

STANDARDS FOR ASSISTED REPRODUCTIVE TECHNOLOGY FACILITY - EMBRYOLOGY LABORATORY AND OPERATION THEATRE



The Standards For Assisted Reproductive Technology (ART) was prepared by Standards For ART Laboratories Working Committee, Medical Development Division, Ministry of Health and is based on Laboratory Accreditation Scheme of Malaysia (SAMM), STR 2.7 – Specific Technical Requirements For Accreditation Of Assisted Reproductive Technology (ART) Laboratories, Issue 1, 30 August 2008 published by Department of Standard Malaysia, with their kind permission via JSM/AD-700/01/09 dated 27 July 2010.

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FOREWORD



Assisted Reproductive Technology (ART) is a fast growing field in the medical world. In a short period of time since the 1980's, it has developed from the basic in-vitro fertilization (IVF) using male and female gametes from natural cycles to intracytoplasmic sperm injection (ICSI) following stimulated cycles to achieve a pregnancy.

Malaysia is still lagging behind in this field, with the service available only in the big cities. However, since 1995 the Ministry of Health has taken the initiative to train more specialists in the field of Reproductive Medicine. This will inevitably lead to the establishment of more fertility centres in both the government and private sectors in future.

As such, there is a need for proper guidelines in the setting up of ART centres so that minimum standards are met. These guidelines includes the minimum standards required for clinical and laboratory practice. A committee comprising of infertility specialists, embryologists and officials from the government agencies, universities, Family Planning Board and the private sector was established to draw up this guideline. It is envisaged that this guideline would be useful for both clinicians and embryologists in the establishment of fertility centres and provision of related services. It would also serve as a useful guide for scientific personnel and clinicians in maintaining a high standard of practice, thereby ensuring the safety of couples undergoing treatment and their embryos.

The cost of fertility treatment in Malaysia is still low compared to that of our neighbouring countries. This should make fertility treatment in Malaysia very attractive, thus promoting Medical Tourism as proposed by our Prime Minister. These standards will ensure that a high quality service in ART will be readily available to infertile couples in this country. In view of this, ethical and good clinical practices must always be upheld and maintained by all clinicians and scientific personnel involved in providing these services.

A handwritten signature in black ink, consisting of a large, stylized loop at the top and a series of horizontal strokes below it, all contained within a light gray rectangular box.

DATO' SRI DR HASAN BIN ABDUL RAHMAN
Director-General of Health, Malaysia

STANDARDS FOR ASSISTED REPRODUCTIVE TECHNOLOGY (ART) FACILITY - EMBRYOLOGY LABORATORY AND OPERATION THEATRE

1 . Introduction

- 1.1 This document describes the minimum standards required for any ART facility operating in Malaysia.
- 1.2 This document shall be read in conjunction with MS ISO 15189 Medical Laboratories.

2. Scope Of ART Facility For Accreditation

The areas for which the scope of services that will be offered for accreditation purposes of the ART facility are as listed below:

2.1 Embriology laboratory

- 2.1.1 Semen Analysis (recognized standards e.g. WHO)
- 2.1.2 Sperm preparation (Fresh sample/frozen sample/ MESA/PESA/TESE/TESA/Open Biopsy)
- 2.1.3 Sperm cryopreservation
- 2.1.4 In Vitro Fertilization (IVF)
- 2.1.5 Gamete Intra Fallopian Transfer (GIFT)
- 2.1.6 Intra Cytoplasmic Sperm Injection (ICSI)
- 2.1.7 Assisted Hatching
- 2.1.8 Oocyte/Embryo/blastocyst cryopreservation
- 2.1.9 Preimplantation Genetic Diagnosis (PGD)
- 2.1.10 Other procedures involving manipulation of gamete, embryo, and gonadal tissue

2.2 Operation theatre

- 2.2.1 Oocyte retrieval
- 2.2.2 Percutaneous Epididymal Sperm Aspiration (PESA)
- 2.2.3 Testicular Sperm Aspiration (TESA)
- 2.2.4 Testicular Sperm Extraction (TESE)
- 2.2.5 Micro Epididymal Sperm Aspiration (MESA)

3. Terms And Definitions

- 3.1 ART facility means any premise which is involved in treatments or procedures that includes in vitro handling of human oocytes, spermatozoa and embryos, for the purpose of establishing a pregnancy, including but not limited to, in vitro fertilization and embryo transfer, gamete intra - fallopian tube transfer, zygote intra fallopian tube transfer, gamete and embryo donation,

cryopreservation and storage of gametes and embryo but does not include intrauterine insemination.

The ART facility should include the consultation clinic, andrology laboratory, embryology laboratory and operation theatre.

- 3.2 Embryology laboratory is the area where the process of IVF and ICSI are performed and this area should be separated from the andrology laboratory.
- 3.3 Andrology laboratory is part of ART facility where semen is analysed, processed and/or cryopreserved.
- 3.4 Clinical director is the person overall in-charge of the ART centre responsible for all clinical and laboratory operational management.
- 3.5 Laboratory director is the person-in-charge of the laboratory who will be responsible for all operations, administration (including the performance of technical procedures) and recording of test results and for ensuring compliance with applicable regulations. The post shall be a full time resident position.
- 3.6 Clinician in attendance is the authorized doctor (see Clause 4.1.3) who is the person overall in-charge of the patient's fertility treatment.
- 3.7 Embryologist is the qualified technical person (see Clause 4.1.4) who performs the relevant laboratory procedures for Assisted Reproductive Technology (ART) as stated in Clause 2.
- 3.8 Medical Laboratory Technologist is the person assisting the embryologist in performing semen analysis, semen preparation and certain diagnostic tests in an ART facility.

4. Technical Requirements

4.1 Personnel (clause 5.1 of MS ISO 15189)

4.1.1 Clinical director shall be a registered medical practitioner who is registered as such under the Medical Act 1971 [Act 50] and who holds a valid practising certificate with a postgraduate qualification in O & G and registered as a subspecialist in Reproductive Medicine by the National Specialist Register.

- 4.1.2 The laboratory director shall have a minimum qualification of Bachelor of Science Degree in a related Biomedical field with at least two years of post qualification supervised training and a minimum of 100 complete hands on cycles of IVF/ICSI (either as part of the degree programme or as post-degree training).
- 4.1.3 The clinician in attendance shall be a registered medical practitioner who is registered as such under the Medical Act 1971 [Act 50] and who holds a valid practising certificate with a postgraduate qualification in O & G and registered as a subspecialist in Reproductive Medicine by the National Specialist Register.
- 4.1.4 The embryologist shall be registered under the law regulating the allied health profession or in the absence of such law, holds such qualification and experience as are recognised by the Director General of Health. The embryologist shall have a minimum qualification of Bachelor of Science Degree in a related Biomedical field with at least one year of post qualification supervised training and a minimum of 50 complete hands on cycles of IVF/ICSI (either as part of the degree programme or as post-degree training).
- 4.1.5 A medical laboratory technologist shall be a person with at least a Diploma in Medical Laboratory Technology or an equivalent, recognised by the Director General of Health and at least 6 months of supervised training in related area of the laboratory services (either as part of the diploma programme or as post-diploma training).

4.2 Accommodation And Environmental Conditions

As in MS ISO 15189 Clause 5.2.1 in addition:

- 4.2.1 The laboratory should be in a low-traffic, secure area separated from other general laboratory activities and operating theatre.
- 4.2.2 Minimum floor area requirement for this embryology laboratory is 100 square feet (9.29 sq. m) with minimum ceiling height between 9 to 11 feet (2.74-3.35 m) to accommodate the minimal equipments required for an embryology laboratory which are the incubator,

micromanipulator, laminar flow, stereo microscope and ICSI manipulator.

- 4.2.3 All workbenches should be purposed-built and of non toxic surface. The ICSI micromanipulator should be preferably placed on anti vibration work top.
- 4.2.4 Design and materials used in construction should be compatible with a high level of cleansing and disinfection.
- 4.2.5 Use of toxic chemicals, radioisotopes, aerosol and pest control substances shall not be permitted in the laboratory.
- 4.2.6 Use of strong smelling personal hygiene products e.g. perfume, deodorant, hair spray, after shave lotion etc shall not be permitted in the confines of the laboratory.
- 4.2.7 The paint for the laboratory should be lead free and odourless.
- 4.2.8 Foodstuff shall not be permitted in the laboratory area.
- 4.2.9 Incoming air should be ducted via ceiling mounted air conditioning system. The air should be filtered by HEPA filters to remove particulate matter.
- 4.2.10 If the laboratory and ART operation theatre are not adjacent to each other, portable incubators should be used for maintenance of gamete/embryo temperature at 37 °C and pH between 7.2 – 7.4 during transportation as required.
- 4.2.11 A separate area should be provided for record keeping, data entry, computer data storage and related administrative functions.

4.3 Embryology Laboratory Equipment

- 4.3.1 The minimum requirement for equipments in the embryology laboratory equipments are the incubators and microscopes (stereoscopic microscope) for egg collection and inverted microscope for ICSI.
- 4.3.2 The embryology laboratory should have incubator(s) with emergency power back-up and preferably alarm systems. The alarm system should monitor both power failure and high and low deviations from set points for temperature and percentage

of CO₂ where applicable. Provision shall be made to access a back-up incubator should the main incubator malfunction.

- 4.3.3 Stereoscopic microscope should be of minimum range of 60 times magnification and inverted microscope should be of 40-400 times magnification for the procedure to which they are used.
- 4.3.4 Warming devices and mechanisms shall be in place to ensure proper maintenance of temperature at 37°C. The pH between 7.2 – 7.4 for media, gametes and embryos during the various phases of all procedures must be ensured and documented.
- 4.3.5 Where in-house media preparation is practiced there shall be access to a pH meter and osmometer for media adjustment to defined standards using appropriate calibration. All laboratory chemicals and reagents shall be labelled to indicate date received, date opened and shelf life where applicable.
- 4.3.6 All containers in contact with body fluids shall be disposable and compatible with tissue culture standards.
- 4.3.7 Gas cylinders should be placed outside or in a separate room with a backup system. Gas supplies to incubators must be of a suitable quality with mechanisms in place to ensure continuity of supply. Certificate of purity shall be available at all times. Appropriate filters to be placed to ensure quality of gas supply to incubator maintained.
- 4.3.8 Gamete and embryo manipulation shall be done in laminar flow work station.
- 4.3.9 Written protocols shall be in place such that treatment outcome will be minimally compromised in the event of malfunction of essential equipment or non-availability of key personnel.
- 4.3.10 All laboratory environment parameters should be documented daily and verified.

4.4 Requirement For ART Operation Theatre And Basic Equipment

- 4.4.1 Minimum floor area requirement for the operation theatre is 100 square feet (9.29 sq. m) to accommodate the basic

equipments required for ART Operation Theatre equipment as in 4.4.12

- 4.4.2 The ART Operation Theatre is preferably attached to the Embryology Lab with access via window or door as suggested in appendix 1.
- 4.4.3 The Changing Room should be a separate area and located within the operation theatre complex.
- 4.4.4 Surgical light source should be made either mobile or attached for adequate exposure.
- 4.4.5 The scrubbing area should be attached to the Operation Theatre.
- 4.4.6 The Operation Theatre shall have a jointless ceiling with covered ceiling lights to prevent particles from above the ceiling having direct access to the operation theatre area.
- 4.4.7 Ventilation
 - i. The operation theatre shall be mechanically ventilated to provide 100 percent fresh air without recirculation.
 - ii. The operation theatre shall be provided with a minimum ventilation rate of twenty room volumes of air change per hour by mechanical supply and exhaust air system. The outdoor air intakes shall be located as far as practicable but not less than 23 feet (7.6 m) from the exhausts of any ventilating system, combustion equipment, medical surgical vacuum system or plumbing vent areas which may collect noxious fumes.
 - iii. The bottom of the outdoor air intake shall be located as high as practical but not less than 3 feet (0.9 m) above the ground level or if installed through the roof, not less than 3 feet (0.9 m) above the roof level.
- 4.4.8 The operation theatre temperature should be maintained at 24° - 26° C.
- 4.4.9 Preferably there should not be any opening that allows sunlight into the operation theatre. However, if there are such openings with direct exposure to sunlight, they shall be covered with ultra violet protector.

4.4.10 Interior finishes

- i. Heavy duty vinyl shall be used for the floor with minimum of 4 inches (10 cm) height at the edges.
- ii. Interior finishes of the operation theatre shall be smooth, jointless and non- interrupted. It shall be able to facilitate and withstand frequent cleaning and disinfecting.

4.4.11 The recovery area shall be adequately equipped which includes:

- i. trolleys with the capability of tilting patient's head downwards.
- ii. oxygen supply and the appliance for delivering oxygen to the patient.
- iii. adequate suction apparatus.
- iv. equipment and drugs for resuscitation.
- v. accessibility to electrocardiogram and pulse oxymeter .
- vi. accessibility to specialised equipment as necessary for the continuing care of the patient.

4.4.12 Basic equipment requirement for ART operation theatre:

- i. A 2-D ultrasound machine for transvaginal scan and transabdominal scan with availability of a needle biopsy guideline on TV monitor for the purpose of transvaginal oocyte retrieval.
- ii. Oocyte retrieval system with vacuum system and tube warmer attached to it to maintain the tubes at 37°C throughout the procedure.
- iii. Patient monitoring must be present – pulse oxymeter for PaO₂ and continuous blood pressure (BP) and pulse rate (PR) monitoring.

- iv. Resuscitation trolley with adequate drugs and equipment to treat any medical emergencies that may be faced in the course of managing ART patients.
- v. Adjustable operation theatre table with suitable surgical stool for oocyte retrieval and embryo transfer.

4.5 Preparation Prior To Procedure

4.5.1 Preparation of patients

- i. A consent form shall be signed by the patient and a copy kept in the patient's record for any ART procedures that the patient and/or couple have to undergo.
- ii. A separate consent form is to be signed by both partners for cryopreservation procedures and subsequent use of the surplus embryos and gametes.

4.5.2 Laboratory safety and infection control

- i. Couples undergoing treatment shall be subjected to appropriate infectious disease screening and quarantine to ensure the gametes and embryos are free from infectious diseases. The minimum diseases to be screened for are HIV1, HIV 2, Hepatitis B and Syphilis. HIV positive patients are referred to the appropriate medical specialist for further treatment. Syphilis carriers are treated with the relevant antibiotic prior to proceeding with ART.
- ii. HIV and Hepatitis carriers shall be listed as the last case and the operating theatre shall subsequently be closed and cleansed using the standard hospital procedure for such cases. The laboratory personnel should handle all gametes from such patients using the standard double-gloving technique in addition to the aseptic techniques. The gametes shall be incubated separately from those of other patients.

4.6. Procedure For Collection And Handling Of Gametes

- 4.6.1 Oocyte retrieval should be performed under standard sterile technique as applicable in an operation theatre. Subsequent handling of gametes shall be undertaken using aseptic techniques (e.g. with proper gowning and wearing of mask, gloves and theatre cap).

- 4.6.2 The quality assurance system should be such as to detect clerical, transcriptional and analytical errors. Identity of gametes and embryos must be double checked at critical steps. Double checking should be indicated in the records by signatures and identifications of the personnel involved. There shall be adequate documentation to indicate this process.
- 4.6.3 Biosecurity
- i. To protect the security of gametes, only authorised personnel are allowed to enter the laboratory or storage area. Security measures shall be in place to prevent unauthorised entry.
 - ii. All containers and storage for gametes shall be properly labelled and recorded.
 - iii. All disposables for handling gametes shall be used only once.
 - iv. All storage containers shall be locked and stored in secure facilities.
- 4.6.4 The procedure should be performed at least under sedation as a minimum to conform to the standard requirements in Private Healthcare Facilities and Services (Private Hospitals and Other Healthcare Facilities) Regulations 2006.
- 4.6.5 Person allowed to administer anaesthesia:
- i. General or regional anaesthesia should be administered only by an anaesthetist or a registered medical practitioner, on condition that he has experience in anaesthesiology and is under supervision of an anaesthetist.
 - ii. A registered medical practitioner may administer local anaesthesia/sedation in treatment and procedures requiring such anaesthesia/sedation.
- 4.6.6 Administration of anaesthesia:
- 4.6.6.1 Before any anaesthesia is administered to a patient, there shall be entered on the medical record of the patient;

- i. history of the present illness
- ii. the results of appropriate laboratory investigations essential to the proper assessment of the patient's physical condition
- iii. the findings on physical examination

4.6.6.2 Before anaesthesia is administered to the patient, the person administering the anaesthesia shall;

- i. take a medical history and make a physical examination of the patient, sufficient to enable him/her to evaluate the physical condition of the patient and to choose a suitable anaesthesia for the patient;

and

- ii. enter on the anaesthetic record, and sign, a statement of data relevant to administering the anaesthesia from the patient history, laboratory findings and physical examination.

4.6.7 The procedure shall be performed by an O&G specialist trained in ART.

4.6.8 The nursing services shall be under the supervision of a registered nurse with training and experience in operation theatre nursing.

4.7 Assuring Quality Of Examination Procedures

4.7.1 Incubator performance shall be monitored daily for temperature and gas composition. Calibration shall be performed at regular intervals.

4.7.2 Water purification systems where applicable shall be maintained to the manufacturer's specifications for tissue-culture quality and performance monitored and recorded on a daily basis. Screening for pyrogens is essential.

- 4.7.3 In-house media, where applicable, shall be of an accepted preparation method to ensure suitability for use with human gametes or embryos.
- 4.7.4 Data from the laboratory shall be regularly analysed to determine that the following minimum criteria are achieved:
- i. fertilisation rate of at least 60% in couples without male factor infertility.
 - ii. fertilisation rate of at least 60% following ICSI.
 - iii. A minimum pregnancy rate of 25% per embryo transfer for IVF/ICSI treatment.

4.8 Procedure For Storage, Transfer And Disposal Of Gametes Or Embryos

- 4.8.1 Facilities shall be made available for cryopreservation of remaining viable embryos either in the same laboratory or other associated laboratory.
- 4.8.2 The following protocol shall be adhered to, for transfer of gametes or embryos from one ART facility to another:
- i. Patients are required to complete the necessary documents to authorize the transfer.
 - ii. Once the above requirement have been completed, staff will contact the receiving facility to arrange the transfer.
 - iii. The facility should label each package containing gametes and embryos with the identity of the patient.
 - iv. The embryos and gametes must be held in a temperature controlled container (minimum temperature should be at least -130°C) in order to preserve them in frozen state.
- 4.8.3 Safe disposal of tissue samples no longer required shall be carried out in accordance with existing regulations or recommendations for biohazard material.

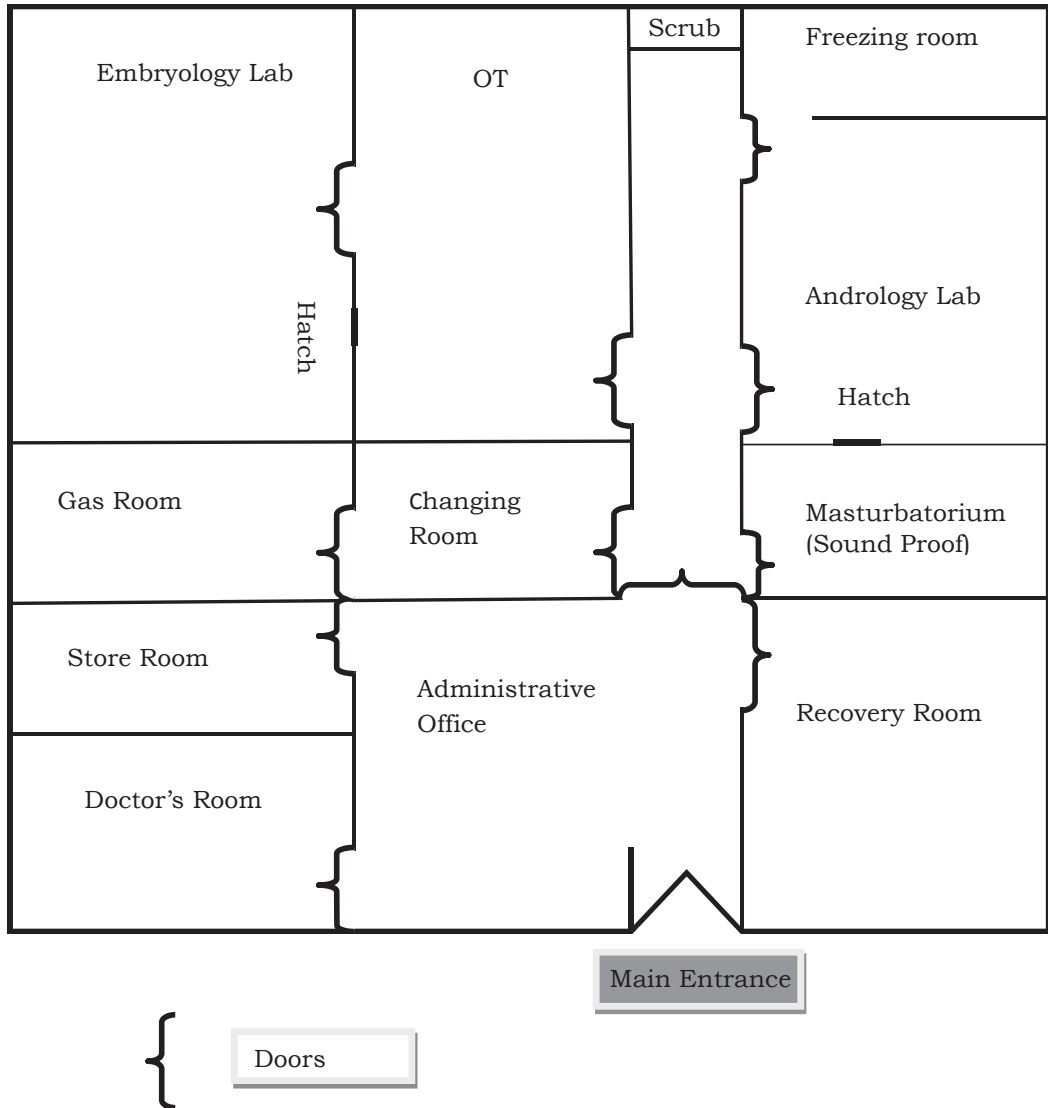
4.9 Reporting Of Results

- 4.9.1 All laboratory issues concerning patients' treatment and the source and fate of all gametes and embryos shall be documented.
- 4.9.2 All results and reports pertaining to embryology shall be validated by the embryologist.
- 4.9.3 A report shall be prepared and made available to the Ministry of Health as requested. The report should include data such as:
 - i. number of all the various ART cycles (In Vitro Fertilization, Intra Cytoplasmic Sperm Injection and Frozen Embryo Transfer).
 - ii. fertilization rates for IVF and ICSI using ejaculated spermatozoa.
 - iii. fertilization rate for ICSI using aspirated sperm from PESA, TESA, TESE, MESA.
 - iv. cleavage rate for 4.9.3.ii and 4.9.3.iii where applicable in the centre.
 - v. frozen embryo thaw survival rate.
 - vi. pregnancy rates from fresh and frozen-thaw cycles.
 - vii. cancellation rate with reasons.

5. Ethics

Confidentiality relating to patient information shall be maintained at all times.

6. Layout Plan For ART Laboratory



7. Standards For Assisted Reproductive Technology (ART) Facility Working Committee

1. Prof. Dr. Zainul Rashid Mohamad Razi (Chairman)
MD(UKM), MOG(UKM), MRCOG(London), AM (Malaysia)
DM(Nottingham), FICS(USA), FRCOG(London)
Dean of Postgraduate
Faculty of Medicine
UKM Medical Centre
2. Y. Bhg. Dato' Dr. Mukudan Krishnan
MBBS(UM), FRCOG(London)
Senior Consultant and Head of O&G Services
Hospital Raja Permaisuri Bainun, Ipoh
3. Dr. Ahmad Razid Bin Salleh
MBBS(UM), MPH(UKM)
Director
Medical Practise Division
Ministry of Health, Malaysia
4. Dr. Haji Mohamad Farouk Bin Abdullah
MBBS (Mal), FRCOG (London), CRM (Malaysia)
Senior Consultant & Head of O&G Department
Hospital Tengku Ampuan Rahimah, Klang
5. Dato' Dr. Prashant Nadkarni
MBBS(Mal) FRCOG(London)
Consultant Gynaecologist & Fertility Specialist
KL Fertility Center
6. Dr. Noor Haliza binti Yussoff
M.D (UKM), M.Med (O&G), Fellow Reproductive Medicine
Senior O&G Consultant
Hospital Kuala Lumpur
7. Dr. J. Ravichandran Jeganathan
MD. M.MED (O&G), Fellow Maternal Fetal Medicine (UK)
Senior Consultant and Head of O&G Department
Hospital Sultanah Aminah, Johor Bahru
And Advisor for O&G Services(MOH)
8. Dr. Rosliah Harun
BSc (Hons) Microbiology (Wales, UK); MSc in Medical Sciences (ART)
(Nottingham, UK); PhD Stem Cells (Sheffield, UK)
Embryologist
National Population and Family Development Board
9. Dr. Ruhaima Ramli
BSc. (Zoology), M.PHIL (Biotechnology Of Animal Reproduction),
Embryologist
Prince Court Medical Centre

10. Dr. Komathy Thiagarajan
M.D. (UKM)
Medical Officer
Human Reproduction Division
National Population and Family Development Board

11. Dr. Noor Aziah Zainal Abidin
MD (UKM), MPH (Hospital Management) (Mal)
Senior Principal Assistant Director
Medical Development Division
Ministry of Health

12. Dr. Arpah Binti Ali
MD (UKM)
Senior Principal Assistant Director
Medical Development Division
Ministry of Health

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Ministry of Health**

- 3. Dato' Dr. Azmi Bin Shapie
Director
Medical Development Division
Ministry of Health, Malaysia**



Kementerian Kesihatan Malaysia
Bahagian Perkembangan Perubatan
Kementerian Kesihatan Malaysia
Blok E1, Parcel E
Pusat Pentadbiran Kerajaan Malaysia
62590 Putrajaya
MALAYSIA

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