This meeting is organised by
the ESHRE Special Interest Group "Embryology"

# The search for excellence in IVF laboratories: towards "the best"

it is not an option, but an obligation

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ESHRE Campus 2009
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## ESHRE guidelines for good practice in IVF laboratories

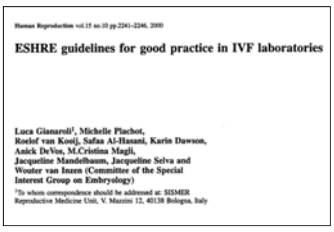
**Education has always been a priority for ESHRE; many efforts have been dedicated to promoting knowledge of the techniques, procedures and strategies in order to ensure use of the highest quality practices in reproductive medicine.**

**Set of guidelines for IVF laboratories → Focus on Reproduction, 1990**

**→ Human Reproduction, 1995**

## ESHRE guidelines for good practice in IVF laboratories

**In the year 2000, the ESHRE Special Interest Group on Embryology introduced guidelines constituting the minimal requirements for any laboratory offering assisted reproduction techniques (ART).**


Human Reproduction vol.15 no.10 pp.2241–2246, 2000

ESHRE guidelines for good practice in IVF laboratories

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## Revised ESHRE guidelines for good practice in IVF laboratories


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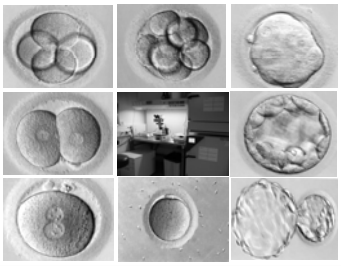
ESHRE Pages

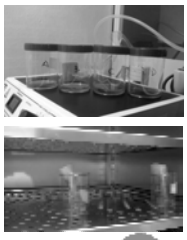
**Revised guidelines for good practice in IVF laboratories**

M. Cristina Magli, Etienne Van den Abbeel*, Kersti Lundin, Dominique Royere, Josiane Van der Elst and Luca Gianaroli for Committee of the Special Interest Group on Embryology

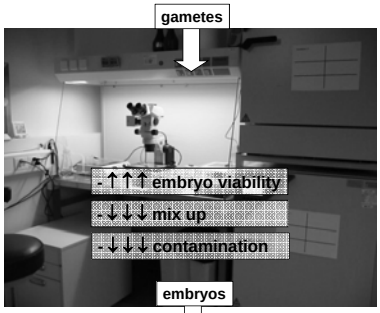
## Why the need for guidelines?

- To implement a quality system for all embryologists and IVF laboratory staff, in the understanding that the embryologist has a responsibility for the correct and justified application of ART in the laboratory.





## Why the need for guidelines?



## Why the need for guidelines?

In March 2004, the European Parliament issued the Directive 2004/23/EC 'On setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

The Directive applies to human tissues and cells, including fresh or frozen reproductive cells for application to the human body, and is mainly concerned with increasing quality and safety through the implementation of a quality management system.

## European Parliament Directives

L 102/48 EN Official Journal of the European Union 7.4.2004

DIRECTIVE 2004/23/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 31 March 2004
on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

**Into force by 7 April 2006**

L 38/40 EN Official Journal of the European Union 9.2.2006

COMMISSION DIRECTIVE 2006/17/EC
of 8 February 2006
implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells

**Into force by 1 November 2006**

L 294/32 EN Official Journal of the European Union 25.10.2006

COMMISSION DIRECTIVE 2006/86/EC
of 24 October 2006
implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells

**Into force by 1 September 2007**

## Revised ESHRE guidelines for good practice in IVF laboratories

**The guidelines for good practice in IVF laboratories issued by ESHRE:**

- **respond to the need of embryologists for support and guidance in their duties**
- **are a complement to the requirements issued by the Tissue and Cell Directive**
- **may represent a point of reference for the national competent authorities inspecting according to the Directive**

## Revised ESHRE guidelines for good practice in IVF laboratories

The implementation of ESHRE guidelines for good practice in IVF laboratories and of the Tissue and Cell Directive requires a quality management program to be in place that encompasses and integrates the operative units, the processes and procedures that represent the core of ART clinics.

## Quality Control & Quality Assurance

- Compliance with a quality management system is mandatory
  - Validated and written procedures for all processes including the occurrence of incidents or hazards
  - Assuring that all media/reagents/disposables are tested for quality with the appropriate assay
  - Maintaining and calibrating equipment regularly
  - Verifying conformance to specifications
  - Taking corrective action to conform

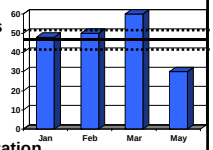
## Quality Control & Quality Assurance

A systematic monitoring of the testing process can be performed under Quality Assurance, aimed at improving the entire process by identifying problems, errors or improvements that may have occurred.

For this internal quality assurance, results should be evaluated on a regular basis, indicators should be objective and relevant, and adequate thresholds set up.

## Quality Control & Quality Assurance

- The following internal indicators should be regularly reviewed, analyzed and discussed with the clinical team:
  - Numbers/rates of errors/adverse events
  - Rates of normally fertilized oocytes
  - Cleavage rates
  - Rates of top quality embryos
  - Proportion of patients with failed fertilization
  - Ongoing clinical pregnancy rates (fresh and frozen-thawed transfers)
  - Multiple pregnancy rates
  - Implantation rates
  - Rate of survival of zygotes/embryos after thawing




## Quality Control & Quality Assurance

- External quality assurance programmes are also recommended

- The results should be related to those reported in the specialized literature, including national data and data from the European registry collected by the European IVF-monitoring programme for ESHRE

Within this framework of quality assurance, ESHRE, in collaboration with several national embryology societies, has setup a programme for Certification of Clinical Embryologists in order to contribute to the assurance of good laboratory practice and to define the concept of qualified embryologists.

## 1- Staffing & Direction

- Laboratory Director – qualified, experienced and responsible
- Responsibilities include:
  - Laboratory facilities are appropriate and safe
  - Written procedure manuals and staff compliance
  - Review and update procedure manuals
  - All process in compliance with quality management system
  - Staffing the laboratory to an appropriate level with qualified personnel
  - Orientation of new staff, with beginners following a supervised training scheme
  - Ensure ongoing scientific and medical education of laboratory staff
  - Ensure that written procedures exist for each staff member as to their individual responsibilities and their position in the chain of command
  - Regular exchange and discussion with clinical colleagues

## 2- Policies & Procedures

- Unique patient identifications for corresponding biological material
- Updated version of all procedures manuals present in laboratory
- Written, signed and dated protocols for every procedure performed in laboratory
- Written procedures for dealing with and documenting incorrect or incomplete identification of biological material or documentation, as well as for non-compliance, emergency and adverse events
- Laboratory and clinical results regularly updated, summarised and discussed by all staff and appropriate responses initiated if required

## 2- Policies & Procedures

- A log book should be maintained by laboratory personnel to permit evaluation of results and performance
- Communication with other specialty units within the clinic should be specified by written procedures
- Phone calls to and from the laboratory should be kept to a minimum

Even with the latest in hands free phones

## 3- Laboratory Safety

- Laboratory Design
  - Adequate space to permit good laboratory practice
  - Close as possible to operating room
  - Construction should permit aseptic and optimal handling of gametes/zygotes/embryos throughout treatment HEPA & VOC filtration of air as well as positive air pressure should be considered to maintain a clean air environment
  - Changing rooms & hand washing facilities should be located near to the laboratory

## 3- Laboratory Safety

• Laboratory Design

- Access to the laboratory should be permitted only to authorized personnel
- Pass throughs for biological material entering the laboratory are recommended
- Location of storage areas and equipment should be planned for efficiency and safety within the working area
- Separate office space should be provided for administrative work
- A general wet area for washing of equipment and sterilization must be separate from the embryo laboratory – if fixatives are involved, procedures must be performed in a fume-hood

## 3- Laboratory Safety

• Laboratory Equipment

- Must be adequate to the needs of the procedures and easy to clean and disinfect
- Critical items of equipment such as incubators and frozen storage facilities should be appropriately alarmed and monitored
- Automatic emergency generator backup should be available in the event of power failure
- A minimum number of 2 incubators is recommended - gas cylinders should be located outside the laboratory and be fixed with an automatic back-up system
- Incubators should be cleaned frequently and sterilized
- Records of routine and extraordinary maintenance on all equipment must be documented and retained

## 3- Laboratory Safety

• Laboratory Equipment

- Devices for the maintenance of temperature of media/gametes/zygotes/embryos during each phase of the procedure when out of the incubator should be in place
- Regular checks of functional parameters for devices used to maintain temperature and $CO_2$ should be performed using calibrated devices – a record of these measurements as well as those shown on the digital displays must be retained
- Instruction manuals for all instruments should be available in the laboratory
- Written instructions should be available to all members of staff for action in the case of equipment failure

## 3- Laboratory Safety

Equipment failure can be catastrophic

## 3- Laboratory Safety

• Infectious agents

All assisted reproductive technologies (ART) involve handling biological material, and pose a potential hazard of transmitting diseases to personnel and to other patients' gametes, zygotes or embryos (cross-contamination). Each unit should establish procedures and policies for the safety of personnel and for preventing cross contamination, taking national and/or local safety regulations into consideration.

- Vaccination of the personnel
- Screening patients and gamete donors
- The laboratory staff must be informed about the risks of handling infected biological material, whenever the information is available (clinical files).

## 3- Laboratory Safety

• Infectious agents

- The treatment of patients positive for HIV or Hepatitis B/C (diagnosed as infectious after PCR control for the presence of the viral genome) should be only performed in laboratories having dedicated areas, in which the adequate safety measures are followed.
- Alternatively, patients with positivity for HIV or Hepatitis B/C could be allocated to specific series or time slots during the working day, which are followed by an accurate cleaning and disinfection of the laboratory.
- A Class II laminar flow cabinet that protects both the operator and the specimen should be used when contaminated samples are handled.

## 3- Laboratory Safety

• Protective measures

The purpose of the protective measures is both to protect laboratory staff and to ensure aseptic conditions for gametes, zygotes and embryos.

- Strict observation of staff hygiene regulations.
- Use of laboratory clothing.
- Use of non-toxic (non-powdered) gloves and masks where appropriate.
- Use of eye and face protection, and of cryogloves if cryogenic materials are handled.
- Use of vertical laminar-flow benches.
- Use of mechanical pipetting devices.
- Use of fume-hood in case of fixatives.

## 3- Laboratory Safety

• Protective measures

- Use of disposable material; after usage, discard it immediately in the proper waste containers. Potential infectious materials must be disposed of in a manner that protects laboratory workers and maintenance, service, and housekeeping staff from exposure to infectious materials in the course of their work.
- Needles and other sharps should be handled with extreme caution and discarded in special containers. If possible, omit glassware in the laboratory; otherwise discard the Pasteur pipettes and broken glassware in special containers.
- Food, drinks, cigarettes and cigars are strictly forbidden.
- The use of make-up and strong perfumes should be limited.

## 4- Identification of patients and their gametes, zygotes and embryos

Unique patient identifications for corresponding biological material

- Verification of patients' identity should be performed at critical steps: before ovum pickup, at semen recovery, at insemination or ICSI, at cryopreservation and at embryo transfer procedures.

- Double checks are recommended at least at: insemination of oocytes, replacement of embryos, zygote or embryo freezing and thawing.

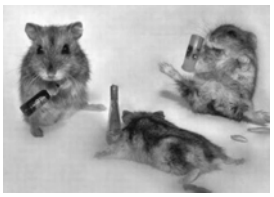
Not everyone plans for a rainbow family

## 5- Culture Media Preparation & Quality Control Testing

- Culture media should be of tissue culture grade, preferably mouse embryo tested and with purity appropriate for the purpose.

-Use of commercially produced, quality controlled tested media is recommended.

- Donor serum or follicular fluid is not recommended as medium additives.



## 6- Handling of Embryos, Zygotes & Spermatozoa

- It should be performed in a laminar flow hood equipped with heating stages and pre-warmed heating blocks.

- Class II hoods should be used for documented contaminated samples, since they provide protection also to the operator.

- Aseptic technique should be used at all times.

7- Oocyte Retrieval

8- Sperm Preparation

9- Insemination of Oocytes

10- Scoring for Fertilization

11- Embryo Culture and Transfer

12- Cryopreservation of Gametes, Zygotes and Embryos

13- Assisted Zona Hatching

14- Preimplantation Genetic Diagnosis

## Conclusions

**The ESHRE guidelines for good practice in IVF laboratories and the European Tissue and Cell Directives, no longer represent an option, but a prerequisite, to operate and provide the best clinical outcome in a safe working system.**

**The SIG in Embryology hopes that this document may assist the laboratory staff to operate according to the requirements of harmonization, implementation, inspection and certification that are now common to all European member states.**