

State of Kuwait

Ministry of Health

Infection Control Directorate

**Task Force Group for Designs and
Constructions of Health Care Facilities**

**Infection Control Guidelines
for Assisted Reproductive Technology
(ART) Unit Design**

2008

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INTRODUCTION

Assisted reproductive technology (ART) definition according to Center for disease control and prevention (CDC) includes all fertility treatments in which both eggs and sperms are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body.

The types of ART include

- IVF (in vitro fertilization)
- GIFT (gamete intra fallopian transfer)
- ZIFT (zygote intra fallopian transfer)

Scientific societies around the world, such as the ASRM (American society of reproductive medicine), SART (society for assisted reproductive technology), ESHRE (European society of human reproductive and embryology) and HFEA (Human fertilization embryology authority) have drawn up guidelines for the safe practice of ART

The European Union and the Governments of several countries such as Australia, the UK and the USA have taken steps to establish perfect models of ART units. Accordingly we aimed to offer ART unit's design that is equivalent with those available in such countries

These guidelines are meant to ensure that ART unit is constructed and operated in accordance with the infection control principles.

IVF Department

Sterile

Non-Sterile

Operation
Theatre Wing

Waiting Area +
Reception

Room for
IUT transfer
of embryo

Record Room

Embryology
Lab
Complex

Examination Room

Store Room

Semen
Collection
Room

Semen
Processing Lab

Clean Room
for IUI

I. Minimal Physical Requirements for an ART Unit

A. The non-sterile area

The non-sterile area must include what is listed under

A reception and waiting room for patients:

A reception and waiting room with adequate space depending upon the load of work are essential.

Examination Room:

A room with privacy for interviewing and examining male and female partners independently is essential. The room must be equipped with an examination table and gynecological instruments for examining the female per vagina, an appropriate ultrasonographic machine. Color Doppler would be useful but not essential.

Store room:

A well-stocked store is needed for keeping essential stock. Facilities must be available for storing sterile (media, needles, catheters, petri dishes and such-like items) and non-sterile material under refrigerated and non-refrigerated conditions as appropriate.

Record room:

Record keeping must be computerized as far as possible so that data is accessible retrospectively for analysis or when called upon by the supervisory agency.

Semen collection room:

This must be a well-appointed room with privacy and an appropriate environment; it should be located close to the semen processing laboratory. This room must have a wash basin with availability of soap and clean towels. The room must also have a toilet and must not be used for any other purpose.

Semen processing laboratory:

There must be a separate room with a laminar air flow for semen processing, preferably close to the semen collection room. This laboratory must also have facilities for microscopic examination of post-coital test smears. Good Laboratory Practice (GLP) guidelines as defined internationally must be followed. Care must be taken for the safe disposal of biological waste and other materials (syringes, glass slides, etc.).

Clean room for IUI:

There must be a separate area/room with an appropriate table for Intra-Uterine Insemination of sperms (IUI).

B. The sterile area

The sterile area shall house the operation theatre, a room for intrauterine transfer of embryos and an adjoining embryology laboratory. Entry to the sterile area must be strictly controlled by an anteroom for changing footwear, area for changing into sterile garments and a scrub-station.

Sterile area includes:

1- Operation theatre (Oocyte collection room):

This must be well equipped with facilities for carrying out surgical endoscopy and trans-vaginal ovum pickup. The operation theatre must be equipped for emergency resuscitative procedures. The Operation Theatre and the embryology Laboratory are adjacent to each other. The theatre is equipped with the latest anesthetic machines, oxymeters & cardiac monitors.

2- Room for intrauterine transfer of embryo (IUT):

This is also called procedure room. It must be a sterile area having an examination table on which the patient can be placed for carrying out the procedure and rest undisturbed for a period of time.

3-The embryology laboratory complex:

The embryology laboratory should have adequate space to follow good laboratory practice. More specifically:

- The construction of the laboratory should ensure aseptic and optimal handling of gametes and pre-embryos during all phases of the treatment.
- The location of storage areas and equipment such as incubators, centrifuges and cryo equipment should be logically planned for efficiency and safety within each working area.
- The most recent developments in equipment and facilities should be applied. Bench height, adjustable chairs, microscope eye height, efficient use of space and surfaces, sufficient air-condition and the amount of daylight, all contribute to a working environment that minimizes distraction and fatigue. Consideration should also be given to local health and safety requirements.

4-The cryostorage room:

- It should be close to the laboratory complex with adequate built in ventilation.
- The cry dewars containing sperms and embryos should be locked for security.
- The liquid nitrogen level is monitored electronically and will alarm if drops below a pre determined level.
- There should be separate dewars for hepatitis B, C and HIV patients.

II. Physical environment of Oocyte Collection, Procedure Room & Embryology Laboratory:

Location:

- Location of ART unit should be ideally close to or within existing obstetrics and gynecology department. Being sensitive to particular needs of these patients(away from labor ward).
- Close proximity to gynecology ward is helpful.
- The laboratory should be located in higher floors to avoid the contamination at ground level.
- The embryology laboratory and theatre should communicate with each other through a window/ hatch, as well as an intervening door, which is kept closed during most of the procedures. This ensures that the eggs, which are being retrieved from the patient or the embryos that are being transferred back into the patient's womb, are not exposed to the detrimental effect of fluctuating environments.
- Laboratory should ideally be located next to procedure room for embryo transfer as well.

Size:

- The oocyte collection/procedure room must meet all of the requirements of a general operating room, with a minimum clear area of 22.5 m² exclusive of fixed and movable cabinets and shelves. It should have adequate space and mutual accessibility.
- The laboratory must be constructed and arranged to ensure adequate space for the performance, reporting of test and for equipments.

Entry restriction:

- Entry is restricted to laboratory personnel only. This is not only helps to maintain a sterile environment but also prevent positive pressure disruption.
- There should be designated separate changing area for theatre and laboratory staff.
- A set of theatre cloths, caps, masks and antistatic shoes should be available.
- All staff entering laboratory, theatre , procedure room should have hand washing facilities, which should be near entry and exit door.
- All personnel must wash hands with antibacterial fragrance free soap on both entry and exit.1

Air quality:

- Air quality is a very important factor for growing high quality embryos. The air quality is improved by making use of special HEPA filters and special air conditioners.
- The air filtration system for the oocyte collection, procedure room and the embryology Laboratory must provide 20 ACH (air changes per hour).
- Recent control studies have shown that embryos are at great risk of the hazardous effect of volatile organic compounds (VOCs) and chemical air contaminants (CACs) because of high metabolic rate and high cell division rate.
- HEPA filter does not remove vapor or gases thus the air quality is improved by making use of newer technology such as CODA tower system which incorporates four stage filter :
 1. Special HEPA filter 99.99% which removes particulate generally called aerosols such as microorganisms from air.
 2. Special layers of active carbon and potassium permanganate filter to absorb auto mobile exhaust fumes, organic hydrocarbons and formaldehyde from particles boards used in construction, paint, solvents, chlorine, cleaning chemicals ,VOCs, CACs and other harmful agents.
 3. Photo catalytic oxidizing agent which convert malignant toxic compounds (even nitrous oxide and carbon monoxide) into constituents such as H₂O and CO₂ and eliminate odor.
- Air conditioning systems should re-circulate hepa filtered air rather than drawing air from outside

Temperature:

The temperature in the procedure room and in the embryology laboratory must be maintained between 20-25°C.

Humidity:

The humidity in the procedure room and in the embryology laboratory must be maintained between 35-50 %.

Pressure:

If the rooms are adjacent, there must be positive pressure from the embryology laboratory room to the operation theatre & procedure room.

Walls and Floors:

- Walls and floors must be composed of materials which are easily washed and disinfected and that are not physically affected by germicidal and cleaning solutions.
- Solvent based paint is lethal to embryo so the use of low fume or water based paint is recommended. Paint work should be completed at least two weeks before starting work.
- Wall bases must be made integral and covered with the floor, tightly sealed within the wall, and constructed without voids that can harbor insects.
- Best for flooring is to have vinyl or single layered flooring which is antistatic.
- Wooden or tiled floors should be avoided as their crevices and ridges can trap dirt.
- Use of carpeting must be strictly avoided.

Ceilings:

Ceilings must have a smooth finish which is washable and waterproof.

Safety:

- Aerosols and toxic pest control substances must not be used.
- Toxic fumes which could be harmful to gametes and embryos must be eliminated.
- All compressed gas cylinders must be secured to prevent falling.

III. Specifications of Laboratory Equipment:

The embryology laboratory must have the following:

- A laminar flow working cabinet with a thermostatically controlled heating plate
- A stereo microscope
- A routine high-powered binocular light microscope
- A 'high resolution' inverted microscope with phase contrast or Hoffman optics, preferably with facilities for video recording
- A micromanipulator (if ICSI is done)
- Carbon dioxide incubator, preferably with a back up unit
- In line filter
- A laboratory centrifuge
- Media sterilizing autoclave
- An equipment for freezing embryos in a programmed manner
- Liquid nitrogen cans
- A refrigerator

Working cabinet, incubator and inline filter are considered as the most crucial equipment and thus their specifications are listed in details below.

Working Cabinet

All work in the Laboratory is done in sterile chambers with laminar flow with the following specifications:

- Vertical laminar flow (class II) protects the operator and the oocytes and embryos while horizontal laminar flow (class I) protects only the operator thus it has been suggested that vertical flow cabinet to be used to handle samples from HIV or hepatitis B or C patients.
- Now the introduction of IVF chamber has afforded substantial protection of the operator from contamination by any inadvertent aerosols or spills.
- It is controlled environmental mobile chamber which is specifically designed to control temperature, PH and CO₂ level (5-6%) during handling of gametes and embryos.
- Usual access to the IVF Chamber is through two arm ports with iris seals. While this protection does not reach Class II biohazard standards, it far exceeds the level of protection afforded by a typical laminar flow hood.
- It is provided with positive pressure in relation the laboratory environment.
- Temperature is maintained at 37°C.
- From April 2007 Human fertilization embryology authority (HFEA) requires

cabinet providing air quality of at least grade C* in the critical work area with a back ground environment as close as to grade D**.

- The workstation interior is constructed of stainless steel, making the work zone easy to clean. The interior surface need not to chip, rust or generate particles.
- Built-in warm electronically ballasted lighting to provide excellent illumination of the work zone and to reduce operator fatigue.
- anti-vibration surface ensuring optimum conditions for ICSI procedures is recommended.

Incubator

- The heart of the IVF Laboratory is the Carbon Dioxide Incubator in which the eggs are fertilized, the embryos are formed and the blastocysts are grown.
- A good IVF laboratory should have at least two incubators. One is used for oocytes and embryos and the other one for andrology, PH equilibration and warming of tubes and dishes of media.
- These incubators maintain temperature at a steady 37°C, 24 hours a day, 7 days a week, thus imitating the human body.
- **Incubator filter** needs special HEPA filter 99.99% , special layers of active carbon, potassium permanganate and photo catalytic oxidizing agent
- Incubator interior should be stainless steel for easy washing and cleaning
- Incubators should be frequently cleaned and disinfected.
- It should have the advantage of built in auto disinfection module.
- It should be organized in order to facilitate identification of embryos, oocytes and spermatozoa.
- Exterior should be smooth and washable.
- Low noise incubator is recommended.

Inline filter

The average CO₂ and other gases cylinders contain high levels of heavy metals, VOCs, CACs and other contaminants.

*grade C is the grade with air quality provided by HEPA filter , >10 ACH and the operator put on a suit with wrist seal, hair and beard cover. It is equivalent to class 10000 (ISO class 7)

** grade D is the grade with air quality provided by air filtration of class F8-F9, ACH =5 and the operator put on 2-piece suit with hair & beard cover. It is equivalent to class 100000 (ISO class 8)

- Inline filter removes and reduces the level of contaminants introduced into the incubator or equipment from gas sources.
- Inline filter needs special HEPA filter 99.99% , special layers of active carbon and potassium permanganate and photo- catalytic oxidizing agent

IV. Infection Control Considerations:

- Standard precautions: must be observed.
- Protective measures:
The purpose of the protective measures is also to ensure aseptic conditions for gametes and embryos. The procedures should deal with, but not be limited to, the following:
 - Use of laboratory clothing.
 - Use of non-toxic (non-powdered) gloves and masks.
 - Use of mechanical pipetting devices.
 - Use of fume-hood in case of fixatives.
 - Disinfection and sterilization of potentially infected equipment.
 - Use of disposable material; after usage, it must be discarded immediately in the proper waste containers. Potential infectious materials must be disposed of in a manner that protects laboratory workers, maintenance service, and house keeping staff from exposure to infectious materials in the course of their work
 - Goggles or glasses and face masks as appropriate must be worn while handling gametes and embryos and if cryogenic materials are handled.
- Needles and other sharps should be handled with extreme caution and discarded in special containers. If possible, glassware should be omitted in the laboratory, otherwise the Pasteur pipettes and broken glassware should be discarded in special containers.
- The facility must comply with Regulations for Management of Medical Waste
- No cloths, boots, lab coats or any equipment contaminated with blood or any other animal tissue should be permitted in the embryology Lab. room areas.
- All bench and work areas should be kept with the fewer amounts of items and apparatus as possible

- Keep the access door for the embryology Laboratory closed when the incubator door is opened.
- No items should be stored inside the hoods
- All glassware, pipette tips and containers used in the hoods during media preparation or gamete manipulation must be sterile.
- All other items such as pipetting devices, bottles of pre-warmed media, aliquots, etc. must be wiped down with 70% ethanol when practical before being placed inside the hoods
- Vaccination of the personnel against hepatitis B or other available viral disease is recommended.
- Cross-contamination with infectious material from one patient to another could occur during the cryopreservation procedure when straws with semen or embryos are filled by dipping the straw in patient medium, sealing it or passing it into liquid nitrogen without external disinfection.
- Material stored in the cryopreservation tanks should be kept in a way to avoid contact of the liquid nitrogen phase with the biological substances.
- Safety cryopreservation straws have been conceived in order to fulfill this requirement. Specimen known to be contaminated should be stored in such high security straws.
- Adequate steps for vermin proofing should be taken to the whole unit, with suitable traps for preventing insects and other forms of unwanted creatures entering the clinic. This essential detail should be planned at an early stage because no pesticide can be used in a fully functional IVF clinic, as it could be toxic to the gametes and embryos.

V. General Considerations:

- **Back-up power supply:**

There should be no interruption in power supply to the incubator, cryopreservation freezer and to other essential services in the clinic.

- **Maintenance of the laboratories:**

- IVF chamber, laboratory tables, incubators and other areas where sterility is required must be periodically checked for microbial contamination and a record of such checks must be kept.
- The embryology laboratory must have a daily logbook which records the temperature,
- Carbon dioxide content, humidity of the incubators and the manometer readings of the laminar air flow.
- All instruments must be calibrated periodically (at least once every year) and a record of such calibration should be maintained

- **Quality of consumables used in the laboratory:**

- All disposable plastic ware must be procured from reliable sources after ensuring that they are not toxic to the embryo.
- Culture media used for processing gametes or growing embryos in vitro should be preferably procured from reliable manufacturers.
- Most media are supplemented with serum they should therefore be tested for antibodies to HIV 1 and 2, Hepatitis B Surface Antigen and Hepatitis C RNA.

References

- Accreditation standards and guidelines for IVF laboratories, Human Fertility, Volume 3, Number 3 , August 2000 , pp. 174-180 (7)
 - Air quality in the clinical laboratory , Nordic IVF Laboratory society- 9th annual meeting- Gothenburg, 2005.
http://www.enerma.cit.chalmers.se/Cleanroom/AQ_IVF_NILS_meeting_Ekberg.pdf
 - ESHRE guidelines for good practice in IVF laboratories
 - Luca Gianaroli¹, Michelle Plachot, Roelof van Kooij, Safaa Al-Hasani, Karin Dawson, Anick DeVos, M.Cristina Magli, Jacqueline Mandelbaum, Jacqueline Selva, Wouter van Inzen and Committee of the Special Interest Group on Embryology
 - Human Reproduction vol.15 no.10 pp.2241-2246, 2000
 - Rules and regulations for in-vitro fertilization pursuant to ACT 920 of 1991, State Board of Health of Arkansas, Little Rock, Arkansas, 1993
 - Introduction, brief history of ART and requirements of ART clinics
 - Advisory Committee of the ICMR's Institute for Research in Reproduction and the Ethics Committee for Human Experimentation of the KEM Hospital INDIA.
 - In-vitro fertilization, Kay Elder director of continuing education, Bourn Hall Clinic
 - Brian Dale director of centre for reproductive biology, Naples
 - CAMBRIDGE UNIVERSITY PRESS
- General considerations standard operating procedures for cell culture rooms
- Maria B. Padua and Peter J. Hansen February 6, 2007
- (Standard Operating Procedures of the University of North Carolina Tissue Culture Facility <http://www.unc.edu/depts/tcf/info.html>)
- Personnel & Product Protection, A Guide to Bio-safety
 - Labconco Corporation www.labconco.com
- How To Select The Right Laboratory Hood System
- Labconco Corporation www.labconco.com

- Ambient air and its potential effects on conception in vitro, Cohen, J., Gilligan, A., Esposito, W., Schimmel, T. & Dale, B. (1997)

- Ambient air and its potential effects on gametes and embryo
J Cohen, A Gilligan, W Esposito, T Schimmel and B Dale
The Institute for Reproductive Medicine and Science of Saint Barnabas, Livingston,
New Jersey, USA.

- Summary of air quality information

<http://www.hfea.gov.uk/en/1333.html>

- VOC levels in a new IVF Laboratory with both central and in- Laboratory
photocatalytic air purification unit.

www.alphascientists.com

- Clean room

[http://www.ee.washington.edu/research/microtech/cam/PROCESSES/PDF%20FILES/
CleanRooms.pdf](http://www.ee.washington.edu/research/microtech/cam/PROCESSES/PDF%20FILES/CleanRooms.pdf)

- Technical report THE BENEFITS OF USING THE “IVF CHAMBER IN THE
HUMAN ASSISTED CONCEPTION LABORATORY

- Report prepared by Oozoa Biomedical Inc (Vancouver, Canada), April 2002.

Good Clinical Practice in Assisted Reproduction by Paul Serhal (Editor), Caroline
Overton, Caroline Overton(Editor) Publisher: Cambridge University Press Pub. Date:
July 2004