

DIRECTIVES FOR PRIVATE HEALTHCARE INSTITUTIONS PROVIDING ASSISTED REPRODUCTION SERVICES : REGULATION 4 OF THE PRIVATE HOSPITALS AND MEDICAL CLINICS REGULATIONS (CAP 248, REG 1)

1 DEFINITIONS

- 1.1 *Assisted Reproduction Centres (“AR Centres”)* in these Directives refers to all licensed private hospitals and medical clinics which have been authorised by the Director of Medical Services to provide Assisted Reproduction services.
- 1.2 For the purposes of these Directives, *Assisted Reproduction (“AR”) services* include all treatments or procedures which involve the handling of human oocytes or embryos, as well as related procedures, including the removal or the attempted removal of oocytes from a woman, either with a view of reintroducing them (whether fertilised or otherwise) into the body, or for research purposes.
- 1.3 An *embryology laboratory* is defined as an establishment which performs any or all of, but not limited to the following:
 - (i) Culture medium preparation and quality control testing
 - (ii) Examination of follicular aspirates with oocyte identification
 - (iii) Oocyte quality and maturing grading
 - (iv) Sperm preparation: semen collection and analysis, sperm washing and capacitation
 - (v) Insemination of oocytes
 - (vi) Determination of fertilisation and zygote quality evaluation
 - (vii) Embryo culture and embryo grading
 - (viii) Embryo transfer (either uterine or tubal)
 - (ix) Embryo/ sperm cryopreservation
 - (x) Micromanipulation of human oocytes and/or embryos

2 FACILITIES

- 2.1 AR Centres must make provisions for high-risk pregnancies conceived through AR technologies to be delivered and cared for in a hospital with Level 3 neonatal intensive care facilities.
- 2.2 AR Centres must have an embryology laboratory equipped to support AR technologies (ART) like In-vitro fertilisation (IVF) and Gamete Intrafallopian Transfer (GIFT) programmes.
- 2.3 AR Centres and its 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.
- 2.4 The embryology laboratory shall be:
 - (i) in a low-traffic, secure area and conveniently located with respect to the procedure room.
 - (ii) “Wet area” work (i.e. media preparation, equipment, sterilisation etc) shall not be done in a manner to prejudice the outcome of the handling of oocytes and embryos.

3 PERSONNEL

3.1 The AR Centre must have a minimum of one medical practitioner and one embryologist authorised by the Ministry of Health to perform clinical and laboratory work in AR technologies respectively.

3.2 Only medical practitioners or embryologists authorised by the Ministry of Health are allowed to carry out AR activities independently in the AR Centre.

3.3 Credentialing

Director of AR Centre

3.3.1 The Director of the AR Centre must be an authorised medical practitioner with at least 5 years of experience in AR technologies in an AR Centre or other recognised overseas Centres. Alternatively, the Director of the AR Centre must have 3 years of experience and performed 250 Assisted Reproduction Cycles independently before the appointment as Director.

Authorised Medical Practitioner

3.3.2 Doctors who wish to be considered for authorisation to perform ART procedures must satisfy the following criteria:

- (i) be accredited by the Specialist Accreditation Board and registered as a specialist in Obstetrics and Gynaecology with the Singapore Medical Council Register of Specialists
- (ii) be credentialed or have met Academy of Medicine Guidelines for credentialing to perform L2 laparoscopy
- (iii) have at least 18 months' training in an AR Centre which should include
 - a) reproductive endocrinology particularly in the use of ovulation-inducing agents and hormonal control of the menstrual cycle
 - b) ultrasound-guided oocyte retrieval techniques
 - c) gynaecological endoscopy
 - d) gamete/ embryo transfer
- (iv) have at least 6 months practical hands-on experience in ART under the supervision of an authorised medical practitioner
- (v) have satisfactorily performed a minimum of 20 follicular aspirations and embryo transfers under direct supervision of an authorised medical practitioner
- (vi) attended at least one course/ seminar on ART.

Authorised Embryologist

3.3.3 Embryologists who wish to be considered for authorisation to perform ART procedures must satisfy the following criteria.

- (i) hold a degree in Bachelor or Master of Science or equivalent
- (ii) have at least 6 months of practice in ART procedures under supervision
- (iii) have satisfactorily performed a minimum of 50 ART procedures under direct supervision of an authorised embryologist (A procedure is defined as a combination of examination of follicular aspirates, oocyte classification, sperm preparation, oocyte insemination [including Intra-cytoplasmic Sperm Injection], documentation of fertilization and preparation of embryos for transfer)
- (iv) attended at least one course/ seminar on ART.

3.4 Responsibilities of the Director of AR Centre

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

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

3.4.3 The Director of the Centre must ensure that:

- (i) the qualifications and experience of anyone carrying out AR activities are suitable for those activities
- (ii) proper equipment is used
- (iii) proper arrangements are made for the keeping and disposal of genetic material
- (iv) suitable practices are used in carrying out the AR activities
- (v) the Centre complies with the conditions of its licence
- (vi) the authorized medical practitioner and the embryologists practicing in the centre remain competent to perform AR procedures, including monitoring their participation in continuing education activities.

4 CLINICAL PRACTICE

4.1 General

4.1.1 IVF procedures and related AR technologies shall be carried out only when there are sufficient indications for the procedure, namely:

- (i) Tubal disease and/ or obstruction
- (ii) Endometriosis – failed alternative approaches to treatment
- (iii) Male factor
- (iv) 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 female patients above 35 years old
- (v) Premature ovarian failure
- (vi) Other conditions acceptable to the local medical obstetric/ gynaecology community.

4.1.2 IVF procedures and related AR technologies shall only be carried out on a married woman and only with the consent of her husband, whether or not her husband's semen is used. It is the responsibility of the authorized medical practitioner managing the patient to obtain the informed consent from the patient's husband. It is also the responsibility of the authorized medical practitioner to ensure that the patient produces documentary proof of her married status e.g. the Marriage Certificate.

4.2 Age Limit for Acceptance into AR programme

4.2.1 Women aged 45 and above shall not be accepted into the AR Programme.

4.3 Counselling

4.3.1 No IVF procedures or related AR technologies shall be carried out unless the woman and her husband have been adequately counselled and informed of:

- (i) 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 have given their explicit written consent to the procedure after such information has been explained to them.
- (ii) the lower chances of success with AR technologies for women above 40 years old, and the higher risk of complications
- (iii) the risk of genetic anomalies in the foetus e.g. Down's Syndrome for patients above 35 years old at her estimated date of delivery
- (iv) 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 to treatment, and compulsory insurance for neonatal care (applicable to Singaporean and foreign patients who intend to deliver in Singapore).

4.4 Screening Tests

- 4.4.1 All persons who will be undergoing AR procedures, including those who are donating sperms, oocytes or embryos, shall be screened for hepatitis B antigen, syphilis, rubella antibody and Human Immunodeficiency Virus (HIV) antibody. Tests for other transmissible diseases should be carried out when necessary.
- 4.4.2 All blood tests on the patients for HIV antibody, hepatitis B antigen, syphilis, rubella antibody and any other tests must be carried out in Singapore before the AR procedures are carried out. Foreigners who have these tests carried out in another country must have them repeated in Singapore.
- 4.4.3 The AR Centre may screen for Thalassaemia if the woman and/or her husband are at risk of Thalassaemia. If the result of the test is positive, the couple shall be counselled on the risk and consequences of having a child with Thalassaemia before the IVF procedure or related AR technologies are carried out.

Rubella

- 4.4.4 No IVF procedures or related AR technologies shall be carried out unless the woman and her husband have been adequately counselled and informed of the risks to the foetus of a patient with negative rubella antibody contracting rubella infection during pregnancy. The couple should also be counselled on the need for rubella immunisation 1 month prior to conception for the woman who has tested negative for rubella antibody.

HIV

- 4.4.5 All persons undergoing AR procedures who have been tested negative for HIV shall be screened at least six monthly while still on the programme.
- 4.4.6 Donors of gametes and/or embryos must be 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 eggs have to be used before the second test, the couple must be informed of the risks of infection and consent has to be taken.

4.5 Maximum number of Treatment Cycles

- 4.5.1 For women who entered the AR Programme at age 40 years and below:

- (i) A maximum of 10 stimulated and/or natural cycles reaching the stage of embryo transfer is permitted. (Women should be strongly discouraged after undergoing 5 cycles without achieving a pregnancy).
- (ii) These 10 stimulated and/or natural cycles refer to consecutive cycles in a nulliparous woman or following a live birth.
- (iii) These cycles include those performed in one or more local / overseas AR Centres.

4.5.2 For women who entered the AR programme at above 40 years of age:

- (i) A maximum of 5 stimulated and/or natural cycles reaching the stage of embryo transfer is permitted.
- (ii) Treatment must be stopped when the woman turns 45 years of age, irrespective of whether she has completed the 5 cycles.

4.5.3 There is no limit to the number of thawed cycles that may be carried out for any woman on the AR programme.

4.6 **Gametes and Embryo Donation**

4.6.1 IVF procedures and related AR technologies can be carried out using donated eggs, sperms or embryos.

4.6.2 Wherever possible, a genetic link to one of the said parents of the child should be maintained. Where it is not possible to maintain a genetic link to at least one of the social parents, embryo adoption (i.e. implantation of an embryo conceived through a donated egg and donated sperms) is permissible. Signed consent of the couple donating the embryo must be obtained.

4.6.3 In vitro fertilisation of eggs donated by her husband's sister with her husband's sperm is not allowed. Similarly no woman is allowed to have eggs transferred into her which have been donated by her husband's sister if her husband's sperm is used.

4.6.4 No woman is allowed to use sperm donated by her brothers for the fertilisation of her eggs.

4.6.5 Only eggs donated by women between 18 to 35 years old can be used for IVF procedures and related AR technologies.

4.6.6 Where a donor of gametes or embryos has, as a result of such donations, achieved 3 live birth events, it is expected that the donor's gametes or embryos will not be used on a subsequent occasion. The limit of 3 live birth events may be exceeded only in exceptional cases such as where the recipient wished to have a subsequent child from the same donor. 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'.

4.7 **Number of Oocytes/Embryos Replaced**

4.7.1 No more than 3 oocytes/embryos shall be replaced in the patient's body at any one time. However, up to a maximum of 4 oocytes/embryos can be replaced if all of the following 3 conditions are satisfied:

- (i) 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; and
- (ii) the patient has undergone not less than 2 previous stimulated ART cycles which were unsuccessful; and
- (iii) the patient is above 35 years of age.

4.8 Combined AR Technologies

4.8.1 Combined AR technologies of GIFT and IVF-ET or GIFT and ICSI-ET within the same cycle for any patient are strongly discouraged.

4.9 Embryo and Fetal Sexing

4.9.1 Embryo and fetal sexing will only be allowed on medical grounds and limited to sex-linked diseases e.g. haemophilia and muscular dystrophy. Prior approval of the Ministry of Health is required and each case will be considered on a case-by-case basis.

4.9.2 In carrying out embryo and fetal sexing, the carrier status of the woman must be established. Proper counselling for the family must be carried out. The course of actions available to the couple must be made clear to them.

4.10 Storage/Disposal/Transfer of Gametes/Embryos

4.10.1 Prior to the commencement of AR procedures, the AR Centre shall seek written instructions from every couple whose gametes/embryos are to be stored, regarding their future plans for the gametes/ embryos, including:

- (i) specification on maximum period of freezing of gametes/embryos;
- (ii) provisions for disposal of gametes/embryos in the event of separation of the couple (e.g. premature death or divorce of a partner);
- (iii) preferred method for disposal of gamete/embryos in the event of incapacitation of one or both partners such that the person is incapable of varying or revoking his/her consent.

4.10.2 All storage of gametes/embryos and their disposal shall be strictly in accordance with the instructions of the couple.

4.10.3 If no clear instructions regarding the disposal of their gametes/embryos were obtained from couples whose embryos were stored prior to the release of these Guidelines, and the couples cannot be traced, AR Centres shall promptly inform the Director of Medical Services of all actions or measures that have been taken.

4.10.4 Embryos should not ordinarily be stored beyond 5 years from the date of their fertilisation. Storage beyond this period should only be carried out where there is exceptional need for the embryos. Under no circumstances shall embryos be used if they have been stored beyond 10 years from the date of their fertilisation.

4.10.5 Centre-to-centre transfer of embryos is allowed between local centres and between local and overseas centres.

4.10.6 It is the responsibility of the receiving AR Centre to ensure that effective consent has been given for the use and storage of any gametes or embryos that are transferred to its Centre. This includes consent for the creation of embryos in-vitro where donor sperm is being provided for use in AR technologies.

4.10.7 The AR Centre is responsible for ensuring that the quality and security of genetic material are maintained, whenever and wherever the material is in its premises.

4.11 Others

4.11.1 AR centres must seek MOH's approval before providing pre-implantation genetic testing/screening services or other new services.

4.11.2 The following activities shall not be carried out in any AR Centre:

- (i) The buying and selling of embryos, ova and sperm;
- (ii) Surrogacy (surrogacy is where a woman is artificially impregnated, whether for monetary consideration or not, with the intention that the child is to be the social child of some other person or couple);
- (iii) Fetal reduction purely for social and financial reasons;
- (iv) Sperm sorting techniques in sex selection.

5 LABORATORY PRACTICES

5.1 Procedure manuals detailing all aspects of the AR technologies and related procedures shall be available in each laboratory. These manuals shall describe the laboratory procedures in sufficient detail.

5.2 These procedure manuals should be reviewed and validated at least annually.

5.3 The laboratory shall have an appropriate labeling system to ensure identification and traceability of gametes/embryos from their collection to storage, transfer, freezing, thawing and disposal.

5.4 Maintenance manuals for all laboratory equipment shall be available in the laboratory. These shall include regular maintenance to be performed on each piece of equipment, documentation of maintenance completed and corrective actions taken, if any.

5.5 All embryology laboratories shall check and maintain its equipment and facilities to be in good working order at all times. A record of such checks shall be available for inspection at any time.

5.6 All laboratory chemicals and reagents must be labelled to indicate date received, date opened, and shelf life, where applicable.

5.7 Procedures and policies on laboratory safety must be available to all laboratory personnel, and should be reviewed annually. Laboratory personnel are required to comply with existing guidelines in effect for laboratories and guidelines on infection control in Singapore.

5.8 As far as possible, disposable materials should be used for steps that involve exposure to tissues and body fluids.

5.9 Use of toxic chemicals or radioisotopes in the laboratory is not permitted. This includes toxic cleaning materials.

5.10 Use of aerosols and pest control substances is not permitted in the laboratory.

5.11 The quality control programme for the laboratory shall be documented and clearly defined to include goals, procedures, policies and corrective actions taken. The quality control records shall be well organised with a defined system to permit regular review by appropriate supervisory personnel.

6 RECORD KEEPING

- 6.1 There shall be a register of children conceived through IVF and other AR technologies and delivered in Singapore, identified by their birth certificate numbers. [The AR Centre should inform couples of all the information that will be recorded.]
- 6.2 The medical records of patients of the AR Centre must be kept in the Centre in a secure place and accessible only to AR personnel authorised by the Director of the AR Centre. A record must be kept of AR personnel authorised to access these medical records.
- 6.3 The AR Centre shall have clear documented security procedures to prevent unauthorised access to records.
- 6.4 A high standard of record keeping must be maintained to ensure proper identification and labelling of gametes and embryos which are cultured and stored.

7 QUALITY ASSURANCE

- 7.1 The AR Centre shall have a documented Quality Assurance (QA) 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. The AR Centre shall also have a Quality Assurance Manual which shall include:
- (i) Philosophy and Objectives of the AR Centre
 - (ii) Policies and Procedures for the AR Centre
 - (iii) Professional Staff Development and Education Programme
 - (iv) Monitoring and Evaluation on practices and standards of the AR Centre

8 RESEARCH

- 8.1 No research on oocytes (including those obtained from excised ovarian tissue) or on human embryos shall be carried out without the prior written approval of the Ministry. Ministry's approval is also required for release of human oocytes (including those obtained from excised ovarian tissue) and/or embryos to other research centres. 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 MOH for consideration. The prospective oocyte donor shall undergo superovulation only in Singapore after the Ministry's approval.
- 8.2 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.
- 8.3 Human ova fertilised with human sperm shall not be cultured in-vitro for more than 14 days (excluding any period when the development of the embryo is suspended).
- 8.4 Under no circumstances shall 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).

- 8.5 No research or experimentation shall be carried out on or using any human gametes/embryos without the explicit consent of the person from whom the gametes/embryos were obtained. Information provided to the donors of gametes and embryos must be comprehensive, and there must not be any inducements, coercion or undue influence.
- 8.6 All prospective oocyte donors (i.e. patients who come primarily to donate their oocyte for research and not as part of fertility treatment) must be reviewed by a panel (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 must interview the prospective donor before commencement of the ovarian stimulation and be satisfied that the prospective donor (a) is of sound mind (b) has clear understandings of nature and consequences of the donation and (c) has given explicit consent for donation (freely without coercion or inducements) before allowing procedures leading to the donation to proceed. In addition, the panel should take into consideration the public interest and community values when assessing an application for donation of oocyte for research.
- 8.7 Trans-species fertilisation for the purpose of reproduction is not allowed. Where trans-species fertilisation is done to assess or diagnose sub-fertility, the resultant hybrid must be terminated at the 2-cell stage.
- 8.8 Under no circumstances shall a human embryo be placed in the uterus of another species for gestation. Similarly no other gametes/embryos except human gametes/embryo shall be placed in a woman.

9 LICENCE APPLICATIONS

9.1 Centres for AR Services

- 9.1.1 All centres intending to carry out AR services must obtain prior approval from the Ministry of Health before commencing such work. The request for approval should specify the AR Centre's objectives, range of services, facilities and staffing resources.
- 9.1.2 The authorisation for an approved AR Centre is subject to the establishment having obtained a hospital or clinic licence issued under the Private Hospitals & Medical Clinics Act. The Director of Medical Services may in his discretion refuse to issue or withdraw the authorisation for an approved AR Centre as he may think fit to impose.
- 9.1.3 The Application Form to set up an AR Centre must 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 on-line at the MOH website or in the eLA system.
- 9.1.4 Any change in the information furnished in support of any application must be immediately notified to the Ministry.
- 9.1.5 Where approval as an approved AR Centre is withdrawn, the Centre shall not proceed with any new treatment cycles, and must make the necessary arrangements to complete all outstanding and any ancillary matters with the Centre's patients, including the completion of cycles already commenced and transfer of cryopreserved gametes/embryos, before the cessation of operation of the AR Centre.

9.1.6 The AR Centre that had its approval as an approved AR Centre withdrawn by the Ministry of Health will be given a grace period from the date of notification to make arrangements with at least one other AR Centre for continuation of services and care of all its patients before the AR Centre ceases operation.

9.2 Authorisation for Medical Practitioners & Embryologists

9.2.1 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.

9.2.2 AR Centres are required to regularly update the list of AR personnel authorised by the Ministry of Health, and to communicate this list to relevant staff of the AR Centre.

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

9.2.4 Where approval to carry out AR work is withdrawn, the AR personnel concerned is, with immediate effect, not allowed to carry out AR work, either to start with new treatment cycles nor continue with existing AR work.

10 OTHERS

10.1 Information on every patient undergoing AR procedures, including those who consented to research, will have to be notified to MOH using relevant prescribed forms.

10.2 All AR Centres shall furnish to the Ministry such information as the Ministry may from time to time require regarding assisted reproduction 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.

Dated this 31st day of March 2006

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Published	December 1990
1 st update	July 1991(para B3)
2 nd update	August 1993(para A5, B1.4, B5, B6, B7, B8)
3 rd update	March 1994(para B2, B3.3, B6, B7, B8.1)
4 th update	June 1996 (para A1, A2, A3, B2.1, B3.1, B3.2, B3.4, B7, B9.2, B10, C8 VII, Form A, Form B, Form C, Form D)
5 th update	September 2001
6 th update	March 2006