LICENSING TERMS AND CONDITIONS ON

ASSISTED REPRODUCTION SERVICES

IMPOSED UNDER SECTION 6(5) OF THE PRIVATE HOSPITALS AND MEDICAL CLINCIS ACT (CAP 248)

1. APPLICATION

1.1 These licensing terms and conditions apply to licensees of private hospitals and medical clinics providing assisted reproduction (AR) services ("licensees") and are imposed under section 6(5) of the Private Hospitals and Medical Clinics ("PHMC") Act (Cap. 248), with immediate effect, save in relation to:

(a) paragraphs 5.4, 5.6(b), 5.7(e), 5.10, 5.13(c), 5.14(c), 5.15, 5.26, 5.27, 5.38, 5.43, 5.44, 8.2, 9.4, 9.8, 9.10, 9.11,10.1 and 10.3, which shall come into effect on 1 June 2011; and

(b) paragraphs 3.5, 4.2(b), 5.3, 5.30 which shall come into effect on 24 October 2011.

1.2 Insofar as the paragraphs referred to in the first column of the Schedule are concerned, the Ministry of Health's *Directives for Private Healthcare Institutions Providing Assisted Reproduction Services* (March 2006) as set out in the second column of the Schedule shall apply until 1 June 2011 or 24 October 2011 as specified in the third column of the Schedule.

1.3 These licensing terms and conditions set out the requirements for the provision of AR services, which is a specialised procedure or service in private hospitals listed in the Second Schedule of the PHMC Regulations and a special care service in medical clinics listed in the Third Schedule of the PHMC Regulations. Licensees are required to obtain prior approval from the Director of Medical Services under regulation 18 or regulation 37 of the PHMC Regulations as the case may be before commencing this specialised procedure/service or special care service.

1.4 Approval may be granted subject to compliance with these licensing terms and conditions as assessed by:

(a) the Ministry of Health; and/or
(b) a certifying body approved by the Ministry.

1.5 Save as set out in the Schedule hereto and without prejudice to paragraph 1.2 above, these licensing terms and conditions shall supersede the requirements set out in all previous directives and licensing terms and conditions issued to AR Centres in relation to AR services including the Ministry of Health's *Directives for Private Healthcare Institutions Providing Assisted Reproduction Services* (March 2006) *and the Licensing Terms and Conditions on Assisted Reproduction Services* issued on 4 November 2010.

1.6 A breach of these licensing terms and conditions may attract potential consequences under the PHMC Act, including but not limited to:

(a) Suspension or revocation of the approval to provide AR services;
(b) Suspension or revocation of hospital licence or medical clinic licence; and/or
(c) Prosecution.

2. DEFINITIONS

2.1 *Assisted Reproduction Centres ("**AR Centres**")* in these licensing terms and conditions refer to all licensed private hospitals and medical clinics which have been authorised by the Director of Medical Services to provide AR services.

2.2 For the purposes of these licensing terms and conditions, Assisted Reproduction ("***AR***") involves clinical treatments and laboratory procedures that include:

(a) the removal or attempted removal of oocytes from a woman for any purpose; and

(b) the handling of human oocytes or embryos for the purpose of procreation.

This includes In-vitro Fertilisation (IVF); Gamete Intrafallopian Transfer (GIFT); Zygote Intrafallopian Transfer (ZIFT); Intra-cytoplasmic Sperm Injection (ICSI); gamete/embryo/ovarian tissue cryopreservation; gamete/embryo donation (for any purpose); and embryo biopsy for Preimplantation Genetic Diagnosis (PGD).

However AR does not include the surgical excision of ovarian tissue.

Notwithstanding the above, AR Centres may collect, process, analyse or inseminate sperm or seminal fluid in accordance with the requirements of these licensing terms and conditions and such other licensing terms and conditions as may from time to time be issued by the Director.

2.3 An ***embryology laboratory*** is defined as an establishment which performs any or all of, but not limited to the following:

(a) Culture medium preparation and quality control testing;
(b) Examination of follicular aspirates with oocyte identification;
(c) Oocyte quality and maturing grading;
(d) Sperm preparation: semen collection and analysis, sperm washing and capacitation;
(e) Insemination of oocytes;
(f) Determination of fertilisation and embryo quality evaluation;
(g) Embryo culture and embryo grading;
(h) Embryo transfer (either uterine or tubal);
(i) Embryo/ sperm cryopreservation; and/or
(j) Micromanipulation of human oocytes and/or embryos.

3. FACILITIES

3.1 AR Centres shall make provisions for high-risk pregnancies conceived through AR to be delivered and clinically managed in a hospital with Level 3 neonatal intensive care facilities.

3.2 AR Centres shall have an embryology laboratory equipped to support the AR procedures, including but not limited to the following:

(a) In-vitro fertilisation (IVF);
(b) Intra-cytoplasmic Sperm Injection (ICSI); and
(c) Gamete Intrafallopian Transfer (GIFT) programmes.

3.3 AR Centres and its facilities including embryology laboratory shall have adequate space to accommodate all personnel, fittings and equipment and to allow procedures and movements to be carried out in safety and comfort.

3.4 AR Centres shall provide all patients and donors privacy, dignity and respect in order to allow consultation and counselling to be conducted discreetly and confidentially.

3.5 AR Centres shall ensure that procedures involving manipulation of gametes/embryos are performed in a controlled environment with appropriate air quality, in order not to compromise the quality and safety of the AR processes. The air quality in the critical work area should be at least Grade C and at least Grade D in the background environment.[1]

3.6 AR Centres shall be equipped with backup and emergency facilities, e.g. lighting, power, water and alarm systems, that are:

(a) appropriate to the level of risk involved in the type of procedure, either clinical or laboratory, being performed in the AR Centre; and

(b) adequate, functional and effective to cope with the types of emergencies known to occur in AR.

3.7 AR Centres shall ensure that:

(a) the embryology laboratory shall be located in a low-traffic, secure and convenient location with respect to the physical room for performing AR procedures; and

(b) "wet area" work (i.e. media preparation, equipment, sterilisation etc.) shall not be performed in a manner

[1] EU Guidelines to Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use http://ec.europa.eu/health/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf

that may adversely affect the handling, manipulation and/or quality of oocytes, embryos and sperm; and

(c) access to the embryology laboratory shall be restricted to persons who are authorised by the Director of the AR Centre.

4. PERSONNEL

4.1 The AR Centre shall permit only medical practitioners and embryologists, all of whom must be authorised by the Director of Medical Services to perform clinical and laboratory work in AR respectively in the AR Centre, save that unauthorised medical practitioners and embryologists may perform such work under the supervision of an authorised medical practitioner or embryologist, as the case may be.

4.2 The AR Centre shall have a sufficient number of staff including authorised medical practitioners and authorised embryologists) commensurate with its workload e.g. number of cycles performed, to provide an adequate standard of care to patients. At the minimum, there shall be at least:

(a) one authorised medical practitioner; and
(b) two authorised embryologists;

working at the AR Centre.

4.3 The AR centre shall maintain formal documentation clearly defining organizational reporting relationships, responsibilities and accountability of its staff.

4.4 The AR centre shall establish policy and procedures which ensure that all staff have:

(a) basic training and updated training in their respective areas;
(b) regular and continuous competence assessment, with audits of this assessment; and
(c) an annual joint appraisal with their supervisor.

4.5 The AR Centre shall maintain updated staff records, which shall include:

(a) job description;
(b) terms and conditions of employment;
(c) a record of staff induction and orientation;
(d) a record of health and safety training;
(e) a record of education and training, including continuing professional development;
(f) relevant educational and professional qualifications;
(g) certificate of registration, if relevant;
(h) absence record;
(i) accident record;
(j) a record of annual joint appraisal;
(k) occupational health record; and
(l) a record of any disciplinary action.

Credentialing

Director of AR Centre

4.6 The Director of the AR Centre:

(a) shall be an authorized medical practitioner with:

(i) at least 5 years of experience as an authorized AR practitioner in an AR Centre and who has independently performed at least 200 AR treatment cycles; or

(ii) at least 3 years of experience as an authorized AR practitioner in an AR Centre and who has independently performed at least 250 AR treatment cycles before the appointment as the Director of the AR Centre; and

(b) shall have practiced AR i.e. performed AR treatment cycles continuously in an AR Centre in the three years prior to the date of appointment as Director of the AR Centre.

Authorised Medical Practitioner

4.7 Doctors who wish to be considered for authorisation to perform AR shall satisfy the following criteria:

(a) be accredited by the Specialists Accreditation Board and registered as a specialist in Obstetrics and Gynaecology with the Singapore Medical Council Register of Specialists;

(b) be credentialed or have met the "Academy of Medicine Guidelines for credentialing to perform L2 laparoscopy;

(c) have at least 18 months' training in an AR Centre which shall include:

(i) reproductive endocrinology, particularly in the use of ovulation-inducing agents and hormonal control of the menstrual cycle;
(ii) ultrasound-guided oocyte retrieval techniques;
(iii) gynaecological endoscopy; and
(iv) gamete/ embryo transfer;

(d) have at least 6 months' practical hands-on experience in AR under the supervision of an authorised medical practitioner;

(e) have satisfactorily performed a minimum of 20 oocyte retrieval procedure and embryo transfers under direct supervision of an authorised medical practitioner; and

(f) have attended at least one course/ seminar on AR.

Authorised Embryologist

4.8 Embryologists who wish to be considered for authorisation to perform AR procedures shall satisfy the following criteria:

(a) hold a degree (i.e. at least Bachelor of Science) or equivalent;
(b) have at least 6 months' practical hands-on experience in carrying out AR procedures[2] under supervision;

[2] For purposes of paragraph 4.8, 'procedure' is defined as a combination of examination of follicular aspirates, oocyte classification, sperm preparation, oocyte insemination (including Intra-cytoplasmic Sperm Injection), documentation of fertilisation and preparation of embryos for transfer.

(c) have satisfactorily performed a minimum of 50 AR procedures under direct supervision of an authorised embryologist; and

(d) attended at least one course/ seminar on AR.

Responsibilities of the Director of the AR Centre

4.9 The Director of the AR Centre shall ensure that only authorised personnel carry out AR activities independently at the AR Centre.

4.10 The Director of the AR Centre shall be responsible for overseeing the care of patients at the AR Centre as well as the overall operation of the AR Centre, including the embryology laboratory.

4.11 Without limiting the generality of paragraphs 4.9 and 4.10 above, the Director of the AR Centre shall ensure that:

(a) Adequate processes are in place to ensure all AR procedures are carried out by an authorised medical practitioner, authorised embryologist or other qualified person who has adequate qualifications, training and experience in such procedures;

(b) the AR Centre is provided with adequate and appropriate equipment for the AR service to be carried out accurately and safely, and adequate processes are in place to ensure that the equipment is operated by suitably trained person or persons;

(c) proper arrangements are in place at the AR Centre for keeping and disposing all genetic material, including gametes and embryos;

(d) adequate processes are in place to ensure that AR activities are carried out in accordance with international best practices;

(e) the authorised medical practitioners and authorised embryologists practising in the AR Centre are competent to perform AR procedures;

(f) the submission of information through the "real-time database on assisted reproduction" system to the Ministry of Health is done in a timely and accurate manner;

(g) all staff (including authorised medical practitioners and authorised embryologists) take part in continuing professional education activities specifically on AR;

(h) all staff are aware of and understand relevant legislation, regulations, licensing terms and conditions and directives;

(i) all staff preserve the privacy and confidentiality of all patient information; and

(j) adequate processes are in place to acknowledge and follow up on complaints and feedback received from patients and stakeholders.

4.12 The responsibilities of the Director of the AR Centre in paragraphs 4.9 – 4.11 above are non-delegable.

5. CLINICAL PRACTICE

General

5.1 AR Centres shall carry out IVF and related AR procedures only when there are sufficient indications for the procedure, namely:

(a) Tubal disease and/ or obstruction;
(b) Endometriosis – failed alternative approaches to treatment;
(c) Male factor;
(d) Idiopathic subfertility – no cause to be found after full investigation, at least 3 years of marriage, and having completed alternative approaches to fertility management for at least 1 year (however, this will not apply to women above 35 year of age);
(e) Premature ovarian failure; and
(f) Other conditions acceptable to the local medical obstetric/ gynaecologic community.

5.2 Where IVF or other AR[3] procedures are carried out for procreation, AR Centres shall carry out such procedures only on a married[4] woman and only with the consent of her husband (in accordance with the requirements at paragraphs 5.8 to 5.10 below), whether or not her husband's semen is used. The AR Centre shall ensure that informed consent for IVF or other AR procedure is obtained from the patient's husband and that documentary proof of her married status (e.g. the marriage certificate) is produced and a copy retained by the AR Centre.

The above paragraph shall not apply to the storage of oocytes under paragraph 5.35 below i.e. where the storage of oocytes is medically indicated or for research.

5.3 When sperm or seminal fluid purporting to be from the husband is received at AR Centres, AR Centres shall:

(a) require the husband to attend at the AR Centre in person;
(b) verify the identity of the husband and obtain from him a signed written declaration confirming that the sperm specimen is his own; and
(c) document the date and time of the attendance.

Acceptance into an AR Programme

5.4 The AR Centre shall not carry out IVF (including ICSI) unless insurance for neonatal care has been purchased by the couple, where:

(a) either the husband or wife, or both of them, are Singaporeans or Singapore Permanent Residents; or

(b) in the case of foreign patients, the couple intends to deliver in Singapore.

5.5 AR Centres shall not accept women aged 45 and above into an AR programme. The authorised medical practitioner may however submit an appeal to the Director of Medical Services to carry out AR procedures on a woman aged 45 and above if:

[3] As described in paragraph 2.2 above.
[4] For the purpose of these licensing terms and conditions, "married" means heterosexual marriage i.e. marriage between a biological male adult and a biological female adult.

(a) the authorised medical practitioner has considered all relevant circumstances, including the woman's health and the risk of complications, and in his professional judgment, is of the view that AR procedures may be carried out safely on that woman; and

(b) without prejudice to the requirements in paragraph 5.6 below, the authorised medical practitioner has counselled the couple comprehensively in relation to the success rates and risks involved with a pregnancy at the woman's age, as well as the potential impact on the welfare of the child.

5.6 Any appeal submitted to the Director of Medical Services for acceptance into an AR programme (women 45 years and above) shall be accompanied by a copy of the couple's written consent confirming that they have been counselled on:

(a) the risks of AR procedures and pregnancy at her age; and
(b) the prevailing AR success rate for women at her age at the specific AR Centre.

Counselling and Consent

5.7 AR Centres shall not carry out IVF or related AR procedures unless the woman and her husband have been adequately counselled and informed of all relevant and material information, including but not limited to the following:

(a) the possible consequences of the procedure, including the possibility of ovarian hyperstimulation syndrome, multiple births and the medical, social, financial and other consequences of such births, and the couple have given their explicit written consent to the procedure after such information has been explained to them;

(b) the lower chances of success with AR procedures for women above 40 years old, and the higher risk of complications;

(c) the increased risk of genetic anomalies in the foetus e.g. Down's Syndrome, for patients above 35 years old at her estimated date of delivery; and

(d) on or before admittance into the AR programme, the estimated total charges per type of treatment cycle which are likely to be incurred in respect of treatment; and

(e) on or before admittance into the AR programme the requirement of compulsory insurance for neonatal care (applicable only if either the husband or wife, or both of them, are Singaporeans or Singapore Permanent Residents or if they are foreign patients, the couple intends to deliver in Singapore).

5.8 AR Centres shall obtain an acknowledgment from the couple, in writing, of the counselling provided and consent obtained in paragraph 5.7 above, and shall keep all information obtained during counselling strictly confidential. AR Centres shall ensure that written records of the counselling are kept in a secure place.

5.9 AR Centres shall ensure that prior written consent from the woman and her husband, which shall be witnessed, is obtained for AR services.

Such consent shall include consent for carrying out all key procedures and processes, including but not limited to:

(a) the examination and treatment procedures;
(b) the number of embryos to be transferred;
(c) the storage/ disposal/ transfer of gametes/embryos; and
(d) any intended donation of gametes/embryos.

5.10 In the event the woman and her husband intend to donate gametes/embryos, the couple shall be given sufficient time of at least 1 week to reflect on their decision before consent is obtained.

5.11 AR Centres shall keep a copy of the signed consent and shall also make a copy available to the couple. The signed consent form shall contain the names, signatures and identification numbers such as NRIC/ FIN/passport number/ MCR number of the couple/ patient, doctor and witness.

5.12 AR Centres are required to obtain a fresh consent, in writing, from the couple before a procedure if the interval between the earlier consent and the date of the procedure is more than 3 months.

Screening Tests

5.13 AR Centres shall ensure that all persons undergoing AR procedures, including those who are donating sperm, oocytes or embryos, are screened for:

(a) Human Immunodeficiency Virus (HIV) antibody;
(b) hepatitis B antigen;
(c) hepatitis C virus antibody;
(d) syphilis; and
(e) rubella antibody;

Tests for other transmissible diseases shall also be carried out when necessary by the AR Centres.

5.14 AR Centres shall ensure that all blood tests on patients for:

(a) HIV antibody;
(b) hepatitis B antigen;
(c) hepatitis C virus antibody;
(d) syphilis;
(e) rubella antibody; and
(f) any other tests;

are carried out in Singapore before the AR procedures are carried out. Foreigners who have these tests carried out in another country shall have them repeated in Singapore.

5.15 AR Centres shall screen all donors for Cytomegalovirus (CMV).

5.16 AR Centres may screen for Thalassaemia if the woman and/or her husband are at risk of Thalassaemia. AR Centres shall counsel all couples who test positive on the risk and consequences of having a child with Thalassaemia before IVF or related AR procedures are carried out.

Rubella

5.17 AR Centres shall not carry out IVF or related AR procedures unless the woman and her husband have been adequately counselled and informed of the risks to the foetus if a patient with negative rubella antibody contracts a rubella infection during pregnancy. The couple shall also be counselled on the need for rubella immunisation 1 month prior to conception if the woman has tested negative for rubella antibody.

HIV

5.18 AR Centres shall:

(a) ensure that all persons undergoing AR procedures who have tested negative for HIV shall be screened at least every six months while still on the AR programme; and

(b) ensure that donors of gametes and/or embryos are tested for HIV antibody at the time of donation and must remain HIV antibody negative, with the second HIV test done not earlier than 6 months from the time of donation, before the donor gametes/embryos can be used. If the donated gametes/ embryos have to be used before the second test, the AR Centre must inform the couple of the risks of infection and consent has to be taken.

5.19 AR Centres shall separately store all gametes/embryos from patients whose screening results are:

(a) positive;
(b) negative; and
(c) who are unscreened including those awaiting the results of screening;

in order to minimise the risk of cross contamination.

Maximum Number of Treatment Cycles

5.20 AR Centres shall ensure that for women of or below 40 years of age who enter an AR programme, a maximum of 10 stimulated and/or natural cycles reaching the stage of embryo transfer only is permitted. AR Centres shall strongly discourage women from continuing the AR programme after undergoing 5 cycles without achieving a pregnancy. For the avoidance of doubt, these 10

stimulated and/or natural cycles refer to consecutive cycles in a nulliparous woman or following a live birth and these cycles include those performed in one or more local / overseas AR Centres.

5.21 AR Centres shall ensure that for women above 40 years of age who enter an AR programme:

(a) A maximum of 5 stimulated and/or natural cycles reaching the stage of embryo transfer only is permitted; and

(b) Treatment must be stopped when the woman turns 45 years of age, irrespective of whether she has completed the 5 cycles, unless approved by the Director of Medical Services on an appeal under paragraph 5.5 above.

5.22 For the avoidance of doubt and subject to these licensing terms and conditions, there is no limit to the number of thawed cycles that may be carried out for any woman on an AR programme.

Ovarian Hyperstimulation Syndrome (OHSS)

5.23 AR Centres shall implement policies and procedures to minimise the incidence of ovarian hyperstimulation syndrome (OHSS) including policy and procedures:

(a) to identify and manage patients at risk of or experiencing OHSS;

(b) to monitor the incidence of OHSS in the AR Centre; and

(c) to document the efforts taken to minimise the incidence of OHSS.

Gametes and Embryo Donation

5.24 AR Centres may carry out IVF procedures and related AR procedures using donated oocytes, sperm or embryos.

5.25 AR Centres shall ensure that wherever possible, a genetic link to one of the parents of the intended child is maintained. Where it is not possible to maintain a genetic link to at least one of the intended parents, the AR Centre may permit embryo adoption (i.e. implantation of an embryo conceived through a donated oocyte and donated sperm) provided written consent of the couple donating the embryo is obtained.

5.26 AR Centres shall ensure that the sperm of the recipient woman's husband shall not be used for fertilisation of oocytes donated by any person who is kindred of, or has affinity to, the recipient woman's husband within any of the prohibited degrees of relationship as specified under the First Schedule of the Women's Charter (Chapter 353). Similarly, AR Centres shall ensure that no woman is allowed to have any oocytes or embryo transferred into her which have been donated by any such person, if her husband's sperm is used.

5.27 AR Centres shall ensure that no woman uses sperm donated by any person who is kindred of, or has affinity to, the recipient woman within any of the prohibited degrees of relationship as specified under the First Schedule of the Women's Charter (Chapter 353) for the fertilization of her oocytes.

5.28 AR Centres shall ensure that only oocytes donated by women between 18 to 35 years old are used for IVF and related AR procedures.

5.29 AR Centres shall ensure that where a donor of gametes or embryos has, as a result of such donations, achieved 3 live-birth[5] events, the donor's gametes or embryos shall not be used on a subsequent occasion. The limit of 3 live-birth events may be exceeded only in exceptional cases where the recipient wishes to have a subsequent child from the same donor.

Oocytes/Embryos Replaced

5.30 AR Centres shall ensure that no more than 2 oocytes/embryos are transferred to the patient's body at any one time. However, AR Centres may transfer up to a maximum of 3

[5] A 'live-birth event' is the birth of a live child or children. This means that the birth of twins or triplets is considered a single 'live-birth event'

oocytes/ cleavage stage embryos if all the following conditions are satisfied:

(a) all children conceived as a result of the procedure will be delivered and cared for in a hospital which has Level 3 neonatal intensive care facilities;

(b) the patient is at least 37 years of age; and

(c) the patient has undergone not less than 1 previous stimulated AR cycle which was unsuccessful or there is no good quality embryo available.

5.31 AR Centres shall monitor regularly and at least annually multiple pregnancy rates and implement corrective actions to reduce the incidence of multiple pregnancies in all treatment cycles.

Combined AR Procedures

5.32 AR Centres shall not carry out combined AR procedures of GIFT and IVF-ET or GIFT and ICSI-ET within the same cycle for any patient.

Embryo and Fetal Sexing

5.33 AR Centres shall not conduct embryo and fetal sexing unless with the prior written approval of the Director of Medical Services. The Director of Medical Services will consider each request from the AR Centres on a case-by-case basis. The request for approval shall include confirmation of the following by the AR Centre

(a) Carrier status of the biological mother; and
(b) Counselling of the couple on the courses of action available.

Storage/Disposal/Transfer of Gametes/Embryos

5.34 Prior to the commencement of an AR procedure, the AR Centre shall inform every couple, whose embryos are to be stored, of the maximum permitted period for storage and use under paragraph 5.39 below, and shall seek written instructions from them regarding their future plans for the gametes/ embryos, including:

(a) the maximum period of storage of gametes/embryos;

(b) provisions for use or disposal of gametes/embryos in the event of a separation of the couple (e.g. premature death or divorce of a partner) or if the couple is not contactable after reasonable efforts by the AR Centre; and

(c) the preferred method for use or disposal of gametes/embryos in the event that one or both partners become incapable of varying or revoking his/her consent.

AR Centres shall ensure that the storage and disposal of gametes/embryos shall be carried out strictly in accordance with the written instructions of the couple.

5.35 AR Centres shall only store gametes and embryos where such storage is medically indicated or which have been donated for research.

5.36 If no clear instructions regarding the disposal of the gametes/embryos were obtained from the couple whose gametes/embryos were stored and the couple cannot be traced, AR Centres shall seek the advice of an independent 3rd party e.g. Hospital Ethics Committee for follow-up actions and shall inform the Director of Medical Services of all actions or measures that have been taken.

5.37 AR Centres shall separately store all such gametes/embryos as provided for under paragraphs 5.35 and 5.36 above.

5.38 AR Centres shall ensure that the termination of the development of gametes/embryos and the disposal of any remaining material is handled ethically and sensitively.

5.39 AR Centres shall ensure that embryos are not stored beyond 10 years from the date of their fertilisation, unless consent had been obtained from the couple for their storage for a purpose other than for treatment. Under no circumstances whatsoever shall AR Centres use embryos for treatment where more than 10 years have elapsed from the date of their fertilisation.

5.40 The AR Centres shall have a proper inventory system on gametes/ embryos stored for each patient.

5.41 AR Centres shall perform an inventory check at least once every two years on stored gametes/embryos which shall include:

(a) Reviewing the purpose and duration of storage; and
(b) Identifying and implementing any follow-up action needed to comply with these licensing terms and conditions

5.42 AR Centres may carry out centre-to-centre transfers of gametes/embryos between local AR Centres and between local and overseas AR Centres.

5.43 In the case of importation of gametes, the authorised medical practitioner of the AR Centre shall :

(a) ascertain that the overseas bank, and the handling of the import comply with the standards set out in these licensing terms and conditions in relation to collection, processing, storage, transport, and consent-taking of gametes/embryos; and

(b) ensure that the couple is counselled on the risks of using imported gametes/embryos from overseas banks.

5.44 AR Centres shall ensure that gametes and embryos are packaged and transported in a manner that minimises the risk of contamination and maintains their required characteristics and biological functions. AR Centres shall ensure that an instruction sheet accompanies all gametes/ embryos transported/transferred. The instruction sheet shall contain the following information:

(a) The appropriate storage condition prior usage;

(b) Information regarding any special care required by the recipient AR Centre for the safe and most effective use of the gametes/embryos; and

(c) Actions to be taken if there is evidence of breakage, mislabelling, etc.

AR Centres shall keep tracking sheets of all movements of gametes/embryos, as well as signed receipts at every receiving point/centre.

5.45 The receiving AR Centre shall ensure that written consent has been given by the couple for the use and storage of any gametes or embryos from them that are transferred to its AR Centre. This includes consent for the creation of embryos in-vitro using donor gametes.

5.46 The AR Centre shall ensure that the quality and security of genetic material are maintained at all times whilst the material is in the AR Centre.

Others

5.47 AR centres shall seek the approval of the Director of Medical Services before providing pre-implantation genetic testing/screening services or other new AR-related services.

5.48 AR Centres shall **not** carry out any of the following activities:

(a) The buying and selling of embryos, oocytes and sperm;

(b) Surrogacy (surrogacy is where a woman is artificially impregnated, whether for monetary consideration or not, with the intention that the child is to be given and adopted by some other person or couple);

(c) Selective fetal reduction;

(d) Sperm sorting techniques in sex selection; and

(e) Placing a human embryo in the uterus of another species for gestation under any circumstances. Similarly no other gametes/embryos except human gametes/embryo shall be placed in a woman.

6. LABORATORY PRACTICES

6.1 AR Centres shall ensure that procedure manuals detailing all aspects of AR and related procedures shall be available in each laboratory. These manuals shall describe the laboratory procedures in detail. AR Centres shall review and validate these procedure manuals at least annually.

6.2 AR Centres shall apply the same standards to sperm preparation and processing for IUI as for IVF from the point of collection to the point of despatch.

6.3 AR Centres may only process semen that is to be used for IVF or IUI and for no other purpose. AR Centres shall not carry out any sperm/semen analysis except in the course of IVF treatment which has commenced. As a good practice AR Centres should (where possible) ensure that sperm preparation and processing for IUI is performed in a place separate from where the sperm processing for IVF is performed, e.g. in an andrology laboratory.

6.4 AR Centres shall ensure that the laboratory shall have an appropriate labelling system to ensure identification and traceability of gametes/embryos from their collection to storage, transfer, freezing, thawing and disposal.

6.5 AR Centres shall ensure that every specimen must be labelled clearly with the full name of the patient and a unique identifier. This also applies to all test tubes, pipettes and other apparatus that are in contact with any of the specimens. If donor sperm is used, AR Centres shall ensure that all labels accurately reflect the full identification number assigned to the donor.

6.6 AR Centres shall ensure that traceability procedures shall cover any materials or equipment that could affect the quality or safety of gametes and embryos, e.g. culture media, serial numbers of equipment and materials coming into contact with gametes and embryos, and records of the monitoring and maintenance of the temperature, CO2 and liquid nitrogen in incubators and storage tanks.

6.7 AR Centres shall have witnessing protocols in place to counter check the identification of specimens and the patients or donors at all critical points of the clinical and laboratory procedures. These checks must be completed and documented at the time the relevant clinical or laboratory procedure takes place.

6.8 AR Centres shall assign the most appropriate staff to counter-check and counter-sign clinical and laboratory procedures.

6.9 AR Centres shall adopt the following procedures requiring validation of identification of the patient/specimen by double signing:

Sperm collection

(a) when sperm is collected from the husband (the husband shall also be asked to confirm and provide written acknowledgment that the specimen is his own);

Sperm preparation

(b) when the sperm from the sperm pot is transferred to the washing tube;
(c) after recovery of the swim-up;
(d) when sperm is transferred to the final sperm tube;

Oocyte Retrieval

(e) before patient undergoes oocyte retrieval;
(f) when oocytes are transferred into the wash dish during oocyte retrieval;
(g) when all the oocytes are finally transferred to the culture dish after oocyte retrieval;

Insemination (IVF and ICSI)

(h) before commencing an insemination (both containers containing oocytes and sperm shall be checked. For ICSI, the dish containing the fertilisation drops shall also be checked);
(i) when the oocytes are transferred to the culture dish for overnight culture soon after ICSI;

Fertilisation Checks

(j) before commencing transfer of fertilised oocytes (the dish to which fertilised oocytes are transferred shall be checked);
(k) before commencing the changing of culture medium for extended embryo culture on day 3 and day 5 (the dish to which the embryos are transferred shall also be checked);

Embryo Transfer (ET)

(l) before patient undergoes embryo transfer;
(m) before commencing transfer of embryo from culture dish to ET dish;
(n) before loading into the ET catheter from the ET dish;

Cryopreservation of Embryos/Gametes

(o) the tubes and dishes from where the gametes/embryos are transferred from;
(p) straw/cryo vial labelling;
(q) after freezing and when the straws/cryo vials are transferred to the liquid nitrogen tank;

Embryo thawing

(r) when removing the straws from the liquid nitrogen tank;
(s) labelling of thawed dish or tubes;
(t) when performing thawing of embryos ;
(u) after thawing, when the thawed embryos are transferred to the culture dish;

Discarding of gametes/embryos

(v) before discarding (storage containers shall be checked); and

Transporting gametes/embryos

(w) before transfer (storage containers shall be checked).

6.10 AR Centres shall ensure that a specimen (whether sperm, oocyte or embryo) from a single patient only is processed at any one time at every stage of processing. The only exception to this condition would be when performing IVF or ICSI where the

specimen belongs to the couple (which includes donor if applicable) for whom the procedure is undertaken.

6.11 AR Centres shall ensure that the processing cabinet/workstation (e.g. laminar flow cabinet) shall accommodate the specimen from only a single patient at any one time during processing, subject to the exception in paragraph 6.10 above.

6.12 AR Centres shall ensure that any interruption or distraction in the laboratory (e.g. phones, external noises) are minimised especially while embryologists or technicians are performing procedures.

6.13 AR Centres shall ensure that maintenance manuals for all laboratory equipment are available in the laboratory. These manuals shall include the regular maintenance to be performed on each piece of equipment, records of maintenance completed and corrective actions taken, if any, etc.

6.14 AR Centres shall ensure that all embryology laboratories, equipment and facilities are checked and maintained and are in good working order at all times. A record of such checks shall be available for inspection at any time. AR Centres shall ensure that procedures are carried out using equipment and facilities designated for the purpose and maintained to suit their intended purpose.

6.15 Where equipment or facilities affect critical processing or storage parameters (eg, temperature, CO2 pressure, particle counts, microbial contamination levels), AR Centres shall identify and monitor the same to ensure that the critical parameters are maintained within acceptable limits at all times.

6.16 AR Centres shall ensure that all equipment used for critical measurement are calibrated against a traceable standard if available.

6.17 AR Centres shall ensure that all laboratory chemical and reagents are labelled to indicate date received, date opened, and shelf life, where applicable.

6.18 AR Centres shall ensure that procedures and policies on laboratory safety are available to all laboratory personnel, and are reviewed annually by the AR Centre. AR Centres shall ensure that laboratory personnel comply with prevailing guidelines for laboratories and guidelines on infection control in Singapore.

6.19 AR Centres shall ensure that only disposable consumables are used when processing the patient's specimen.

6.20 AR Centres shall ensure that non-touch aseptic techniques are used at all times including when transferring sperm into the ICSI dish, i.e. before transferring sperm into an ICSI dish, dispensing the sperm into a Petri dish by using a graduated pipette or Pasteur pipette before drawing the sperm into the pipette tip e.g. Eppendorf tip. For the avoidance of doubt, the pipette tip shall not be inserted directly into the test tube to aspirate the sperm.

6.21 AR Centres shall ensure that biohazards and other hazardous waste items are disposed of in a manner that would minimize the hazards to the AR Centres, including personnel and the environment, and AR Centres shall conform to existing legislation and relevant guidelines issued by the Ministry of Health and the National Environment Agency in this regard.

6.22 AR Centres shall ensure that no toxic chemical or radioisotope is used in the laboratory including toxic cleaning materials.

6.23 AR Centres shall ensure that no aerosol or pest control substance is used in the laboratory.

6.24 AR Centres shall ensure that the quality control programme for the laboratory shall be documented and clearly defined to include goals, procedures, policies and corrective actions taken. AR Centres shall ensure that the quality control records are well organised and readily reproducible for review/audit, at the request of the Ministry of Health.

7. RECORD KEEPING

7.1 AR Centres shall ensure that a register of children conceived through IVF and other AR procedures (as described in para 2.2), and delivered in Singapore, identified by their birth certificate numbers, is maintained. AR Centres shall inform couples of all the information that will be recorded for the purpose of AR.

7.2 AR Centres shall ensure that their medical records of patients are kept in a secure place and are accessible only to AR personnel authorised by the Director of the AR Centre. A record must be kept of all AR personnel authorised to access these medical records.

7.3 AR Centres shall maintain clear documented security procedures to prevent unauthorised access to all records.

7.4 AR Centres shall ensure proper identification and labelling of gametes and embryos which are cultured and stored. A list of all such cultured and stored gametes and embryos (with proper identification and labels) shall be clearly recorded and readily reproducible for review/ audit, at the request of the Ministry of Health.

8. QUALITY AND RISK MANAGEMENT

8.1 AR Centres shall have a documented Quality and Risk Management Programme to ensure quality patient care through objective and systematic monitoring, evaluation, identification of problems in laboratory, clinical and counselling practices and actions to improve the level and appropriateness of care. AR Centres shall also maintain a Quality Manual which shall include:

(a) Philosophy and Objectives of the AR Centre;
(b) Policies and Procedures for the AR Centre;
(c) Professional Staff Development and Education Programme; and
(d) Monitoring and Evaluation on practices and standards of the AR Centre

8.2 Without limiting the generality of paragraph 8.1 above, AR Centres shall document written procedures for:

(a) risk management of potential cross contamination (e.g. what the AR centre would do to the rest of the gametes/embryos stored in the same tank if there is one specimen found positive with an infectious condition); and

(b) recall of gametes/embryos or notification of recipient centres of adverse incidents e.g. potential contamination, defects in processing, preparation of distribution, or other factors affecting suitability of the gametes/embryos for their intended use.

8.3 AR Centres shall maintain a system for regular review of the performance and complications of all treatment cycles carried out in the AR Centre with an aim to improve the quality of care and ensure the safety of the patient.

9. RESEARCH

9.1 AR Centres shall ensure that no research on oocytes (including those obtained from excised ovarian tissue) or on embryos shall be carried out without the prior written approval of the Director of Medical Services. Approval from the Director of Medical Services is required for the release of human oocytes (including those obtained from excised ovarian tissue) and/or embryos to other research centres.

9.2 Research protocols (including protocols to select oocytes/embryos for research) shall be reviewed and approved by the respective institutional review board (IRB) or the ethics committee of the AR Centres' parent institution before submission to the Director of Medical Services for consideration. If there is more than one agency/ institution involved in the proposed research, approval from the IRB or ethics committee of each agency/ institution is required. The prospective oocyte donor may undergo oocyte donation procedures in Singapore only after the approval from the Director of Medical Services is obtained by the AR Centre.

9.3 AR Centres shall ensure that the principal physician and embryologist in charge of the patient's AR treatment must not be

the principal investigator of the research team working on the same oocyte and/or resulting embryo obtained from his/her patient.

9.4 If the principal physician and the embryologist in charge of the patient's AR treatment is part of the research team, such links to the research team shall be made known to the patient / research subject **before** she/the couple makes an informed decision on whether to participate in the research.

9.5 AR Centres shall ensure that no human oocyte fertilised with human sperm is cultured in-vitro for more than 14 days (excluding any period when the development of the embryo is suspended).

9.6 AR Centres shall ensure that under no circumstances shall any research be carried out on or using human embryos which are more than 14 days old from the time of creation of embryo (excluding any period when the development of the embryo is suspended).

9.7 AR Centres shall ensure that no research or experimentation shall be carried out on or using any human gametes/ embryos without the express consent of the person from whom the gametes/embryos were obtained. Where reasonably practicable, AR Centres must provide comprehensive information to the donors of gametes and embryos of the intended research and shall ensure that no inducement, coercion or undue influence is exerted over the said donors.

9.8 AR Centres shall ensure that the express consent for research is obtained at no earlier than (1) week after the information referred to in paragraph 9.7 above is given to the donor.

9.9 AR Centres shall ensure that all prospective oocyte donors (i.e. patients who come primarily to donate their oocytes for research and not as part of fertility treatment) are assessed by an independent panel (which may come from the hospital's ethics committee) consisting of a lay person and 2 medical practitioners, one of whom is an authorised AR practitioner. The panel shall interview the prospective donor before the commencement of the oocyte donation procedures and be satisfied that the prospective donor:

(a) is of sound mind;
(b) has a clear understanding of the nature and consequences of the oocyte donation; and
(c) has given express consent for the donation (freely and without coercion or inducement),

before allowing any procedure leading to the donation to proceed.

In addition, the panel shall take into consideration the public interest and community values when assessing an application for donation of oocytes for research.

9.10 AR Centres shall ensure that prospective donors of oocytes/embryos for research shall be provided with all relevant material information relating to the proposed donation in an understandable form. This shall include, at the minimum:

(a) the purpose and nature of the research;
(b) the risks of the donation procedure, including the possibility of having a reduced chance of achieving pregnancy, if the woman is on an AR programme;
(c) whether the donated oocytes/embryos would be destroyed after being used for research;
(d) whether the oocytes/embryos, or the derived cells, would be kept/ stored for future research; and
(e) the right to withdraw consent or vary the terms of consent at any time before their oocytes/embryos are actually used in research, how to withdraw consent and the implications of a withdrawal.

9.11 AR Centres shall ensure that consent for research on oocytes/embryos shall be separately obtained from any consent for AR treatment. If a potential oocyte donor for research is also a woman undergoing fertility treatment, her consent for oocyte donation shall be taken independently of the treatment team. The potential donor(s) shall confirm in writing that they have been informed of the full implications of the donation and that they do not require these oocytes/embryos for future reproductive use. Only surplus embryos created from gametes of the couple for whom AR treatment was provided may be used for research with their consent.

10. HUMAN-ANIMAL COMBINATIONS (HAC)

10.1 A human-animal combination (HAC) gamete/embryo is a gamete/embryo which contains both human and animal genetic or non-genetic material and includes an embryo created by the fertilization of human and animal gametes.

10.2 AR Centres shall not carry out trans-species fertilisation for the purpose of reproduction unless the trans-species fertilisation is done to assess or diagnose sub-fertility, in which case, the resultant hybrid must be terminated at the 2-cell stage;

10.3 Except as permitted under paragraph 10.2 above, AR Centres shall ensure that no HAC gamete/embryo is created and no research on an HAC gamete/embryo is carried out without the prior written approval of the Ministry of Health. AR Centres shall ensure that under no circumstances shall any HAC gamete/embryo of any HAC be placed in the uterus of human or another species.

11. LICENSE APPLICATIONS

Centres for AR Services

11.1 As set out in paragraph 1.1 above, all AR Centres intending to carry out AR services must obtain prior approval from the Director of Medical Services before providing such services. The request for approval shall specify the AR Centre's objectives, range of services, facilities and staffing resources.

11.2 The authorisation for an approved AR Centre is subject to the establishment having obtained a hospital or clinic licence issued under the PHMC Act. The Director of Medical Services may in his discretion refuse to approve or may withdraw the approval granted to an AR Centre as he thinks fit.

11.3 The application form for approval to set up an AR Centre shall be submitted to the Director of Medical Services not less than 90 days before the intended commencement of operations of the AR Centre. Forms are available online at the Ministry of Health's website or in the eLA system.

11.4 Any change in the information furnished in support of any application must be immediately notified to the Ministry.

11.5 Where approval as an AR Centre is to be withdrawn, the AR Centre will be given a grace period from the date of notification to make arrangements with at least one other AR Centre for the continuation of services and care of all its patients before the AR Centre ceases operation.

Personnel

11.6 Applications for authorisation of medical practitioners and embryologists shall be made through the Director of the AR Centre. The Director of Medical Services may in his discretion refuse to issue or withdraw the authorisation for medical practitioners and embryologists as he deems fit.

11.7 AR Centres shall regularly update the list of AR personnel authorised by the Director of Medical Services, and shall communicate this list to the relevant staff of the AR Centre as determined by the Director of the AR Centre.

11.8 AR Centres shall immediately notify the Ministry of Health of any change in the information furnished in support of any application for approval.

11.9 AR Centres shall ensure that where approval to carry out AR services is withdrawn, all AR personnel concerned, with immediate effect, are not allowed to carry out AR procedures, either to start with new treatment cycles nor continue with existing AR procedures.

12. OTHERS

12.1 AR Centres shall notify the Ministry of Health of all information on every patient undergoing AR procedures, including those who consented to research, using relevant prescribed forms.

12.2 AR Centres shall furnish the Ministry of Health with such information as the Ministry may from time to time require regarding AR and research carried out in the AR Centres. All information received by the Ministry which is subject to medical confidentiality shall be treated as confidential by the Ministry.

THE SCHEDULE

Paragraphs 1.2 and 1.5

	New Paragraph	*Old Paragraph*	*Effective Date*
(i)	4.2(b)	3.1	24 October 2011
(ii)	5.30	4.7.1	24 October 2011
(iii)	5.4 and 5.7 (e)	4.3.1 (iv)	1 June 2011
(iv)	5.26 and 5.27	4.6.3 and 4.6.4	1 June 2011

Dated this 26th day of April 2011.

PROF K SATKU
DIRECTOR OF MEDICAL SERVICES
MINISTRY OF HEALTH, SINGAPORE