

The colour of the five categories was thought appropriate by most of the focus group participants, but one raised concerns over the use of amber and grey *'I think red is good for essential safety concerns as and/or may reduce treatment. I would potentially… The category that is currently amber, I would potentially put that as grey. Because some studies show it works and some don't. It is a grey area. And the one where we cannot rate the effectiveness as a few studies have been done, I potentially would go for a more neutral colour like blue or white. To just say there is just nothing there, we can't say one way or the other.'*

## 4. Additional outcomes

Information on additional outcomes was welcomed by all the focus group participants. In particular information on OHSS risk and Miscarriage risk was sought. Maternal age was considered particularly important *'I think age is incredibly important because the conversations you have at different ages are very different.'*

There was a strong call from the second focus group to provide information on the impact of an add-on *'When you are in a cycle, and you have invested not just money but so much in yourself and your relationship into the cycle. When somebody says to you here is something else that might or might not help you… …if somebody said to me, like a 2%, you know you are going up from maybe 25% chance of having a baby to 27% perhaps chance of having a baby and it is going to cost you a quarter more… I feel like I need those facts to make that decision.'*

## 5. Tables as a way to present information on additional outcomes

While there was support for setting out ratings for additional outcomes in a table there was concern that the table does contain any information on how much an add-on might or might not help, as set out above.

All participants were supportive of having information set out in a layer format so that people were not overwhelmed and could access an appropriate level of information for their needs. *'…having that option with the headlines, if you want more information, if you want to see the research papers, if you want a synthesis of the research papers and why we have come to these conclusions, click here. And I think having those layers, is very useful for your different types of audience.'*

## 6. Other insights from the focus groups

The focus groups raised several other points that, while supplementary to this project, are extremely important, they included:-

- add-ons are very different, with vastly different safety profiles, eg embryoscope is non-invasive, other add-ons are not. Putting them all together as 'add-ons' doesn't convey this variation.
- The term 'add-on' was seen as positive and there are some of the add-ons which the participants felt weren't positive.
- Concerns were raised about informed consent; participants reported that patients are often asked about add-ons mid treatment and raised concerns that it is not ok to be consented in this way. '*Yes I would be asked about embryo glue on the day of embryo transfer.* 'We have your embryo ready to go in to you. Do you want us to use embryo glue or not.?' *And I know in other situations, clinical situations, you cannot consent somebody once a procedure has started.'*
- Add-ons are being used by clinicians to avoid having a discussion about ending treatment *'actually I think the add on was given as a kind of rather than talking about ending treatment, it was kind of well you can try this'*
- HFEA not a first port of call for many patients about add-ons. Participants felt we could potentially improve our presence on forums so we have greater prominence and to direct people to accurate impartial advice on add-ons.
- There has been a move from discussing 'test-tube babies' to 'IVF', but that there now needs to be a move away from talking about IVF to a broader term which encompasses the reality of current practice. Suggestions put forward were fertility treatment or medically assisted reproduction.

# Annex B – Evidence base used by Cochrane, NICE & MHRA

## Cochrane

### Cochrane summary

Allow the use of non-randomised trials, but only in limited circumstances. They list five reasons where they accept the use of non-randomised trials:

1. Where available RCTs only address the question indirectly or are incomplete (e.g. Non randomised Studies of the intervention can be used to provide information on rare treatment outcomes, or very long term effects of treatments where the results may not be available for many years)
2. Where randomisation is not a realistic possibility (e.g. When considering the population effects of specific pieces of legislation or where participants would not agree to randomisation)
3. To provide the case for a RCT to be undertaken, by highlighting the faults with the non-randomised study
4. When an intervention effect is very large (clearly there are ethical concerns with randomisation if the intervention effect is large or if the effect is randomisation would not be desirable to participants, e.g., when one cohort would undergo surgery and the other would not)
5. When RCTs could be used, but very few RCTs are available

They emphasise that they consider the first two reasons as more valid than the third, and all three of these much more valid than the fourth and fifth.

They allow for the publication of an “empty review” when evidence is too limited, rather than including questionable studies.

### Cochrane Full Description

Link

Chapter 24: Including non-randomized studies on intervention effects | Cochrane Training

Broadly, we consider that there are two main justifications for including NRSI in a systematic review, covered by the flow diagram shown in Figure 24.1.a:

1. To provide evidence of the effects (benefit or harm) of interventions that can feasibly be studied in randomized trials, but for which available randomized trials address the review question indirectly or incompletely (an element of the GRADE approach to assessing the certainty of the evidence, see Chapter 14, Section 14.2) (Schünemann et al 2013). Such non-randomized evidence might address, for example, long-term or rare outcomes, different populations or settings, or ways of delivering interventions that better match the review question.
2. To provide evidence of the effects (benefit or harm) of interventions that cannot be randomized, or that are extremely unlikely to be studied in randomized trials. Such non-

randomized evidence might address, for example, population-level interventions (e.g. the effects of legislation; (Macpherson and Spinks 2008) or interventions about which prospective study participants are likely to have strong preferences, preventing randomization (Li et al 2016).

A third justification for including NRSI in a systematic review is reasonable, but is unlikely to be a strong reason in the context of a Cochrane Review:

1. To examine the case for undertaking a randomized trial by providing an explicit evaluation of the weaknesses of available NRSI. The findings of a review of NRSI may also be useful to inform the design of a subsequent randomized trial (e.g., through the identification of relevant subgroups).

Two other reasons sometimes described for including NRSI in systematic reviews are:

1. When an intervention effect is very large.
2. To provide evidence of the effects (benefit or harm) of interventions that can feasibly be studied in randomized trials, but for which only a small number of randomized trials is available (or likely to be available).

We urge caution in invoking either of these justifications. Reason 4, that an effect is large, is implicitly a result-driven or post-hoc argument, since some evidence or opinion would need to be available to inform the judgement about the likely size of the effect. Whilst it can be argued that large effects are less likely to be completely explained by bias than small effects (Glasziou et al 2007), clinical and economic decisions still need to be informed by unbiased estimates of the magnitude of these large effects (Reeves 2006). Randomized trials are the appropriate design to quantify large effects (and the trials need not be large if the effects are truly large). Of course, there may be ethical opposition to randomized trials of interventions already suspected to be associated with a large benefit, making it difficult to randomize participants, and interventions postulated to have large effects may also be difficult to randomize for other reasons (e.g., surgery versus no surgery). However, the justification for a systematic review including NRSI in these circumstances can be classified as reason 2 above (i.e., interventions that are unlikely to be randomized).

The appropriateness of reason 5 depends to a large extent on expectations of how the review will be used in practice. Most Cochrane Reviews seek to identify highly trustworthy evidence (typically only randomized trials) and if none is found then the review can be published as an ‘empty review’. However, as Cochrane Reviews also seek to inform clinical and policy decisions, it can be necessary to draw on the ‘best available’ evidence rather than the ‘highest tier’ of evidence for questions that have a high priority. While acknowledging the priority to inform decisions, it remains important that the challenges associated with appraising, synthesizing and interpreting evidence from NRSI, as discussed in the remainder of this chapter, are well-appreciated and addressed in this situation. See also **Section 24.2.1.3** for further discussion of these issues. Reason 5 is a less appropriate justification in a review that is not a priority topic where there is a paucity of evidence from randomized trials alone; in such instances, the potential of NRSI to inform the review question directly and without a critical risk of bias are paramount.

Review authors may need to apply different eligibility criteria in order to answer different review questions about harms as well as benefits (**Chapter 19, Section 19.2.2**). In some reviews the situation may be still more complex, since NRSI specified to answer questions about benefits may have different design features from NRSI specified to answer questions about harms (see **Section 24.2**). A further complexity arises in relation to the specification of eligible NRSI in the protocol and the desire to avoid an empty review (depending on the justification for including NRSI).

Whenever review authors decide that NRSI are required to answer one or more review questions, the review protocol must specify appropriate methods for reviewing NRSI. If a review aims to include both randomized trials and NRSI, the protocol must specify methods appropriate for both. Since methods for reviewing NRSI can be complex, **we recommend that review authors scope the available NRSI**

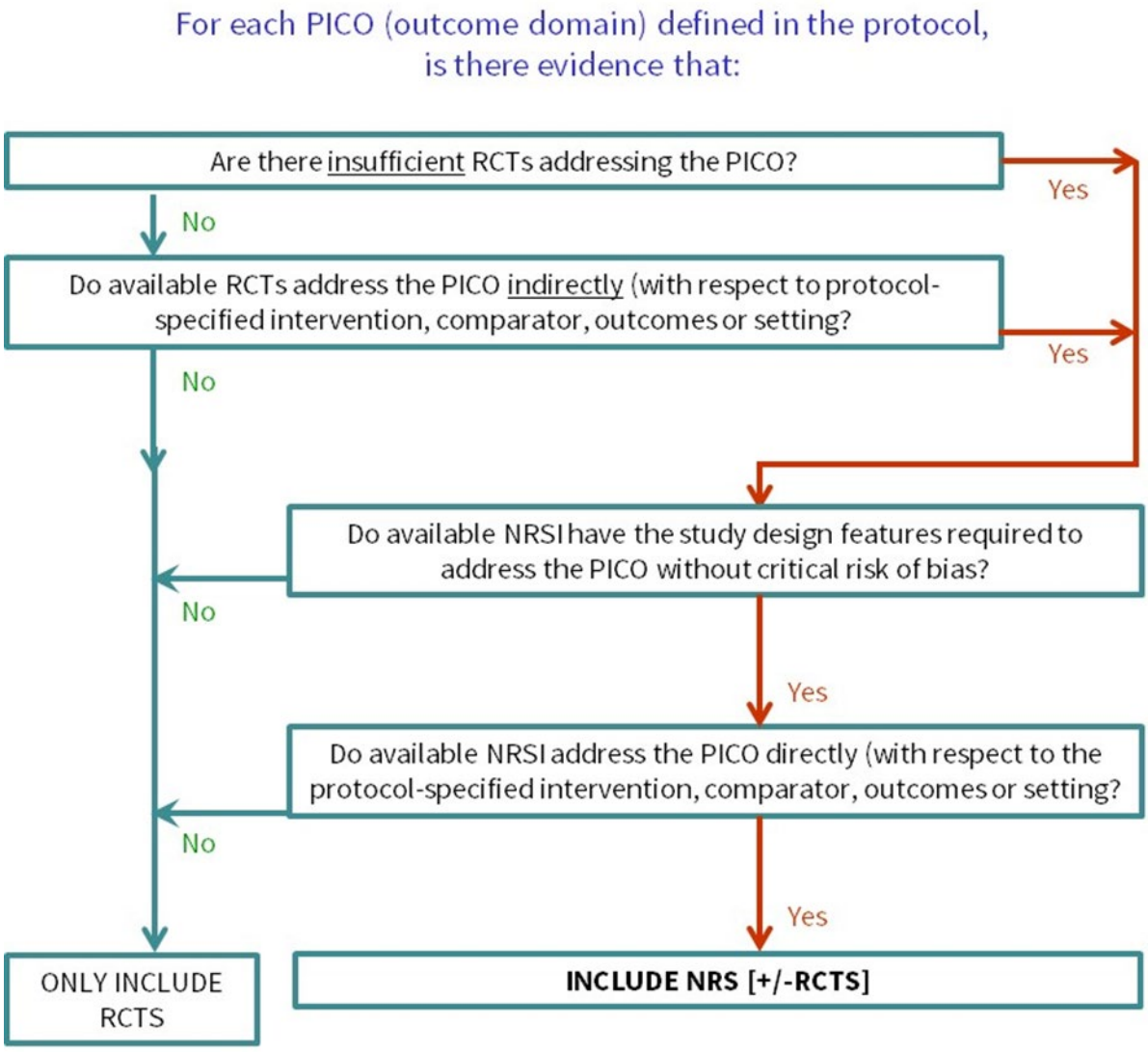
**evidence**, after registering a title but in advance of writing a protocol, allowing review authors to check that relevant NRSI exist and to specify NRSI with the most appropriate study design features in the protocol (Reeves et al 2013). If the registered title is broadly conceived, this may require detailed review questions to be formulated in advance of scoping: these are the **PICOs for each synthesis** as discussed in **Chapter 3, Section 3.2**. Scoping also allows the directness of the available evidence to be assessed against specific review questions (see **Figure 24.1.a**). Basing protocol decisions on scoping creates a small risk that different kinds of studies are found to be necessary at a later stage to answer the review questions. In such instances, we recommend completing the review as specified and including other studies in a planned update, to allow timelines for the completion of a review to be set.

An alternative approach is to write a protocol that describes the review methods to be used for both randomized trials and NRSI (and all types of NRSI) and to specify the study design features of eligible NRSI after carrying out searches for both types of study. We recommend against this approach in a Cochrane Review, largely to minimize the work required to write the protocol, carry out searches and examine study reports, and to allow timelines for the completion of a review to be set.

Their decision tree on the use of non-randomised trials is shown in figure 24.1.a below. Note the following abbreviations:

- RCTs = Randomised Control Trials
- NRS = Non-Randomised Studies
- NRSI = Non-Randomised Studies of Interventions

- PICO = Population, Intervention(s), Comparator(s), Outcomes




## NICE (National Institute for Health and Care Excellence)

**NICE summary**

Largely only use published material. In exceptional circumstances, they allow for the use of pre-prints, but the example of exceptional circumstances they give is a “public health emergency”.

The possible pieces of evidence are gathered, the least relevant are filtered out, and then up to three pieces of evidence are selected using the following priority rankings:

1. Systematic reviews
2. Randomised control trials
3. Cohort/case-control/case series, ranked upon a combination of their size/publication date/clarity of data/inclusion of an “active comparator” (effectively, a placebo option)/how representative the study population is of the relevant UK population

If none of the above can be identified, the search criteria may be broadened

Note, studies ranked below RCTs are **only used if no RCTs are available**, or if they provide data on a specific outcome not discussed in an RCT

Worth noting, they include details in their report of the studies they shortlisted, and reasons for non-inclusion of studies on this list they didn't use

**NICE Full Description**

Link

**6 Developing the evidence summary | Evidence summaries: process guide | Guidance | NICE – Section** (6.5 in particular)

**6.5 Literature search**

6.5.1 Searching for evidence

NICE's information services do a literature search according to the agreed scope and PICO. The aim is to find the best available evidence on the effectiveness, safety and resource impact of the medicine. In exceptional circumstances, the literature search may include preprints from medRxiv and bioRxiv, for example during a public health emergency.

The search strategy and quality assurance of the search process is included as an appendix in the evidence review.

6.5.2 Selecting the evidence

Evidence identified from the literature search is reviewed to find relevant primary research that addresses the use of the medicine within the defined indication and population under review. If robust systematic reviews of randomised controlled trials (RCTs) or RCTs are available, they form the basis of the review. However, the best available evidence may include evidence other than RCTs, such as observational studies.

First sift

The first sift reviews the title and abstract of the study against the scope and PICO and removes evidence of low relevance. This may include non-English language studies, or conference abstracts or studies that have not been published in full (because these cannot be critically appraised). Note that preprints may be considered for inclusion in exceptional circumstances.

Second sift

The second sift of full papers further excludes articles that do not meet the criteria in the scope.

When all relevant studies have been identified, the best available evidence is selected for inclusion in the evidence review. Usually no more than 3 studies are prioritised for inclusion, using these principles:

- systematic reviews of RCTs are prioritised first, followed by single RCTs
- if 1 or more systematic reviews or RCTs are included, lower-quality studies (for example cohort or case-control studies, or case series) would only be included if they provide additional data on outcomes not available from the higher-quality studies
- if further prioritisation is needed, other factors would be considered such as:
    - size of study (number of study participants)
    - date of publication
    - how well the data are reported
    - whether an active comparator was used, and whether this reflects usual UK practice

- whether the population in the study reflects the typical UK population for which this medicine is likely to be used.

If no relevant evidence is identified, the development team will consider if broadening the search to include a wider population may provide useful information for decision making.

A summary of included studies and those studies excluded at second sift (with reasons for non-inclusion) are included as appendices in the evidence review.

Relevant regulatory information such as a European public assessment report (EPAR) or national public assessment report (if this has been published) are also reported to supplement the included studies, if needed.

6.5.3 Appraising the prioritised evidence

The development team appraises the included studies to assess risk of bias or quality of studies using a **NICE quality appraisal checklist** suitable for the type of evidence being reviewed. This quality assessment is included in an appendix in the evidence review.

## MHRA (Medicines and Healthcare products Regulatory Agency)

**MHRA summary**

MHRA's role is to decide whether a treatment should be legal, rather than whether its use should be encouraged. In order to be licenced a medicine must demonstrate safety and efficacy.

The MHRA use different types of evidence at different stages.

Licensing

There are several **potential routes to licence a new medicine** in the UK, including national and international processes (which rely on mutual recognition). Regardless of the route chosen **the licensing of a new medicine relies on evidence from clinical trials,[1] almost exclusively RCTs.** All pre-authorisation clinical trials must be approved by the MHRA, who provide an **algorithm** to identify if a clinical trial is needed.

MHRA state that Clinical trials are used in a risk-proportionate way. There are processes for accelerated routes to the UK market such as the Innovative Licensing and Access Pathways and the Early Access to Medicines Scheme which aim to streamline/add flexibility to the licensing process to allow for earlier patient access to important medicines. However, in essence **medicines do not reach the wider market without clinical trials having been undertaking, usually RCTs, which demonstrate safety and efficacy.**

Post-marketing surveillance

The objective of post-marketing vigilance is to monitor safety in a real-world context and to detect rare adverse events that were not seen in clinical trials which have a more limited study population. There are two major types of post-marketing reporting, mandatory reporting and spontaneous reporting.

Reporting by Marketing Authorisation Holders (MAHs) is mandatory, with MAHs having to report adverse reactions to either the relevant notified body or the European Medicines Agency, depending on which procedure was used to license the medicine.

In addition to mandatory reporting by MAHs there is spontaneous reporting. MHRA have a section of their website ( **Yellow Card | Making medicines and medical devices safer (mhra.gov.uk)** ) where anyone can report an adverse event that they feel is a side effects of treatment. Such pharmacovigilance reports are shared with other international regulators to increase the size of the reporting pool. Spontaneous reporting has traditionally been considered the lowest level of the evidence pyramid, indicating that MHRA consider all forms of evidence about potential dangers of licenced medicines to be valid (though they are not necessarily weighted equally, for an example see Section 3 of **Review paper: Citrin-Diav O et al (publishing.service.gov.uk)**).

Post-marketing surveillance incorporates a wide range of evidence types and methodologies ranging from requirements on marketing authorisation holders to report suspected serious adverse events to the competent authority to spontaneous adverse event reports from individuals into their national ADR reporting scheme. Various different types of evidence can feed into post-market pharmacovigilance, including RCTs and meta-analysis, cohort or observational studies, linkage studies, prescription event monitoring, the use of registries and spontaneous reports.

When we approached them MHRA confirmed that they will use a variety of evidence types, stating

[1] There are different requirements for generics and medicines which have been in widespread use for over a decade.

*'If a new side effect is identified which may impact the balance of risks and benefits of a product, information from different data sources is carefully considered in the context of the overall side effect profile for the medicine, and how it compares with other medicines used to treat the same condition. A regulatory decision is made based on assessment of all relevant data and expert advice from the Commission on Human Medicines and/or its Expert Working Groups.'*

**MHRA Full Description**

**Links –**

**Clinical trials for medicines: apply for authorisation in the UK - GOV.UK (www.gov.uk)**

**Algorithm_Clean__1_.pdf (publishing.service.gov.uk)**

**Clinical trials for medicines: manage your authorisation, report safety issues**

**Apply for the early access to medicines scheme (EAMS) - GOV.UK (www.gov.uk)**

**Yellow Card | Making medicines and medical devices safer (mhra.gov.uk)**

**Notes:**

Clinical trials

In their online guidance on **Clinical trials** MHRA set out the process for authorising a clinical trial, a selection of relevant sections are detailed below including:-

1. **When a clinical trial authorisation (CTA) is needed**.
2. **Risk Proportionate Approaches**, and
3. **Applications that need expert advice**

When a clinical trial authorisation (CTA) is needed

Use the online algorithm **Is it a clinical trial of a medicinal product?** (PDF, 68KB, 2 pages) to find out if your study needs MHRA authorisation.

The algorithm is a set of questions that determine:

- whether the substance you're testing counts as a medicinal product
- whether your trial counts as a clinical trial within the scope of the relevant legislation

You can also read the **Mock examples to assist with the question 'Is it a clinical trial of an investigational medicinal product?'** to help you decide if your study needs a CTA.

For further advice you may also wish to consult your local regulatory department or research governance team. From October 2021 the 'SCOPE' advice service will only be available via self-service using the guidance on this webpage.

Risk Proportionate Approaches

A risk proportionate approach to the initiation, management and monitoring of certain clinical trials is possible. The sponsor should carry out a risk assessment based on the potential risks associated with the IMP. View our guidance on **risk-adapted approaches to the management of clinical trials of investigational medicinal products**.

We will perform a risk adapted assessment of certain 'Type A' trials in which the risk to the patient from the IMP is considered to be no greater than that of standard medical care. These are trials involving medicinal products licensed in any EU Member State if:

- the trial relates to the licensed range of indications, dosage and form of the product, or;
- the trial involves off-label use (such as in paediatrics and oncology) that is established practice and supported by enough published evidence and/or guidelines.

Applications that need expert advice

For certain trials, we will seek advice from the Clinical Trials, Biologicals and Vaccines Expert Advisory Group (CTBVEAG) of the Commission on Human Medicines (CHM). The CHM will then discuss the trial at their meeting, which will take place later in the same week as the CTBVEAG meeting. We will make the decision to refer applications for expert advice based on an assessment of the risks and how the sponsor plans to mitigate them. Areas we look at when considering risk factors include:

- mode of action
- nature of the target
- relevance of animal species and models

We may refer other applications for expert advice if we identify issues during the assessment process. Examples of trials where expert advice may be needed include first-in-human (FIH) trials with novel compounds where the:

- mode of action involves a target that is connected to multiple signalling pathways (target with pleiotropic effects), e.g. leading to various physiological effects or targets that are ubiquitously expressed
- compound acts (directly or indirectly) via a cascade system where there may be an amplification effect which might not be sufficiently controlled by a physiological feedback mechanism
- compound acts (directly or indirectly) via the immune system with a target or mechanism of action which is novel or currently not well characterised
- is novelty in the structure of the active substance e.g. a new type of engineered structural format such as those with enhanced receptor interaction as compared with the parent compound
- level of expression and biological function of the target receptor may differ between healthy individuals and patients with the relevant disease
- is insufficient available knowledge of the structure, tissue distribution, cell specificity, disease specificity, regulation, level of expression and biological function of the human target, including down-stream effects
- compound acts via a possible or likely species specific mechanism or where animal data are unlikely to be predictive of activity in humans

If you are a sponsor of a FIH or early stage clinical trial you should read the **Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products**. You should use the document to help you identify risk factors and create mitigation strategies.

Sponsors should use the criteria above to decide if their trial needs expert advice. You can get pre-submission advice from us if you are unsure if your compound falls into the 'higher-risk' category.

To get advice you should send an email with 'URGENT – EAG/CHM QUERY' as the title to **clintrialhelpline@mhra.gov.uk** including:

- a summary of the nature of the compound

- its target/mechanism of action
- the relevance of the animal model(s)

We will send a response to this email within 14 days.

If we confirm that the application comes within the category of 'higher risk', or you have determined this yourself, you should **select the date of the CTBVEAG meeting** where you want your trial discussed.

You should prepare your complete submission package and submit it in the new part of IRAS as described above. At least 14 days prior to submission you should alert MHRA and HRA (**clintrialhelpline@mhra.gov.uk**; **approvals@hra.nhs.uk**) that the application is planned and it requires EAG/CHM review to ensure an appropriate REC meeting is scheduled. The submission should be made no later than 21 days before the date of the CTBVEAG meeting it will be discussed at, but ideally much earlier to enable a smooth review process. Applications that are received later will be assigned to the next available meeting.

The rest of the application process is as described above for all applications. The combined response letter will be sent to the sponsor as soon as possible after the REC meeting. Please refer to HRA website for further information regarding scheduling of the REC meeting.

Post-marketing surveillance – Spontaneous reporting

Spontaneous reporting has been important in detecting rare side effects which are not seen at a high enough level to be detected by the relatively small numbers of people taking part in clinical trials. Particular attention is paid to medicines which are under additional monitoring requirements, including those which are new to market and vaccines, these are also part of the black triangle scheme.

The **Yellow Card website** states:-

Yellow Card

The Yellow Card scheme is vital in helping the Medicines and Healthcare products Regulatory Agency (MHRA) monitor the safety of all healthcare products in the UK to ensure they are acceptably safe for patients and users.

Reports can be made for:

- suspected adverse drug reactions (ADRs) to all medicines including:
    - vaccines
    - blood factors and immunoglobulins
    - herbal medicines
    - homeopathic remedies
- all medical devices available on the UK market
- defective medicines (those that are not of an acceptable quality)
- fake or counterfeit medicines or medical devices
- nicotine-containing electronic cigarettes and refill containers (e-liquids)

It is important that problems with medicines and medical devices and other nicotine e-cigarette products are reported, as the reports help identify new problems with these products.

MHRA will review the product and if necessary and take action to minimise risk and maximise benefit to patients and the public.

MHRA is also able to investigate counterfeit medicines or devices and if necessary take action.

Black triangle scheme

New medicines and vaccines that are under additional monitoring have an inverted black triangle symbol (▼) displayed in their package leaflet and summary of product characteristic, together with a short sentence explaining what the triangle means – it does not mean the medicine is unsafe. You should report all suspected ADRs for these products.

For products with regards to Northern Ireland, the European Medicines Agency (EMA) is responsible for maintaining the list of black triangle products. For products with regards to the United Kingdom the MHRA is responsible for maintaining the list of black triangle products.

This symbol appears next to the name of a relevant product:

- in the British National Formulary (BNF)
- in the British National Formulary for Children (BNFC)
- in Monthly Index of Medical Specialties (MIMS)
- in the Association of the British Pharmaceutical Industry (ABPI) Medicines Compendium
- on advertising material
- in Drug Safety Update
- in summaries of product characteristics and patient information leaflets

See **the Black Triangle scheme - new medicines and vaccines subject to EU-wide additional monitoring** (PDF, 139KB, 4 pages).

# Annex C – Evidence base used by SCAAC to date

## Evidence Base used by Scientific and Clinical Advances Advisory Committee (SCAAC) to date

The table below shows how many papers have been considered to date by SCAAC when considering each add-on. There are three add-ons where SCAAC has considered fewer than three publications; Endometrial Receptivity Analysis, Intrauterine culture, and IV immunoglobulin.

| Add-on | Number of publications considered |
|---|---|
| Artificial Egg Activation | 10 |
| Assisted Hatching | 4 |
| Embryo Glue | 11 |
| Endometrial Receptivity Analysis | 2 |
| Endometrial Scratching | 29 |
| Freeze All | 11 |
| IMSI | 8 |
| Intralipids | 3 |
| Intrauterine culture | 1 |
| IV immunogloblin | 2 |
| MACS | 4 |
| PGS3 | 9 |
| PGS5 | 5 |
| PICSI | 8 |
| Steroids | 9 |
| Time Lapse | 10 |

# Modernising Fertility Regulation - update

## Details about this paper

| | |
|---|---|
| Area(s) of strategy this paper relates to: | Shaping the future |
| Meeting: | Authority |
| Agenda item: | 7 |
| Meeting date: | 19 July 2022 |
| Author: | Clare Ettinghausen, Director of Strategy and Corporate Affairs<br>Laura Riley, Head of Policy (Scientific)<br>Ana Hallgarten, Public Policy Manager |
| Annexes | Annex 1: Notes of discussion at the Legislative Reform Advisory Group on 6 May 2022 on consent and data sharing<br>Annex 2: Notes of discussion at the Legislative Reform Advisory Group on 27th May 2022 on donor anonymity and information provision<br>Annex 3: Notes of discussion at the Legislative Reform Advisory Group on 27 June 2022 on scientific developments |

## Output from this paper

| | |
|---|---|
| For information or decision? | For decision/ |
| Recommendation: | The Authority is asked to:<br>• Discuss the topics outlined in sections 4-7 and any concerns over the issues raised<br>• Agree the plan for a targeted consultation to take place later this summer<br>• Consider any particular issues they would like to discuss further in September |
| Resource implications: | Staff resources required to ensure this work is kept on track |
| Implementation date: | Ongoing |

| | |
|---|---|
| Communication(s): | As outlined in the paper – through regular public and stakeholder updates |
| Organisational risk: | Medium |

# 1. Introduction

**1.1.** A key HFEA priority is to develop a proposal on legislative change for the Department of Health and Social Care (DHSC) towards the end of the year.

**1.2.** The primary legislation governing fertility treatment and embryo research, including the regulatory activities of the HFEA, is the Human Fertilisation and Embryology Act 1990 (as amended). Although the Act was updated in 2008, and in Regulations at other times, in large parts it remains as written over 30 years ago. Developments in the fertility sector, in science and medical technology, and in social and cultural norms, mean it is time to take a coherent view at which parts need to be modernised.

**1.3.** Previous updates to the Authority during 2021 and 2022 have noted the background to this work and developments to date.

**1.4.** This paper provides an update on activities and issues arising since the last Authority meeting in May 2022. Section 2 summarises the key topics that the Authority have agreed to focus on. Section 3 outlines activity since the last Authority meeting and summarises the views of the Legislative Reform Advisory Group (LRAG) in relation to consent (section 4), data sharing (section 5), donor anonymity and information sharing (section 6) and scientific developments (section 7). Section 8 outlines the targeted consultation plans and section 9 the next steps.

# 2. Key topics

**2.1.** To recap, the key topics that the Authority has previously agreed to look at in more detail are:

## Patient protection

- The Act is silent on patient centred care
- There is a limited range of enforcement mechanisms or sanctions to drive improvement and current sanctions are blunt or slow
- There are no economic sanctions which have been shown to be an effective driver of improvement in other competitive markets
- The Act assumes a clinician ownership model which increasingly no longer exists – where does that leave the 'person responsible'
- Work of the CMA is welcome but raises questions of what should be within our remit and extent to which patients would be better protected if all aspects of the fertility sector were subject 'end to end' regulation by the HFEA
- The Act is overly prescriptive - e.g., requires inspections every two years – which limits the scope to reward good compliance with more streamlined regulation

## Scientific developments

- The Act is at risk of being overtaken by research advances
- 14-day rule has proved effective and any replacement would need to offer the same degree of certainty and regulatory clarity
- Process is overly prescriptive e.g. in relation to mitochondrial donation
- There are no means to encourage new technology or other innovation through trials or regulatory experimentation

## Consent, data sharing, anonymity

- Consent is overly complicated which creates costs for clinics and increases risk of errors
- Patient and donor confidentiality and disclosure of register data maybe out of step with other areas of healthcare and with new challenges such as DNA testing websites. Is the idea of data confidentiality out of date? Where will this go in another 10 years or more?

# 3. Activity since May 2022

**3.1.** We last discussed the modernisation of the Act at the May 2022 Authority meeting. Since then, a range of issues have been outlined at both our professional and patient stakeholder groups; at three different LRAG meetings, and at roundtable discussions with the Nuffield Council on Bioethics (on donation and anonymity), the Medical Research Council and researchers from the Francis Crick Institute (on scientific developments) and with researchers that have used HFEA Register data (on a range of data related questions, which are largely consequential to wider changes to the Act).

**3.2.** The LRAG papers are on the HFEA **website** and the notes summarising the discussion at each meeting are attached for reference at annexes 1-3. Sections 4-7 sets out the emerging conclusions from LRAG in respect of questions relating to consent, anonymity and donation, data sharing and scientific developments.

# 4. Key questions relating to consent

**4.1.** There was agreement on the key issues outlined to LRAG and summarised in the **paper**. It was noted that informed concept in one of the most important principles in healthcare and a fundamental feature of the Act. Taking consent is complex and there are a range of options for reform, from how the administrative arrangement work to embryo donation for research. Key points discussed are below.

**4.2.** The Act should be amended so that consent forms for legal parenthood are not stored over decades only at clinics, which is suboptimal, and potentially risky for practical reasons. Forms should be mandated to be stored for much longer than 30 years under any changes to the Act.

**4.3.** In future, it was suggested that while patients could consent to become legal parents to a resulting child, their consent to treatment could be taken as implied by the patients' presence in the clinic.

**4.4.** All agreed that legal parenthood is often not considered a key issue by patients who are understandably more focused on starting their fertility treatment as soon as possible. The Act's requirements in this area must be therefore kept as simple as possible to avoid issues for patients about legal parenthood further down the line, for example when registering a child's birth.

**Electronic consent**

**4.5.** The Act could in future require clinics to be able to demonstrate evidence of informed consent, but need not specify what method (electronic or otherwise) must be used for recording this consent. The HFEA could determine the appropriate consent recording regimes for clinics.

**Consent for storage and use of testicular and ovarian tissue**

**4.6.** The Act should be amended to resolve complications regarding the statutory responsibilities for the two regulators (HFEA and HTA) over these tissues. LRAG agreed that the Act should be amended such that consent (to storage, for example) should be given and recorded independently without tying it to any time-limited financial arrangements agreed for storage.

**Family limits**

**4.7.** LRAG agreed that the Act should be amended to specify that a family limit must be placed on donation and that HFEA should be given responsibility to determine the specific limit.

**Posthumous consent**

**4.8.** LRAG were content that in a fresh cycle of treatment (without processing and storing), a new Act requirement for consent before using a person's own gametes for their own/their partner's treatment could reduce difficulties if circumstances change in the course of treatment.

**Consent to research**

**4.9.** All concurred that amending the Act to explicitly permit broad consent could allow for more research and less wastage of donated embryos. Recontact should be required as part of this. Patients with stored embryos are already recontacted regularly by their clinic.

**4.10.** The Act should provide under any new consent arrangements, that patients must still be able to donate their embryos directly to specific projects only, if they prefer that.

## 5. Data sharing

**5.1.** LRAG members agreed that amending the Act to permit easier sharing of fertility patient data in medical settings outside the fertility clinic would aid patient protection and safety, improving care, speeding up diagnosis, and providing important centralised records for research or commissioning.

**Sharing patient data in a research setting**

**5.2.** LRAG members were content that that the Act should be amended to allow register information from the donors of gametes and embryos to be shared for all kinds of research, beyond anonymised research.

## 6. Donor anonymity and information provision

**6.1.** A range of different options were discussed with LRAG ranging from the 'status quo plus' to a 'double track' system. LRAG agreed that the double track system was likely the best way forward. Details of these options and the potential impact of each option on donors, donor conceived people, patients/parents of donor conceived people, clinic staff and operations; and the HFEA are outlined in the paper. The summary of the preferred 'double track system' is below.

**6.2.** A double track system – in which donors must choose between the status quo (i.e., donor identifiable information available when the child is 18) and being identifiable from the outset (to

be defined in new legislation). Patients could choose between donors who wish to be identifiable and those who do not. This could provide more autonomy to donors and patients in deciding the type of information/contact they want. However, where patients opt for the status quo, donor-conceived people still might wish to find out details about their donor earlier than 18. This option has the advantage of choice for the patients but the disadvantage of not permitting a uniform set of options for all donor-conceived people. The 'choice' for donors may not be realistic because a high likelihood remains of information coming to light outside of the consented process, with the need for provision in the Act for managing that eventuality

## 7. Regulation of scientific developments

**Regulatory processes**

**7.1.** There was broad agreement that a principles rather than process approach was more appropriate for new research and/or treatments. This would allow licensing applications to be considered and approved or rejected in a more timely way

**Supporting innovation**

**7.2.** The use of a 'regulatory sandbox' may be beneficial, as means of better supporting innovation. Additionally, a 'sandbox' would allow for a greater role of external expert views in the process, but may increase resource demands on the HFEA. There were concerns about the participation of patients in innovative treatments/research that patients have to pay to access. Paying for unproven and novel treatments is unusual outside of the fertility sector, and it would be beneficial to impose license conditions in some research that participating patients should not have to pay. This would ensure that the Act continues to increase patient protection.

**The 14-day limit**

**7.3.** There was no clear consensus on extending the 14-day limit, with at least one member expressing concerns that such a move could lead to a significant public push back to any extension. However, several members agreed that either an extension to 21 or 28 days may be appropriate, given the potential benefits that might flow from such a change. Additionally, there was agreement that any change in the limit would require proper public engagement.

**In vitro-derived gametes, embryo-like entities, and stem cell based embryo models**

**7.4.** LRAG members noted that developments in this field were taking place at a rapid rate and required continuous assessment. At present such activity is not regulated but many felt that there was a case for bringing at least some of these entities into a future Act.

**Use of human embryo in research: 'alternative' models**

**7.5.** LRAG discussed that there were benefits if a future Act could be amended to read that embryos are 'desirable' rather than 'desirable' and 'necessary'.

**Embryonic selection based on Polygenic risk scores**

**7.6.** LRAG members presented different opinions on the future regulation and use of polygenic risk scores. Some considered that the Act continued to be too prescriptive as regards possible embryo testing that may be beneficial in the future, and others were concerned about the ethical issues raised by embryo selection based on polygenic risk scores.

**Germline genome editing**

**7.7.** LRAG members agreed that germline genome editing raises new ethical questions which may require reflection in the future Act, with one member noting that this is the case not only with nuclear genome editing, but also with epigenetic editing.

## 8. Targeted consultation

**8.1.** As noted at previous Authority meetings, a targeted consultation is planned for later in 2022 to gather professional, key stakeholder patient groups and clinic staff views on our emerging proposals for legislative reform.

**8.2.** Initial discussions about the themes we have been looking at have taken place with our professional and patient organisation stakeholder groups, and we have publicly stated that a consultation will be taking place this year.

**8.3.** The consultation will be designed in a format that enables the HFEA to set out why we think specific changes are necessary and the outline proposals we have for reform. The plan is not to consult on changes which are largely technical, and which aim to improve on the operation of the existing policy consensus. Instead, the consultation will focus on proposals which are new, or significantly develop or depart from the existing policy consensus.

**8.4.** It should be noted that there is potentially a great level of public interest in debating some of the details of the Act, for example on embryo research. It is not intended that this consultation can definitively establish public views on these issues in the time we have. As and when the Government do review the legislation, then we expect there to be wider opportunity for public discussion or consultation on the detail of any proposed changes.

**8.5.** The consultation will cover questions relating to the key areas outlined in section 2 of this paper.

**8.6.** The time for detailed Authority consideration of these issues will be in the Autumn, but at this stage it would be useful to know if there are areas in the planned consultation that Authority have any concerns on.

**8.7.** A detailed communications plan will be developed to ensure the consultation is publicised and we have already trailed this in the media, and with stakeholder groups.

## 9. Next steps

**9.1.** The consultation will be drafted and launched later this summer with feedback to be brought back to Authority later this year, with final draft proposals for Authority to consider.

**9.2.** The risks outlined in the **May Authority meeting** are ongoing and in some cases have been challenged further by the intense activity that has been required for the implementation of the new storage laws for July.

## 10. For decision

**10.1.** Authority is asked to:

- Discuss the topics outlined in sections 4 to 7 and any concerns over the issues raised
- Agree the plan for a targeted consultation to take place later this summer
- Consider any particular issues they would like to discuss further in September.

# Annex A Notes of discussion at the Legislative Reform Advisory Group on 6 May 2022 on consent and data sharing

The discussion paper on consent for this meeting can be found here and on data sharing can be found here.

## 1. Legal parenthood

**1.1.** LRAG agreed that legal parenthood continues to be a complex area for patients and challenging to administrate in practice. Legal parenthood forms are complex, because the law is complex, but often delegated to less experienced nurses to discuss with patients, to free up more senior staff's time for other aspects of care.

**1.2.** LRAG members raised that:

- The Act should be amended so that consent forms for legal parenthood are not stored over decades only at clinics, which is suboptimal, and potentially risky for practical reasons. Forms should be mandated to be stored for much longer than 30 years under new amendments to the Act. There was however, no consensus on where else such forms should be stored.
- Because complex family and parenthood arrangements also exist outside of patients seeking fertility treatment. It was suggested that legal parenthood in fertility clinics could be removed from the Act entirely and be dealt with as part of wider family law. One approach would be that (given some members also felt that a review of birth registration legislation would be beneficial), family law questions about legal parenthood could be dealt with in a new, separate Act also covering birth registration. However, it was accepted that any wider review would take years and therefore there was a strong case to improve the position within the constraints of the Act. An alternative view was that the family courts could iterate around legal parenthood via case law, avoiding this area being dealt with by legislation at all.
- Consenting to medical treatment and consenting to legal parenthood under the current Act can become 'muddled' for patients. In future, it was suggested that while patients could consent to become legal parents to a resulting child, their consent to treatment could be taken as implied, by the patients' presence in the clinic.
- Some suggested further that individuals seeking fertility treatment at clinics could be considered by default as wanting to be parents, rather than needing to explicitly give their consent to legal parenthood. Others were concerned by the idea of implied consent and felt strongly that a legal process is needed to agree and evidence who the legal parents are, for example by the patient ticking a box that s/he agrees to be the parent of any child born. Without a clearly recorded consent following specific mandated information-giving, this could raise issues for patients or their families if there were a change of circumstances, for example, with the posthumous use of gametes and embryos.
- All agreed that legal parenthood is often not considered a key issue by patients who are understandably sometimes more focused on starting their fertility treatment as soon as possible. The Act's requirements in this area must be therefore kept as simple as possible to avoid issues for patients about legal parenthood further down the line, for example when registering a child's birth.

## 2. Electronic consent

**2.1.** LRAG agreed that the use of electronic consents in a clinic setting could be helpful to both clinicians and patients. Benefits included reducing admin errors, requiring identity authentications, creating flexible forms for different situations, automatically requiring information to be entered correctly, and offering drop-down details to explain complex issues, or providing mandatory video explanations of consent prior to completion. Patients can easily save electronic consent forms for their own records.

**2.2.** LRAG members raised that:

- The Act could in future require clinics to be able to demonstrate evidence of informed consent, but need not specify what method (electronic or otherwise) must be used for recording this consent. The HFEA could determine the appropriate consent recording regimes for clinics.
- The Act's focus should move to minimising the risks of patients misunderstand consent requirements, eg requiring staff to make it clear what patients are being asked to consent to, and making it clear how patients can provide their consent.
- Nurse consultations should still be compulsory where electronic consent forms are used outside of the clinic, so that patients can seek professional explanations easily, including patients who need more help to understand written information or whose first language isn't English.

## 3. Consent for storage and use of testicular and ovarian tissue

**3.1.** LRAG members raised that:

- The Act should be amended to resolve complications regarding the statutory responsibilities for the two regulators over these tissues. At the point of treatment the samples are the HFEA's responsibility, but when stored, the responsibility of the Human Tissue Authority, causing occasional non-compliances to occur. These might mean that tissue stored for future fertility preservation eg by a child having cancer treatment in hopes of eventual fertility restoration by autologous transplantation, in fact can't be used.
- Furthermore, there has also been significant research progress with in-vitro derived gonads which will require appropriate regulation in law.

## 4. Family limits

**4.1.** LRAG agreed that the Act should be amended to specify that a family limit must be placed on donation and that HFEA should be given responsibility to determine the specific number for this limit.

**4.2.** LRAG members raised that:

- Given sometimes complex family relationships, defining 'family' can be challenging. There were varied opinions regarding whether using the term ' families' was optimal when setting limits.

- A suggestion was for the Act to specify that the limit could pertain to the 'children born, plus their siblings and half siblings' per donor via licensed donation treatment, as a simpler expression of the principle. The relevant number of children per donor could then be set in directions by HFEA.
- Donations from the same donor can be used in the UK under family limits, but also without limit in other countries, for example in the US. Strong concerns for donor-conceived people and recipients were felt about lack of restrictions on family limits overseas, for donations imported into the UK from abroad.
- Some felt the Act should be amended to require increased transparency on the number of children/families already created overseas by donors whose gametes have been imported into the UK for treatment use. Others questioned how achievable this transparency might be, given that overseas clinics and donors may not know of these numbers themselves.
- There were similar concerns about UK clinics' practice of exporting any unused stocks of donations overseas for use, after an individual UK donor has reached the current ten family limit. This was similarly felt to be a breach of patients' or donor-conceived people's expectations.
- The principle for placing limits should be around limiting the risks of consanguinity for donor-conceived people in sexual relationships, but also around allowing donor-conceived people who wish to, to form relationships with a donor and/or relationships with their siblings from the same donor. This relationship-building becomes increasingly difficult where family numbers are very high.

## 5. Payment arrangements coupled with consent

**5.1.** LRAG agreed that the Act should be amended such that consent (to storage, for example) should be given and recorded independently without tying it to any time-limited financial arrangements agreed for storage.

## 6. Posthumous consent

**6.1.** LRAG noted the difficulty in regulating posthumous consent. The example of a current ongoing court case has demonstrated the problems that can arise posthumously when consent forms are not properly completed.

**6.2.** LRAG members raised that:

- Clinic consultations do discuss posthumous consent, but at that time, patients may be stressed or anxious to proceed to treatment, hence errors being made on the forms, or insufficient consideration being given to wishes around posthumous use.
- Consent forms continue to be essential as consent choices must be clearly documented regarding posthumous use.
- For clarity, all forms need to provide a required yes/no choice to be recorded. 'I do not want X to happen' should be required to be recorded as an active choice, not, as sometimes currently happens, leaving the 'yes' box blank for a presumed 'no', with no box provided, because forms have only provided a box to tick for 'yes'.

- The number of consent forms regarding the use of gametes could be reduced, with consent to different types of uses combined together in one form, to simplify the process and reduce the chance of errors between several forms.

## 7. Clarity on consent requirements for procurement/harvesting of gametes and partner treatment of sperm

**7.1.** LRAG were content that in a fresh cycle of treatment (without processing and storing), a new Act requirement for consent before using a person's own gametes for their own/their partner's treatment could reduce difficulties if circumstances change in the course of treatment.

## 8. Consent to research

**8.1.** LRAG noted that most embryo research already falls into easily defined purposes. Because the Act does not currently explicitly permit broad consent to donation of embryos for defined research purposes, this has resulted in at least one instance of wastage of large numbers of embryos donated for research. At present the Act implies that consent must be to donate to specific research projects. Reconsent to any amended individual research project can be very difficult logistically to obtain from patients.

**8.2.** If for example, a renewed research licence is not granted to a project due to changing views at the HFEA licensing system or the **Research Ethics Service** Research Ethics Committee (REC) then the embryos already consented to that project must be destroyed, which is a waste and a reputational risk to research. Research funding ceases with the licence stopping.

**8.3.** LRAG members raised that:

- All concurred that amending the Act to explicitly permit broad consent could allow for more research and less wastage of donated embryos. Recontact should be required as part of this. Patients with stored embryos are already recontacted regularly by their clinic.
- Research gamete and embryo banks could be created under broad consent. Many patients will welcome the opportunity to donate to more than one specified project.
- Specific opt-outs for different research uses must be available within any broad consent. Eg opting out of all research generating an enduring stem cell line, or creating a chimeric embryo.
- The Act must provide under new consent arrangements, that patients must still be able to donate their embryos directly to specific projects only, if they prefer that. Some patients will only want to donate to a project that resonates with them personally.
- More information should be provided about donating to research and the purposes of research in the Code of Practice and on the HFEA website.
- Some members felt that the Act may not need significant change around consent to research, dependent on how the Act and the Code of Practice are interpreted.

## 9. Data sharing

**9.1.** The HFEA Chief Executive outlined the discussion paper.

**9.2.** LRAG members agreed that amending the Act to permit easier sharing of fertility patient data in medical settings outside the fertility clinic would aid patient protection and safety, improving care, speeding up diagnosis, and providing important centralised records for research or commissioning. The group were concerned that when a patient has a miscarriage for example, were hospital staff not to have access to their fertility clinic records adds unnecessary risk. Clinicians said that they had almost never experienced patients saying this would be problematic (though occasionally if patients have a social relationship with their GP they might say they don't want their GP to know).

**9.3.** LRAG members raised that:

- The Act's imposition of an extra layer of confidentiality around fertility treatment above standard medical confidentiality should not be retained.
- HFE Act amendments should dovetail with GMC guidance around confidentiality and data sharing within research as well as care, such as the 'no surprises' test.
- Although many patients consent to data sharing of medical data for research, they may at times not feel clear who this information is being shared with. Maximum transparency should be provided.
- When sharing medical data between professionals, clinicians must be mindful and sensitive about disclosing information. A few fertility patients do not tell anyone at all that they are having treatment.
- Caution was raised where patients using donated gametes did not want their medical record to show donor gametes, which for some patients, particularly from some underserved communities, would be felt to be sufficiently stigmatising for the patients and their potential child that they would seek treatment outside the UK to avoid it.

## 10. Sharing patient data in a research setting

**10.1.** LRAG members were content that that the Act should be amended to allow register information from the donors of gametes and embryos to be shared for all kinds of research, beyond anonymised research.

## 11. Incentivising the use of HFEA Register data in research

**11.1.** LRAG members were content that the HFEA should be able to charge full cost recovery to researchers for access to our register data, regardless of how identifiable it may be, and at a rate set by the Authority (not the Act).

# Annex B Notes of discussion at the Legislative Reform Advisory Group on 27 May 2022 on donor information and anonymity

The discussion paper on donor information and anonymity can be found here..

## 1. Donor anonymity and information provision discussion

**1.1.** The HFEA Chief Executive outlined the issues in the discussion paper. LRAG agreed that this is perhaps one of the most sensitive and potentially contested areas that they expected to discuss as a group, given that impacts of any change on individuals will range widely.

**1.2.** The Chief Executive gave a general overview of the issues, including some of principles around how the HFEA currently works. He asked the group to consider how the Act might require clinics and the HFEA to operate in future around donor anonymity and managed information release, in the interests of donor-conceived people and their families, and donors, bearing in mind that donor anonymity can no longer be guaranteed, due to the huge uptake of direct-to-consumer DNA testing and matching services.

**1.3.** Discussion began with a general exploration of the issues raised in the discussion paper. LRAG members had a range of responses and reflected that both patients and donors would be likely to have equally mixed views, depending on family circumstances, with no 'one size fits all' solutions. They suggested a new principle in the Act, that it should support parents to make the decisions that suits their child and family best.

**1.4.** Other groups also use donor services: under the current Act, donors' own children can't apply to find formal information about their donor-conceived siblings, this information is not held on the HFEA register. All agreed that further consideration should be given to providing some information rights to donor's children in the Act.

**1.5.** All agreed that the Act should continue to require clinic collection, and HFEA safekeeping, of all the data about children born from a donor, for the adult child/ren to request if wished. The Act should continue to make sure that consent is properly taken and in line with existing HFEA Code of Practice guidance, donors and recipients are properly informed about the changes to anonymity due to DNA testing and matching services. Parents should continue to decide when or if to tell their child aged under 18, about her or his donor-conceived status.

**1.6.** Some LRAG members felt that the HFEA's legal relationship should focus only on the clinic and donor. Officially available, identifiable donor information relating to children under 18 years old shouldn't be dictated by the Act, but parents should decide when and if they approach a donor for childhood contact, and when or if to find out about or approach their child's siblings born from the same donor.

**1.7.** Members felt that one of the merits of the current age limits of 16 years (for non-identifying donor information) and 18 years (for identifying information, only for donor conceived people born after 2005) is that it provided time for young people to reflect before contacting their donor. Some felt that some donors would not want to donate at all if they had to be potentially identifiable to a donor-conceived child in their childhood years- although all acknowledged the possibility of donors becoming identified informally via DNA testing and matching services at

any time. Some felt it removed choices from both donor and parent for the law to make identifying donor information available in childhood.

**1.8.** There were some concerns that a change in law could mean that parents (or their children) will feel they should make childhood contact with their donor, even though this might not be a good result for all families. Some LRAG members felt that funded emotional support would be needed for families considering making childhood contact with a donor, including peer support from other families via donor conception.

**1.9.** Other members commented that the HFEA's role should be to provide the donor information, not a support service for those accessing information.

**1.10.** LRAG members commented that if identifiable donor information became available at birth, some patients might want that information before conception, meaning that donation at clinics would have to work very differently.

**1.11.** Turning to the core principles set out in section 4 of the discussion paper, LRAG members recommended that a further principle ought to be added, that any proposal did not impact on the availability of fertility treatment. If this were not addressed, then there was a concern that patients might then seek treatment overseas in less closely-regulated countries.

**1.12.** Some felt that a change in the Act towards identifiable information-sharing during childhood could encourage a cohort of new donors, who had carefully considered the implications of their donation for the donor conceived child. However, all noted that it was important that any change in policy did not impact negatively on some ethnic minority recipients and donors, given that some donor numbers relative to demand are already very low.

**1.13.** Some LRAG members reported that fertility clinics serving specific faith communities can find that some patients from those groups find the concept of the HFEA holding a donor record to be a deterrent, and prefer to seek treatment abroad.

**1.14.** LRAG members pointed out that people with white Northern European or North American ancestry are relatively overrepresented in the DNA testing and matching databases and are thus more likely to receive results of greater specificity, as well as perhaps being culturally more likely to use these services. People from other global majority ethnic backgrounds, or Eastern European or Southern European ethnic backgrounds are less well represented.

**1.15.** Some LRAG members felt that given these aren't universally-used services in the UK, if there was no reason aside from the rise in DTC DNA testing to consider changing the Act, that it may be more appropriate to ask Government to look again at the regulation of Direct-to-consumer DNA testing and matching. Other members thought that because the option to allow donor information in childhood achieved by these services could be very valued by some patients and children, this justified their consideration around the Act.

**1.16.** LRAG members wondered if in future, the Act could need to provide for recipients to choose a donor using information on the donors' genetics, by selecting a close match (or seeking a specific difference) to their own genetic information. They felt the Act may need to respond to growing demand for donors to have enhanced carrier screening. As polygenic risk scoring becomes more understood and reliable over the next decade, this could also radically change how recipients want to choose donors.

## 2. Options discussion

**2.1.** The Chief Executive of the HFEA outlined some initial thoughts on possible options for a new model (further detail in the discussion paper):

**2.2.** A) Status quo plus –keep the current statutory position where all donors must remain anonymous until resulting child is 18 after which the donor-conceived person may seek their identity from HFEA if they wish to, and amend the Act so that clinics must inform donors and recipients about the risk that any children born from their donation could find out the donor's identity before they are 18, including as part of the consent process. This position would make the existing Code of Practice guidance mandatory. However, there would remain the high likelihood of information coming to light outside of the consented process and the need for provision in the Act for managing that eventuality.

**2.3.** B) Early identification by consent – introduce guidance for clinics and a voluntary system for donors to become identifiable earlier on, perhaps under agreed terms about the level of contact/localised arrangements (either from the outset or at any point before children born from their donation are 18 with the consent of the parents, or consent varied by the child after a certain age).

**2.4.** C) Remove Anonymity completely, Amend the Act so that legally, donors' details must be made identifiable to the recipients from the outset: whether from the time of considering all donors, so donor details are always identifiable, or after selecting a specific donor, or when treatment commences, or upon pregnancy, or birth

**2.5.** D) A double track system – in which donors must choose between the status quo (i.e., donor identifiable information available when the child is 18) and being identifiable from the outset (to be defined in new legislation). Patients could choose between donors who wish to be identifiable and those who do not. This could provide more autonomy to donors and patients in deciding the type of information/contact they want. However, where patients opt for the status quo, donor-conceived people still might wish to find out details about their donor earlier than 18. This option has the advantage of choice for the patients but the disadvantage of not permitting a uniform set of options for all donor-conceived people.

**2.6.** Continuing, the HFEA Chief Executive noted that options A and B rely on people not varying their consent, but it may be that some people will want to change their minds. Option C runs the risk of deterring people who would otherwise want to donate and could reduce access to treatment. Option D seeks to give donor and patient a choice on identifiable donor details by offering a double track system.

**2.7.** The Chief Executive invited comment on the four initial options. LRAG members said that:

Option A: Status quo plus

- Seeks to protect donor anonymity until the donor-conceived child is 18 years old, but there is always a risk of information being revealed informally, whether the donor-conceived person is younger or older than 18 years.
- Someone must make a decision on the child's behalf, which is best done by their parents.

Option B: Early identification by consent

- Added more consent options on top of already complex consent requirements, which could be burdensome for some patients and clinics.
- Would be resource intensive.

•Donor-conceived people may find it difficult that their parents actively made a concealing choice - whereas where parents have no choice there can't be blame. Counselling will be key.

Option C: Remove Anonymity completely

• In New Zealand, donors are identifiable from birth.

• Some people are already going online to find their donor in childhood- Why are 16 and 18 the right ages to reveal information.

• Adoption in the UK has removed anonymity completely. Children know from an early age that they are adopted.

• Not everyone will want to know about their biological or genetic origins, even when identifiable information is available.

• Resource heavy, unsure how we would make it work in day to day terms.

Option D: A double track system

• Seems to balance protections for those who need them, with offering more choices for those who want them.

• The law should not push people toward less safe options. This option still contains the current strong advice that anonymity in childhood can't be guaranteed, but it could allow as many people as possible to have regulated UK clinic treatment rather than going overseas for donor treatment or going online informally in the UK.

• Parents should make all the choices and decisions for children, and they have to stand by them- nobody else can make those choices.

•Sometimes parents change their mind about donor anonymity after the child is born, which may happen with this model that relies on consent at the outset

•It doesn't give all donor-conceived children equal rights.

•This option would need careful discussion with patients before treatment, when they may be having to take in a lot of other information already.

## 3. Options decision

**3.1.** The LRAG members did not support options B or C. There was support for continuity (option A) but on balance, members agreed that a consensus could be recorded that option D was their preferred option overall.

# Annex 3 Notes of discussion at the Legislative Reform Advisory Group on 27 June 2022 on the regulation of scientific developments

The discussion papers for this meeting can be found here and here.

## 1. Regulatory Processes

**1.1.** The HFEA Chief Executive outlined the issues in the discussion paper regarding the way in which the Act currently specifies regulatory processes and that the Act and HFEA should be able to support and encourage innovation.

**1.2.** Of particular concern is, for example, the limitation that currently exists regarding mitochondrial replacement techniques. At present, Regulations allow only two specific methods of mitochondrial donation, and were a more efficient and safer technology become available that achieved the same end it would not appear to be accommodated by the current Act.

**1.3.** The Chief Executive recommended that if amended, the Act should offer principles rather than defined processes in order for HFEA to consider new research and/or treatments and approve or reject them in a more timely, proportionate and ideally more 'future-proofed' way.

**1.4.** There was consensus among LRAG members that:

- The use of principles rather than processes would be beneficial.
- Any developed principles would need to be sufficiently detailed.

## 2. Supporting innovation

**2.1.** The Chief Executive noted that the HFEA's ability to support responsible innovation within the current Act is limited. At present, in the procedure that allows HFEA authorisation of novel treatment processes, there is not an appropriate balance between the approval before a new technology or treatment is allowed to take place and after the approval is put in place. The controls for new technologies and treatments are all 'front-loaded'. This can be problematic when some applications cannot fully evidence their safety and effectiveness until after application. The options for change presented to LRAG would allow for greater pre-approval and post-approval control, with increased flexibility in approving new developments and innovations due to the increased control later in the process.

**2.2.** Some LRAG members recommended that amendments to the Act should:

- Introduce a duty for HFEA to support innovation.
- Support HFEA's powers to offer regulatory 'sandbox' model for appropriate new technologies or treatments.
- Involve external expert body views in the assessment and monitoring process, where merited.
- Protect via HFEA licencing, research participants in research studies involving their own fresh sperm. These are currently unregulated by HFEA or HTA as one in every 50 participating men could learn that they are azoospermic, for example, regulatory oversight could require that appropriate information and support.

**2.3.** LRAG members noted that:

- 'Sandbox' models tend to be tailored to each application and require individual oversight which would create greater resource demands on the Executive than the present system.
- The participation of patients in what can amount to research, but where payment is required for them to participate, is concerning. Paying to have unproven medical treatments is unusual outside of the fertility sector. To increase patient protection, LRAG members felt that it may be beneficial for HFEA in some cases to impose licence conditions stating that participants in innovative treatment that is effectively research, should not be required to pay. These areas will require careful definition and HFEA powers to require this, which may need to be explicitly provided for in the Act.

**2.4.** The Chief Executive asked whether the Act should be amended to offer principles for HFEA about supporting responsible innovation and authorising novel processes in the UK. Currently HFEA interpret this area from the requirements of the **2004 European Tissues and Cells Directive**. LRAG members noted that EU Exit had already removed congruence with Europe in future, as any new or updated Tissues and Cell Directives will not be built into UK law.

## 3. Artificial Intelligence

**3.1.** The Chief Executive highlighted that the paper did not present concrete proposals about the rapid development of AI. The aim rather was to note different ways in which AI is being used in several fertility treatment processes in the UK. Across all heath sectors, regulatory responses and statutory responsibilities are still emerging, with a relevant government White Paper expected soon, meaning that there will be some common approaches to consider across health sectors.

**3.2.** LRAG members agreed that regulating AI is possibly beyond the remit of the Act and the HFEA in isolation. They recommended that HFEA reach out to the Ada Lovelace Institute who are working around AI governance in the health sector. It was agreed that any key work or findings from the HFEA's AI Working Group should be shared with LRAG.

## 4. The 14-day limit

**4.1.** The Chief Executive began by thanking the Medical Research Council and the Francis Crick Institute for their time and insights relating to the 14-day limit. They noted that, to a large extent, the 14-day limit has stood the test of time very well but as research progresses, and it is now possible to keep an embryo in vitro for longer than 14 days, it is important to consider the case for extension.

**4.2.** LRAG members raised that:

- The 14-day limit first proposed in the Warnock Report had gathered support for multiple reasons: ethically, in that the 14 day limit considered the moral value of the embryo; politically, as it was considered any further limit may not have passed through Parliament; scientifically, at the time 14-days appeared sufficient for research benefits, as it was not possible to keep an embryo alive beyond 14-days nor to accurately mimic in-vivo development via embryo models.

- One member of LRAG discussed the recent proposals of the **International Society for Stem Cell Research (ISSCR) guidelines** to remove the 14-day limit and replace with strict case-by-case oversight of any research past 14-days where justified, as laid out in the guidelines and after extensive public engagement.
- Some members expressed disagreement with extending the 14-day limit, partly because they felt it was still an appropriate ethical limit, partly bearing in mind how some patients regard their stored embryos, and partly because they felt that the public push back to any proposed extension beyond 14 days could be significant.
- Other members agreed that either an extension to 21 or 28 days may be appropriate in the interests of increasing scientific knowledge and, in time, improving clinical options. There is a window of very early pregnancy between 14 and 28 days of embryo development which is not well researched by any other route. Researching embryo development beyond 14 days could for example, improve understanding around very early pregnancy loss where the cause lies with the embryo. Scientific benefits could include enabling more detailed research into new fertility treatments or possibilities to avoid passing on genetic disorders. These could include around mitochondrial donation, in-vitro derived gametes, and genome editing. Other areas for basic research would include around better understanding of cell differentiation, gastrulation, and the appearance of primordial germ cells.
- For those that supported it, in principle an extension would only be acceptable where there were strict regulatory conditions placed, no alternative research model was available, and where there was a reasonable degree of public acceptance of the work going ahead, justified by high quality public dialogue. The meeting heard that scientists in the field were hopeful that the UK might take the first step given its reputation for public dialogue and the excellence of its regulatory regime.

## 5. In vitro-derived gametes, embryo-like entities, and stem cell based embryo models

**5.1.** The Chief Executive highlighted the development of these new entities, and the similar issues raised by their regulation. None are currently regulated, and some scientists are now of the view that regulating these entities may enable further innovation through the public trust that might flow from such oversight.

**5.2.** LRAG members concurred that the speed at which developments are taking place in this field requires assessment, and that regulation of at least some of these entities within the future Act should be considered.

It was noted that a key goal of the Warnock report was to ensure that the resulting Act would facilitate and enable science. Regulating these entities will increase public confidence. A member argued that an absence of regulation is bad for science, as it is difficult to proceed without public confidence. A balance between regulatory rules and innovation would need to be found, and any amendments will need to focus on the principles and outcomes to be controlled rather than the specific method or process used to develop these entities.

## 6. Use of human embryos in research: 'alternative' models

**6.1.** At present, the Act states that embryo research can only take place where it is both 'necessary' and 'desirable' to use human embryos.

**6.2.** LRAG members were broadly in favour that any future Act should consider removing the term 'necessary' and only require that it be 'desirable'.

## 7. Embryo selection based on Polygenic risk scores

**7.1.** The Chief Executive set out the permitted reasons for PGT-P testing of embryos for use in reproduction and discussed the use of polygenic risk scoring in clinical embryology in other countries.

**7.2.** LRAG members raised that:

- The testing regulations set out in the 2008 Act amendments are unable to adapt to new forms of testing embryos.
- The use of probability and risk calculations in genetic conditions with complex causes is difficult, as is determining the likely outcome of the interaction of genes and environment. The current lack of understanding of polygenic embryo testing and selection as a tool to reduce clinical risk means that fertility patients could be presented with unevidenced claims of clinical risk or of clinical benefit to a future child.
- There were concerns raised regarding the use of these tests, and that any permitted uses in future would require specific reasons for why this testing would be appropriate.

## 8. Germline genome editing

**8.1.** The Chief Executive set out the prohibition of nuclear germline genome editing set out in the Act and presented the options for change.

**8.2.** LRAG members raised that:

- Germline genome editing raises new ethical questions which may require reflection in a future Act.
- There is the possibility of future clinical benefit in strictly defined areas: if germline genome editing techniques could be used alongside mitochondrial replacement therapies in order to eliminate any carry over of mutated mitochondrial DNA, for example.
- The Act does not properly set out restrictions relating to the possible application of epigenetic germline genome editing, which will require consideration as research interest in this area is growing.