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REVIEW

ASEBIR Quality Special Interest Group guidance for quality in assisted reproduction technology

BIOGRAPHY

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KEY MESSAGE

This is a reference document that highlights the critical aspects to consider when establishing an assisted human reproduction laboratory to achieve excellence through optimal functioning and the guaranteed safety of the procedures. It is based on the recommendations of major national and international societies and consensus groups.

ABSTRACT

Assisted human reproduction has undergone rapid advances since its inception 45 years ago. To keep pace with these advances, assisted reproduction laboratories should adhere to a quality management system that addresses staffing and training, physical space and air quality, equipment maintenance and other operational matters, and ensures gamete and embryo handling in accordance with the latest quality and safety standards. Accordingly, this review aims to provide a reference document that highlights the critical aspects to consider when establishing and operating an ART laboratory. The review collates and expands upon published national and international guidelines and consensus documents, providing easier access to this large body of important information.

INTRODUCTION

Since the birth of the first child conceived through assisted reproduction techniques, 45 years ago, the role of embryologists has evolved from performing strictly technical tasks to non-technical ones, such as computerized image evaluation. Moreover, novel techniques and systems have been introduced, with laboratories now required to pass strict quality control to ensure optimal outcomes. Thus, quality management systems (QMS) that enable embryologists to work efficiently and safely are increasingly being implemented. Embryologists perform practical work that requires a high degree of training and experience, knowledge of non-laboratory aspects and assuming of significant responsibility (*Alpha Scientists in Reproductive Medicine, 2015*). Hence, a clinical embryologist is as important and highly valued as effective laboratory design or equipment. Each laboratory must have a sufficient number of embryologists who

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KEYWORDS
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receive regular training and possess certified technical skills. Laboratory protocols should follow universal principles of good general and IVF-specific laboratory practices and patient safety protocols (*Go, 2015*).

The American Society of Reproductive Medicine previously published a comprehensive guide for human embryology, andrology and endocrinology laboratories that includes recommended laboratory staffing requirements based on the embryology cycle volume (*Practice Committee of the American Society for Reproductive Medicine and Practice Committee of Society for Assisted Reproductive Technology, 2008*). This guide was updated in 2021 (*Practice Committees of the American Society for Reproductive Medicine and the Society for Reproductive Biologists and Technologists, 2022*). Similarly, in 2015, the European Society of Human Reproduction and Embryology (ESHRE) published revised guidelines for good practice in IVF laboratories to widen the coverage of key aspects (*ESHRE Guideline Group on Good Practice in IVF Labs et al., 2016a*).

The Spanish Association for Standardization is a legally recognized national standardization body in Spain (formerly called the Spanish Association for Standardization and Certification [Asociación Española de Normalización y Certificación – AENOR]), and among its normative documents are the Una Norma Española (UNE) standards. UNE 179007 is a standard derived from ISO 9001 that defines specific requirements for human assisted reproductive technology (ART) laboratories to improve quality and safety. It establishes common criteria regarding professional qualifications, processes and responsibilities, infrastructure, equipment characteristics and controls, product traceability and safety, as well as quality indicators (*Ortiz et al., 2014*).

This review covers the legal aspects and minimum requirements for establishing an assisted human reproduction laboratory. Furthermore, it reviews an already published proposal for determining staff size, staff training and skill development, necessary physical resources in the laboratory, as well as design and QMS (*Alikani et al., 2014*, *Ferrer et al., 2021*; *Veiga et al., 2022*). The review's primary objective is to create a reference document that includes the key aspects to consider when establishing an ART laboratory based on the bibliography recommended by the main national and international guidelines.

MATERIALS AND METHODS

This review is the product of a team of experts in ART laboratories recruited from among the members of the Association for the Study of Reproductive Biology (ASEBIR) Quality Special Interest Group (A.M., C.O., E.F., E.V., L.S., M.F., N.O.) to create an initial script of the questions to be reviewed. After an internal revision, these questions were further revised to ensure that they were appropriate for the target audience (andrologists, embryologists, urologists and attending physicians with expertise in male infertility) as well as comprehensible for speakers of Spanish as a first language. The bibliographic review and the personal contributions of the experts was conducted for writing the Clinical Embryology Notebook: HR, RRFF and Quality 202 published by the same team of experts (*Ferrer et al., 2021*).

More than 40 online meetings were needed to arrive to an agreement on all the topics presented in the Notebook. Every topic was presented by a member who revised and updated the topic, taking in account all the bibliography as well as the main national and international guidelines. An open discussion with all members was held following every presentation in order to reach points of agreement. Finally, every member wrote their topic common points. When the presentation meetings finished a new round of meetings took place where all key points were written and reviewed, and the final Notebook was edited.

Given the important recommendations provided in the ASEBIR Notebook, the entire Quality Special Interest Group considered it important to disseminate a summary of it to speakers of English as a first language. All members of this interest group (A.M., C.O., E.F., E.V., L.M., L.S., M. F., M.I., M.L.L.R., N.O.), also authors of the review, are accredited clinical embryologists with extensive experience in assisted human reproduction centres and relevant knowledge on IVF QMS, air quality, key performance indicators and staff management in IVF laboratories. More than 10 online meetings were needed to arrive at an agreement on all the topics presented in the review. The meetings were structured around every key topic, as was done for the edition of the original Notebook.

Minimum requirements

For a new ART centre to be authorized, it should fulfil the legislative requirements of the corresponding country. Typically, administrative authorization is required for the installation and operation of equipment as well as for carrying out relevant activities.

Generally, legal requirements refer to the following:

(a) A report describing the ART service offer to be developed.
(b) A description of compliance with structural requirements, equipment and its maintenance programme, as well as the cleaning and disinfection of surfaces.
(c) A description of staff – specifying their qualifications, training and experience in ART.
(d) Clinical documentation or medical records of the users or donors that guarantee their confidentiality, availability of informed consent, data protection management, standard operating procedures (SOP) of the main ART activities, traceability and an activity registry.
(e) A systematization of sample storage in cryopreservation tanks.
(f) A description of how the processing, storage and distribution of human cells and tissues will be managed. and of the labelling system to ensure traceability (e.g. using the single European code [SEC]).
(g) A description of how a QMS integrated into the guidelines and strategies of the centre will be developed and updated.
(h) Assurance of civil liability coverage.
(i) Waste management.
(j) A description of the biovigilance system that allows a reporting, recording and transmitting of information on the observed effects and serious adverse reactions.
(k) A record of periodic inspections performed by the competent authority.

Responsibilities, competencies and training

The staff members of an ART laboratory can be classified based on their training and experience as follows:

(a) Embryologist – a higher university graduate in biomedical sciences or medicine with training and experience in reproductive biology.
(b) Clinical embryologist – an embryologist with certification recognized by a scientific society.
(c) Support staff – laboratory technicians and administrative staff.

In an ART laboratory, the functions and responsibilities in the organization should be distributed among the following members: director, coordinator, embryologists and laboratory technicians. TABLE 1 details the minimum competencies and duties of these members, defined in accordance with the Personal, Administrative, Clinical, Education and Research (PACER) system (*Alpha Scientists in Reproductive Medicine, 2015*; *Asociación Española de Normalización, 2013*; *Ferrer et al., 2021*).

The laboratory director, who is well acquainted with the responsibilities and competencies of all the staff members, ensures that everyone is properly assigned and supervised. To ensure the maintenance of competence, all laboratories should have a person responsible for designing a minimum periodic training plan that includes all staff members. This training plan should comprise internal sessions within the laboratories as well as courses provided by scientific societies and congresses.

Calculation of staff size to run an ART laboratory

The number of embryologists necessary for the safe and efficient operation of an ART laboratory depends on the volumes and types of process performed. The increased complexity and time requirements of the latest reproductive

TABLE 1 RESPONSIBILITIES, COMPETENCIES AND TRAINING OF STAFF IN AN ART LABORATORY

Characteristic	Director	Coordinator	Embryologist	Other personnel
Definition	Responsible for all aspects of the laboratory before the legal representative of the centre	Required in laboratories where the volume of work necessitates the presence of additional management positions	Responsible for the daily supervision of the laboratory, following the guidelines described by the laboratory director In charge of carrying out most of the laboratory's daily activities under the supervision of the director and/or coordinator	Collaborates with the embryologist in certain laboratory tasks and carries out routine maintenance tasks under the supervision of an embryologist
Education certification experience	Has a university degree in biomedical sciences Has a Doctorate or Master's degree related to ART Has a clinical embryologist certificate recognized by a scientific society Has at least 6 years' work experience in ART or in the specific area they direct, or has coordinated an IVF laboratory for at least 2 years	Has a university degree in biomedical sciences Has a university Master's degree related to ART Has a clinical embryologist certificate recognized by a scientific society Has at least 3 years' work experience in ART	Has a university degree in biomedical sciences Has a university Master's degree related to ART Plans to obtain a clinical embryologist certificate recognized by a scientific society	Has an advanced training degree as a laboratory technician Has completed the training programme and the required probationary period
Staff	Manages, leads, and motivates staff to create and maintain a competent team Reachable during and outside normal working hours	Communicates with the rest of the team professionals, coordinating laboratory and clinical activities Communicates with patients about biological aspects related to their case Communicates with the laboratory director Communicates with laboratory personnel and clinical colleagues Has teaching and training capacity	Communicates to patients the results of laboratory procedures and the progress of embryonic development	Applies ethics and integrity, critical thinking, good communication within the team, time management and teamwork skills
Administrative	Validates all official documents and data confidentiality Has knowledge of and complies with current legislation Performs valuation of budgets and effective management of resources Conducts agreements with suppliers to guarantee stock service	Coordinates the transport of gametes and embryos between centres	Manages cryogenic containers Maintains an effective record of laboratory procedures Performs administrative tasks and data recording	Applies and maintains an efficient system of laboratory records Actively participates in the quality management system Is knowledgeable about and has the capacity to fill out different laboratory forms Implements budget and cost control measures Receives orders

(*continued on next page*)

TABLE 1 (*Continued*)

Characteristic	Director	Coordinator	Embryologist	Other personnel
Clinics	Conducts the daily activities of the laboratory, having minimum assistance activity Defines the functional organization chart of the laboratory and the organization of the distinct functions and tasks Participates in the configuration of the staff with an adequate number of qualified personnel to cover the workload, ensuring cover for periods of absence to illness or vacation Prepares and conducts periodic reviews of laboratory protocols Authorizes the introduction of any new techniques Applies the quality management system and assigns a person in charge with whom to coordinate it Prepares and reviews the quality indicators of the different laboratory procedures and implements corrective measures in the event of deviant values Ensures that the laboratory has adequate facilities, environmental conditions and equipment, which comply with current regulations in terms of safety, space and cleanliness, as well as their review and periodic verification Ensures the traceability of samples Implements a labour risk prevention and management policy for the laboratory Updates the emergency and contingency plan Notifies clinical data and adverse events in accordance with European and/or national regulations	Conducts the daily activities of the laboratory, having frequent assistance activity Acts as the deputy director of the laboratory, assuming responsibility for different aspects in the laboratory in the absence of the director Oversees all aspects in the laboratory and its services Coordinates the different areas and participates in the planning and management of cycles Organizes daily laboratory work Contributes to clinical decisions in the laboratory following the established protocols and policies of the centre Reviews and updates quality indicators Ensures that all equipment is working properly and that adequate maintenance is performed	Independently performs all routine technical laboratory procedures Manipulates and evaluates gametes and embryos Contributes to the clinical decisions of the laboratory following the established protocols and policies of the centre Solves problems, considering ethical and legal issues Works in conformance with the guidelines of the established quality system Guarantees that all equipment works correctly Follows the work protocols set by laboratory management	Provides support in laboratory procedures Performs environmental quality control Monitors/controls equipment parameters, temperatures, gas supply, monitoring, and filling of liquid nitrogen from banks and tanks Notifies the director/coordinator about any incident Controls stock and ensures correct storage conditions for consumables
Education	Conducts continuous monitoring and evaluation of laboratory personnel Ensures new staff have an onboarding plan Guarantees the continuous training of laboratory personnel Plans and coordinates attendance at congresses and the annual staff training plan Organizes scientific review meetings	Trains, supervises, and evaluates personnel	Keeps up to date with new guidelines and technologies Participates in ongoing professional development Participates in the training of new members or students	Updates training and skills
Research	Actively searches for clinical and scientific updates Initiates, designs, and executes research and follow-up studies with analysis and publication in national or international congresses or scientific journals Processes the applications for funding of research projects and collaboration with external institutions	Proposes, participates in or implements clinical research studies	Proposes or participates in clinical or basic research studies	Supports or participates in any research activity

ART, assisted reproductive technology.

technologies — including intracytoplasmic sperm injection, preimplantation genetic testing and oocyte vitrification — have significantly increased the amount of time required to perform a treatment cycle. The scarce existing research argues that an embryologist can perform 150 IVF cycles a year, which is obsolete and far from the current requirements that specify a minimum of two embryologists (*Practice Committees of the American Society for Reproductive Medicine and the Society for Reproductive Biologists and Technologists, 2022*). However, the IVF cycle number has decreased over time, with the latest publications, that of Alikani and colleagues (*Alikani et al., 2014*) in particular, establishing a maximum of 100 cycles per embryologist. In other words, the work that an embryologist can undertake is exhibiting a downward trend.

To evaluate workload, it is necessary to calculate the number of hours required to perform each process and know the available work time, which is the sum of the hours worked by each embryologist per year. The number obtained determines the staff required to perform all the processes. During 2019 and 2020, a work squad from the ASEBIR Quality Special Interest Group (seven senior clinical embryologists) conducted a multicentre study to evaluate the different processes (comprising multiple activities) performed in andrology, embryology and cryobiology laboratories. Each laboratory process was assigned a unit workload value (hours) comprising the sum of all activities (minutes) within the process (*Veiga et al., 2022*).

The hours required for a laboratory coordinator or director to perform their tasks have not been included in the calculation of staff requirements. Thus, whenever more than two embryologists are needed to manage the workload in an IVF laboratory, the laboratory coordinator or director should also be present to perform their tasks.

Based on the times collected for each activity, a calculator was developed to determine the minimum staff requirements based on the main processes handled by each ART laboratory according to its characteristics, the number of processes performed and the number of hours worked per day. Furthermore, we added the time that it took employees to conduct daily quality control and instrument maintenance that was recommended by Alikani and colleagues (*Alikani et al., 2014*) to the total times obtained for each process (https://asebir.com/cassandra-calculadora-de-rrhh/).

The recommended staffing level for a clinical embryology laboratory is one full-time embryologist per 120 IVF stimulation cycles per year (*Alpha Scientists in Reproductive Medicine, 2015*). However, according to published studies and guidelines, in practice the number of cycles per embryologist ranges from 31 to 344 per year (*Gardner et al., 2014*; *Kovacic et al., 2015*). Based on Cassandra calculations, a full-time embryologist is recommended for every 119/102 IVF/intracytoplasmic sperm injection cycles with TL (Time Lapse) culture (12.5 total hours per cycle) per year, depending on whether they were working for 8 or 7 h/day. For the calculation, the type of process, workload, daily breaks and types of witness used were considered.

In reality, globally comparable standards are needed for those working in clinical embryology. This study and similar ones (*Alikani et al., 2014*) help support the need for standardization. Despite the lack of standardization, the Cassandra platform, unlike the study of Alikani and colleagues (*Alikani et al., 2014*), is not limited to embryology laboratories. In addition, as activities for the development of different processes are usually uniform and the characteristics of the labour laws of each country can be entered into the interactive online platform, it is believed that the calculator can be used to compute the staffing needs of any centre worldwide.

Laboratory structure and equipment

An ART laboratory should provide sufficient space according to the maximum workload and types of sample to be processed, while ensuring optimal and safe working conditions for both staff and biological samples. Aspects that should be considered at the design level are listed below:

(a) Although no minimum area is recommended, at least 15–20 m^2 should be allocated to each laboratory or area, taking equipment dimensions into consideration.
(b) Walls, floors, and ceilings must be made of non-porous, smooth materials free of volatile organic compounds (VOC). Corners must be rounded, and joints must be sealed for easy cleaning.
(c) Warm and adjustable lights must be used. For natural lighting, UV filters should be placed on all windows.
(d) Enough electrical outlets and an available internet connection are necessary for the future increase or redistribution of equipment and furniture if the need arises. The passage of water pipes through the ceiling of the laboratory should be avoided.
(e) Furniture should be made of non-porous materials (e.g. aluminium, epoxy resin, glass, stainless steel) appropriate to support the equipment's weight, avoiding vibrations that could cause errors in operation or accidents.
(f) The area should be sufficiently spacious to house an appropriate air-conditioning and ventilation system with easy access for maintenance technicians because filter changes and periodic inspections are required.

The total laboratory can be divided into the following three areas:

(1) andrology
(2) embryology
(3) cryobiology.

These three separate laboratories can be separated and independent but must be connected by doors or hatches/transfer chambers that allow for the rapid and smooth communication of personnel as well as the safe transport of biological materials during daily work. Access to the ART laboratory must be restricted to authorized personnel, considering the need for a controlled environment, security and confidentiality. The access door system should separate the dirty from the clean area and maintain positive pressure. The laboratory personnel's changing room should be adjacent to the access door or airlock and have separate clean and dirty areas to prevent the entry of polluting agents into the laboratory. Further, annexed areas are described below:

(a) Liquid nitrogen storage and handling area: this should provide sufficient space for cryogenic containers appropriate for the number and types of sample to be stored. The space allocated to this area should allow the safe movement of tanks, samples and

personnel without shocks. The floor must be resistant to liquid nitrogen. The temperature of the storage area for the cryogenic containers should be between 20°C and 25°C to avoid excessive nitrogen evaporation.

(b) Room for medical gases and liquid nitrogen: this should have an uninterrupted medical gas supply system and an alarm system in case of the gas runs out. As both types of gas are potentially dangerous in the event of a leak or during handling, this room should be located outside the laboratory and ventilated. Ideally, it should have access to the outdoors for natural ventilation and to facilitate access during supply. If this room is indoors, it should be equipped with an extraction system that activates in the event of a leak and allows for air renewal.

(c) Warehouse for storing laboratory materials.

(d) Waste warehouse.

(e) Administrative management area for laboratory personnel conducting administrative procedures: this should be separate to avoid interfering with the handling of biological samples and prevent the paper trail from entering the laboratory. However, it must have rapid and fluid access to the laboratory.

ART laboratory equipment

ART laboratories must have the necessary state-of-the-art equipment to ensure that all processes are conducted with maximum safety and quality. Next, the basic equipment recommended for an ART laboratory in accordance with guidelines, standards and recommendations at national and international levels (*Asociación Española de Normalización, 2020*, *2013*; *Bento et al., 2013*; *Gianaroli et al., 2000*; *Human Fertilisation and Embryology Authority, 2019*; *Mortimer et al., 2018*) is described:

(a) General equipment:
- Uninterruptible power supply (UPS) system: UPS batteries should provide sufficient autonomy to avoid an abrupt shutdown of critical laboratory equipment and damage to biological materials in the event of a power failure, and to filter the electrical current, thereby avoiding damage to the equipment itself.
- Uninterruptible medical gas supply system: at least two tanks — with automatic exchange — must be stored for each type of gas used in the laboratory and be connected online. A third unconnected tank is recommended in case of a leak.
- Air purification system: this should ensure the correct environmental conditions and achieve the level of environmental quality required in an ART laboratory as a clean room. The air treatment equipment must comprise an air-conditioning system to control the temperature and humidity, an aeration system to regulate air renewal, and appropriate filtration stages to purify air entering the laboratory.
- Ambient O_2 and CO_2 sensors with visual and audible alarms should be placed inside and outside the laboratory and liquid nitrogen handling area to prevent the suffocation of laboratory personnel owing to O_2 depletion or CO_2 intoxication caused by a possible gas leak. The ambient sensors must be installed according to the manufacturer's specifications, no more than 120 cm above floor level, and no higher than the shoulder level of authorized personnel.
- Central alarm system: all critical equipment (incubators, refrigerators/freezers and cryogenic containers) should be connected to an alarm system that notifies the user of equipment failure, even outside working hours.

(b) Equipment in an andrology laboratory (*Mortimer et al., 2022*; *World Health Organization, 2021*):
- Incubator at 37°C and/or bath at 37° C (an acceptable range and monitoring).
- CO_2 incubator.
- Heated plate.
- Class 10 (ISO 4) or 100 (ISO 5) vertical/horizontal laminar flow cabinet (LFC) or biological safety cabinet (BSC) for handling biological samples.
- Clinical-grade refrigerator (+4°C) and freezer (−20°C) .
- Programmable centrifuge with safety covers.
- Optical microscope with phase contrast (10 ×, 20 ×, 40 ×) and a 100 × immersion objective (not necessarily phase contrast).
- Cell count chamber.
- Manual multichannel cell counter.
- Automatic/mechanical pipettors for disposable serological pipettes.
- Positive displacement micropipettes with capacities ranging from 2 μl to 1000 μl (e.g. P20, P100, P1000).
- Vortex mixer.
- External measurement equipment: thermometers and gas meter.
- Cryogenic container.
- Straw sealer.

(c) Equipment in an embryology laboratory (*Cairo Consensus Group 2020*; ESHRE Guidelines 2015; *Mortimer et al 2018*; *Practice Committees of the American Society for Reproductive Medicine and the Society for Reproductive Biologists and Technologists, 2022*; UNE 179007:2013):
- CO_2 incubators:
  - Incubators for embryo culture with CO_2 control and, ideally, O_2 as well (low O_2 because of its superiority to high O_2 for embryo culture).
  - CO_2 incubator for equilibration with the gaseous environment of the culture media.
- Sample handling must be carried out under appropriate environmental conditions as established by current environmental quality regulations, through the use of laminar flow or BSC.
- Micromanipulation station:
  - Inverted microscope with phase contrast (10 ×, 20 ×, 40 ×) or Hoffman modulation contrast, Nomarski-type inter-differential contrast or differential interference contrast.
  - Adjustable heated stage.
  - Two motorized micromanipulation systems.
  - Two manual hydraulic air or oil microinjection systems.
  - Anti-vibration table or support.
- Follicular aspirator (vacuum pump) with adjustable pressure.
- Thermo-blocks for tubes and dishes.
- Incubator.
- Refrigerator (+4°C) clinical grade.
- Freezer (−20°C) clinical grade.
- External measurement equipment:
  - Thermometers with surface and immersion probes.
  - Gas meter (CO_2 and O_2).
  - pH measurement equipment.
  - Monitoring systems and continuous control of parameters (temperature, CO_2 and O_2) for critical equipment.
- In addition, other recommended equipment according to techniques is needed.
- Equipment should include an incubator for transporting non-cryopreserved biological materials at a controlled temperature.

- Equipment in case of embryo biopsies for preimplantation genetic testing (*ESHRE PGT Consortium and SIG-Embryology Biopsy Working Group et al., 2020*) should also be included:
  - Laser system adapted to the micromanipulation station.
  - Class II type A BSC with UV light for intubating blastomeres/trophectoderms.
  - Extraction hood located in a separate room with an appropriate vapour extraction system to fix the blastomeres or spermatozoa for fluorescent in-situ hybridization.

(d) Equipment in a cryobiology laboratory (*European Directorate for the Quality of Medicines & HealthCare, 2022*):

- Specific BSC for cryopreservation with temperature control and shutdown options (which can be placed in the embryology area).
- Materials for handling samples in liquid nitrogen (tweezers and tongs) and personal protection equipment (PPE).
- Cryogenic label printer.
- Storage and identification materials for samples resistant to liquid nitrogen, such as markers and cryogenic beakers.
- Appropriate cryogenic containers to store samples at below −150°C (which should have a double metal wall with an air chamber between the two, sealed under vacuum; *Schiewe et al., 2019*).
- Container types include the following:
  - Storage containers for cryopreserved biological materials (separate containers are recommended for storing gametes and pre-embryos).
  - Liquid nitrogen storage containers.
  - Specific sample transport containers with temperature control.
  - Quarantine containers for samples with unknown serologies or for results deferred after processing.
  - Sample containers from serodiscordant patients.
- Transfer system connected to the liquid nitrogen storage containers.
- Continuous monitoring of temperature and/or liquid nitrogen levels in all containers containing cryopreserved biological materials: the system should alert staff even outside business hours. In the absence of an automated system, the nitrogen level should invariably be visually checked to determine signs of vacuum loss over time and container deterioration. This information is also crucial for potential legal claims).
- Other recommended equipment according to the techniques used:
  - A reserve cryogenic container or sufficient space in the rest of the cryogenic storage containers to house samples in case of the need to empty one of them in an emergency owing to damage.
  - Specific sealer for closed oocyte/embryo vitrification devices.
  - Automated filling system for cryogenic containers (used in high-capacity cryogenic containers).

For all critical equipment, a replacement or a protocolized work procedure that details how to act in case of failure is necessary. Equipment failure should be prevented to avoid affecting the viability of biological materials.

In terms of equipment control (*Cairo Consensus group, 2020*):

- All equipment must have the CE (Conformité Européene) marking, and the medical device type should be indicated.
- New or repaired equipment should be validated before use.
- Records of all laboratory equipment containing the following details should be available:
  - Unique code per equipment.
  - Type of equipment, brand, model and serial number.
  - Location.
  - Date of registration and discharge, if applicable.
  - Identification of critical equipment.
  - Technical service.
- An annual preventive maintenance plan should be defined for all laboratory equipment.
- External measurement equipment should be calibrated by an external accredited company.
- The working range, tolerance and maximum admissible uncertainty of the appropriate equipment should be defined.
- The manual for equipment use must be in the local language.
- Critical equipment should be identified, with the control and safety guidelines described for each item.
- Equipment requiring a certified external measurement control and alarm system should be determined.
- Breakdowns and repair of critical equipment should be recorded.
- Equipment and registry cleaning protocols must be established.

Environment and air quality in the laboratory

The Spanish Association for Standardisation includes, among its normative documents, the UNE standards. In 2020, the UNE 171340:2020 standard for validation and qualification of controlled environment rooms, which applies to ART laboratories, was updated (*Asociación Española de Normalización, 2020*) as follows:

- A clean room or controlled environment room is one equipped with the necessary facilities and structures to control environmental contamination in general and biocontamination within levels that do not affect the processes, gametes or embryos managed therein. A protected or work area is one that includes the work area and area for handling gametes and embryos, culture dishes, equipment and other sterile materials, as well as personnel equipped with appropriate clothing (*Pastor, 2012*; *Veiga et al., 2021*). The UNE 171340:2020 standard classifies controlled environment rooms into five risk levels based on the values of their environmental parameters, requiring a medium risk (type 3) for conventional outpatient operating rooms (for follicular puncture), which corresponds to ISO 7 in operational rest or ISO 8 in operation (*Asociación Española de Normalización, 2020*). Annex 2 of the standard describes the specific requirements that must be fulfilled for an ART laboratory (**TABLE 2**).

In an ART laboratory, in addition to environmental and biosafety aspects, VOC must be controlled because of their embryotoxic potential (*Mortimer and Mortimer, 2015*; *Mortimer et al., 2018*). Three sampling methods are outlined in the standard. Any of these methods is equally valid, and certification of the controlled-environment room must be conducted at least once a year (*Veiga et al., 2021*). To provide more information regarding the types of VOC present and locate their source, a species by species analysis (high-performance liquid chromatography/gas

TABLE 2 ENVIRONMENTAL REQUIREMENTS THAT ART LABORATORIES SHOULD COMPLY WITH

Room parameters	IVF laboratory	Andrology and cryopreservation laboratory
ISO classification room based on ISO 14644-1	≤ISO 7 (operational standby): <352.000 particles measuring <0.5 μm, or <2.930 particles <5 μm/m^3 air ≤ISO 8 (working): <3.520.000 particles measuring <0.5 μm, or <29.300 particles <5 μm/m^3 air, measured in every sampling place	
Temperature (°C)	20–26	
Relative humidity (%)	45–55	40–60
Differential pressure (Pa)		>6
Air renewal	≥15	≥10
Biocontamination Aerobic mesophilic (CFU/m^3) Fungi and yeast (CFU/m^3)	 <100 (operational standby) <150 (working) Absence	 <100 (operational standby) <150 (working) <10 (without pathogens)[a]

Cairo consensus on the IVF laboratory environment and air quality (*Mortimer et al., 2018*) accepts <352,000 particles >0.5–10 μm/m^{3}as a normal value (equivalent to <10,000 such particles per cubic foot).

Installation in rest mode: this can be in operational mode (complete installation, with equipment installed and working, but without personnel present) or in standby mode (the same as operational mode but adjusted to the minimum to ensure an acceptable degree of biosecurity and minimize energy consumption).

Installation in operation mode: installation operates in a specified manner, with a specified number of persons present and working in a prescribed manner.

Pressure differential: 15 Pa is between two rooms; the Cairo consensus recommends a total differential of 38 Pa, and the EU recommends 30 Pa (not written in the EU GMP, Good Manufacturing Practice but deducible from the recommendations to have 10 ± 5 Pa between rooms with the need for an anteroom before the IVF laboratory).

Renewals/h: the quotient between the flow of outside air in m^3/h introduced into the room and the volume of the controlled-environment room in m^3.

[a] CFU: a particle that carries a viable microorganism capable of forming a colony in the culture medium. The following genera are considered pathogens: *Aspergillus*, *Rhizopus*, *Mucor* and *Scedosporium*.

ART, assisted reproductive technology; CFU, colony-forming unit; EU, European Union.

chromatography–mass spectrometry) is recommended to help deal with the risk of chemical pollution.

TABLE 3 defines the VOC sampling methods and permitted limits according to UNE 171340:2020/Annex 2 standard and the Cairo Consensus (*Asociación Española de Normalización, 2020*; *Mortimer et al., 2018*).

Culture media and consumables

The culture media must be controlled by following the processes outlined below (Cairo *Consensus Group 2020*; *Ferrer et al., 2021*; *Mortimer et al., 2018*):

- Verify the temperature and integrity of the package at the time of receipt of the media and ensure that the temperature is maintained within the appropriate range using continuous measurement systems during storage in the laboratory.
- Record the expiration and opening dates of batches and/or vials, and consider manufacturers' recommendations regarding stability once a vial has been opened.
- Avoid exposure to light during storage.
- The following are crucial during the preparation of culture dishes:
  - Air out the dishes for at least 24 h to avoid VOC.
  - Follow the equilibration time before use that is recommended by the manufacturer.
  - Avoid preparing multiple dishes simultaneously; prepare them on unheated surfaces and cover them with oil to avoid changes in osmolality (*Swain et al., 2012*).
- For optimal embryonic development, maintain a stable temperature, pH and osmolality, and avoid VOC. The following are crucial during this period:
  - Use the most appropriate type of oil depending on the type of incubator to minimize evaporation of the medium during culture and large

TABLE 3 SAMPLING METHODS FOR VOC AND PERMITTED LIMITS IN ACCORDANCE WITH UNE 171340:2020/ANNEX 2 STANDARD AND THE CAIRO CONSENSUS

Sampling method	Limit	Reference
A. Uptake on an adsorbent tube connected to a low-flow pump and subsequent gas chromatography (*Asociación Española de Normalización, 2019*) B. Photoionization detectors or equivalent methods with a detection limit of 10 μg/m^3 of air C. Passive uptake, quantitative scanning by thermal desorption, and subsequent GC/masses	[VOC] indoor <1% VLA [VOC] indoor < [VOC] outdoor [Total VOC]: 200 μg/m^3 (isobutylene as standard) <5 μg/m^3 referenced to aldehydes	*Instituto Nacional de Seguridad y Salud en el Trabajo (INSST), O.A., M.P (2019)*
	[Total VOC]: 500 μg/m^3 (isobutylene as standard) <5 μg/m^3 referenced to aldehydes	Cairo consensus (*Mortimer et al., 2018*)

ELV: environmental limit values, which are the reference values for concentrations of chemical agents in the air and represent conditions to which most workers may be exposed daily throughout their working life without adversely affecting their health.

GC, gas chromatography; VOC, volatile organic compound.

temperature fluctuations. Avoid overfilling to prevent the oil from sealing the lid of the dishes and interfering with gas exchange (*Mestres et al., 2022*).
- Keep the work surfaces for culture dishes heated and controlled to avoid temperature fluctuations.
- Use activated carbon filters with potassium permanganate in the gas lines that enter the incubator to ensure the absence of VOC.

Like the culture media, fungible materials must be controlled by following the process outlined below:

- Place storage consumables outside the laboratory to avoid negative effects on the air quality inside the laboratory. To avoid fungal contamination, do not bring packaging, especially cardboard, to the ART laboratory.
- Whenever possible, use embryo-tested dishes and tubes.
- Use single-use, sterile, CE-marked and embryo-tested materials.

Maintenance

More than 200 laboratory variables — including equipment, consumables, environmental conditions, work protocols and personnel — can influence the results of an IVF cycle (*Pool et al., 2012*). Therefore, an inventory of all equipment and a plan for its maintenance, verification and calibration must be prepared. The periodicity of the plan is established for each piece of equipment according to its criticality for the process to be conducted, its degree of use, previous actions performed and recommendations included in the technical sheet.

Variables affecting measurements include the following:

- Temperature.
- Types and brands of culture dish.
- Altitude, measurement and adjustment of CO_2 and pH.
- Devices and measurements with acceptable measurement uncertainty.

For all of these, the criteria for acceptance of the measures should be defined and the results recorded. The equipment that should be subject to a verification or calibration plan is described in the tables of Annex 7 of the supplementary material of the Clinical Embryology Notebook Recommendations on Human, Physical, and Quality Resources (*Ferrer et al., 2021*; https://asebir.com/cuadernos/11-recomendaciones.pdf). An effective maintenance programme ensures a high performance, few breakdowns, low repair costs and minimal premature replacement of equipment (*de Monserrat Vallvé et al., 2014*; *Ferrer et al., 2021*; *Jiménez et al., 2019*).

Critical equipment (BSC, LFC, incubators, microscopes, heated surfaces, refrigerators, freezers, automated freezers) must be connected to a UPS system.

As a minimum requirement, the following control parameters must be controlled and recorded:

- Temperature.
- CO_2 and/or pH in incubators.
- Liquid nitrogen levels in cryopreservation containers.

At least one device should be available for the direct measurement of the CO_2 percentage, and one for temperature measurement — calibrated annually by accredited laboratories with calibration certificates and minimum uncertainty values. For all of them, the criteria for acceptance of measures must be defined, and records of the results should be maintained.

For laboratory equipment, the tolerance limits of the measurements should be defined and should not exceed the limit set by the manufacturer. The results of the verification and calibration of the measuring equipment should be recorded.

Moreover, a critical equipment plan is necessary. At least annual preventive maintenance (internal or by an external company) should be conducted for the equipment in accordance with the manufacturer's instructions; corrective maintenance should be performed when an anomaly is detected in any equipment.

Calibration of measuring equipment

The thermometers, gas meters and probes of the continuous monitoring system should be periodically calibrated, and controls should be recorded. The company that performs the external verification or calibration of the equipment should state the inventory code of the equipment on a label.

In the case of verification, a report should certify that the equipment or measurement system works correctly and meets specifications. The maintenance procedures and their records should be defined in a document that allows an exhaustive evaluation of any problems that may arise and should be available for review throughout their use.

Cleaning and waste management

At the entrance to the controlled environment areas of the ART laboratory, staff must do the following:

(a) Use appropriate clothing:
  - A clean scrub suits or single-use disposable gown with closure at the back.
  - A hat that completely covers the hair.
  - Clean surgical shoes or clogs.
  - A mask.
  - Clothing that covers cuts, burns or skin lesions.

(b) Wash their hands before entering the clean room.

(c) Use PPE when handling biological samples:
  - Gloves.
  - A mask covering the nose, mouth and chin.

Cleaning, disinfection/sterilization procedure

Cleaning and disinfection procedures should be included in the SOP and be approved by the laboratory director.

For proper disinfection/sterilization of medical devices (*Official Journal of the European Union, 2017a*, *2017b*; *Rutala et al., 2008*), the following are necessary:

(a) Cleaning with automatic machines or manually.

(b) Disinfecting with sanitary products.

In an ART laboratory, cleaning/disinfection should be manual and always conducted after the use of material/equipment or at the end of the working day. For high or difficult-to-access areas, disinfection by air using H_2O_2 nebulization techniques is recommended, as is performance in cabinets. A record of cleaning zones/areas/equipment with the date and time of cleaning and the person(s) who performed it (initials of the names and surnames, as well as the signatures) should be kept.

Waste management

Protocols for the classification and management of biological waste should be established by law in each country (*Instituto Nacional de Seguridad e Higiene*

en el Trabajo, 2009a, *2009b*; *Official Journal of the European Communities, 1994*) and made available to staff. However, depending on specific regulations, the containers used for the collection of waste from separate groups must be adequately marked.

In all ART laboratories, the waste management plan should be formulated as an SOP. Technical criteria for waste management should be established based on the legal framework, and a management plan specific to the laboratory's activities should be designed. Effective segregation should be conducted at the point of production following the established classification. Biological waste is usually classified into two large groups according to its associated risks (FIGURE 1).

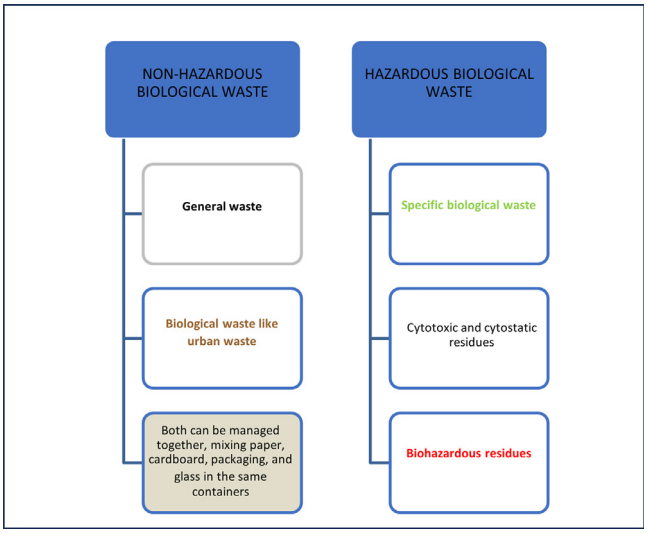

FIGURE 1 Waste grouped according to risk. General waste: paper, cardboard, packaging, food scraps, plastics in **black bags** in a brown/ grey container.
Biological waste such as urban waste:
– Printer toner cartridges: specific cardboard boxes with **brown bags**.
– Mixtures of edible oils and water: **blue container** with metal spring ring closures.
– Clothing and textiles, waste metal, non-hazardous electrical and electronic equipment.
Specific biological waste:
– Low liquid content: gauze, tape, bandages, sharp objects, serum systems, probes, gloves, mineral oil with culture medium, seminal preparation in **green bags**, using trash cans as a base in a brown/ grey container.
– High liquid content: urine bags without an emptying system, aspiration systems, blood/urine tubes or bottles, urine bottles with non-bloody follicular fluid in green containers with **green bags** with a self-closing system.
Cytotoxic/cytostatic residues (not generated in assisted reproductive technology laboratories) in **blue containers** with an airtight closure and a specific label.
– Biohazardous residues:
– Biological remains (semen) from patients with infectious diseases, containers with blood (bags, tubes, urine bottles with follicular fluid) in **red bags** with a self-sealing system in reusable black containers with a non-hermetic closure.
Sharp items in **yellow safe boxes**.
– Minor human remains such as testicular and ovarian tissue, and placentas placed in **blue containers** labelled 'biological for incineration'.

Traceability and control of stocks and expiration

A person should be responsible for the stock control of media and consumables, and their traceability, and the following should be recorded:

– Batch opening and end dates as well as the person responsible.
– Treatments wherein the batch is used.
– Stock and expiration dates of culture media and consumables used for handling gametes and embryos.

These materials should meet the appropriate specifications for use in humans and, in Europe, carry the CE mark. Similarly, continuous availability of stocks must be ensured following the scheduled activity. Laboratories should have an SOP and the necessary records regarding how these procedures are performed.

Quality management

According to European directives and recommendations (*ESHRE Guideline Group on Good Practice in IVF Labs et al., 2016b*; *European Directorate for the Quality of Medicines & HealthCare, 2022*; *Official Journal of the European Union, 2006a*, *2006b*), the implementation of a QMS is mandatory in units in assisted human reproduction centres. This system should have all the critical aspects under control, and its implementation should offer an effective, efficient and safe provision of services; satisfy patients' needs and expectations; comply with medical and scientific standards, legal obligations and ethical codes; and protect the rights of all parties involved (including children born using RHA (Assisted Human Reproduction) techniques). The system to be implemented is specific and unique to each centre, but should include and develop the following:

– A quality policy involving all areas, objectives and resources.
– Quality objectives with clear and defined deadlines that integrate human resources, facilities, technology, economic planning and the definition of actions aimed at achieving them.
– Quality planning. The organization should:
  • Appoint a person responsible for quality management.
  • Describe the responsibilities and promote the commitment and participation of all team members.
  • Guarantee sufficient personnel for QMS implementation.
  • Guarantee resources for quality training and the implementation of new techniques.
  • Participate in the creation of objectives and definition of actions.
  • Schedule periodic reviews of quality management, evaluation of the degree of compliance, and QMS effectiveness.

Different tools enable allow the goals of quality management, quality cycles and risk management to be achieved.

Quality management

This integrates three key activities – quality control, quality assurance and quality improvement (*Mortimer and Mortimer, 2015*). It should be implemented in both processes (set of related or interacting activities that transform input elements into results) and systems (several

TABLE 4 FACTORSTO ENSURE AN EFFICIENT QUALITY MANAGEMENT SYSTEMS

Human resources	Organizational chart, definition of jobs and defined responsibilities
	Qualified and competent personnel
	Continuous training and accreditation
Environmental or physical factors	Design of facilities and laboratories
	Equipment: choice of equipment; maintenance, calibrations and verifications
	Culture conditions: temperature, CO_2, pH, humidity and osmolality
	Culture media and fungible materials: they must be of guaranteed quality
	Environment and air quality
Methodology	Election of appropriate standard operating procedures, writing all instructions for each process
	Complete identification and traceability of the cells, materials, equipment and personnel involved in laboratory activities
	Communication with patients: have established operational guidelines
	Guidelines for cleaning and waste management
	Research, ethics and code of good practices
Security	Risk management systems
	Contingency and emergency plans
	Biological safety and biomonitoring
Quality	Management and quality control
	Analysis of indicators and establishment of reference values
Documentation and records	Laboratory and centre databases
	Technical bulletins
	National and international registration

processes methodically related and organized). Examples of QMSs include the processing of maps, SOPs, and indicators.

Quality cycle

The Deming cycle comprises four stages ('PDCA'): Plan, wherein objectives are planned, and the necessary resources are defined and chosen; Do, wherein the plan is implemented; Check, wherein the result is verified; and Act, wherein decisions are made, or actions executed. This cycle allows for continuous quality improvement.

Risk management

Prevention activities should be developed to eliminate or reduce all types of risk. Risk management allows a guarantee of the efficiency, safety and quality of the procedures, as well as the identification of opportunities for improvement. Different risk management tools include failure mode and effect analysis, root cause analysis and the 'SWOT' (Strengths, Weakness, Opportunities, and Threats) matrix.

An ART laboratory should develop emergency and contingency plans that are reviewed, periodically updated and made available to all members of the laboratory. A QMS should be implemented by applying good practices, which ensure the uniformity and repeatability of an auditable system with consistent and precise results. Therefore, the skills of the personnel and culture conditions should be maximized, and the key aspects to control should be selected to optimize the laboratory. TABLE 4 presents the key points to be considered.

Use of indicators for continuous quality improvement

Laboratory quality management is performed by applying tools such as benchmarking. This technique compares the results of laboratory's own indicators with those of reference indices to determine the state of the laboratory and, if necessary, introduce improvement guidelines. The practice of this continuous measurement technique helps the laboratory manage risk, avoid serious failures and perform better.

Different types of indicator should be included and monitored: programme indicators, laboratory indicators, efficiency indicators, best practice indicators, laboratory operations indicators and financial indicators. Sentinel indicators are important to detect adverse events (*Hammond and Morbeck, 2019*).

The indicators selected must be described, including their formulas, exclusions and review periodicity (*Asociación Española de Normalización, 2013*; *Bento and Esteves, 2016*; *Mortimer and Mortimer, 2015*; *Sánchez et al., 2021*). Ranges, reference values and the sources/publications from which they are obtained must be defined (*Alpha Scientists in Reproductive Medicine, 2012*; *ESHRE Clinic PI Working Group et al., 2021*; *ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine, 2017*).

ASEBIR uses the limits defined by the Spanish Association of Pharmaceutical Analysts to calculate analytical quality specifications, describing three levels of specification, namely, minimum, desirable and optimal (*Ardoy et al., 2016*). ASEBIR publishes updated standard values of the indicators extracted from the data presented annually in the National Activity Registry. These data are published on the ASEBIR website (https://asebir.com/grupos-de-interes/grupo-de-interes-de-calidad-del-laboratorio-de-reproduccion-asistida/). If a laboratory has an indicator for which reference values have not been published, these should be defined based on the centre's previous experience.

The frequency of calculation and review of indicators, including the type of centre and number of processes and techniques, must be programmed. Additionally, relevant results should be recorded. A computer system that allows the automatic extraction of indicators from the database itself should be available. This would include file cards for each indicator, with its characteristics, reference values, historical results and graphs, allowing for quick periodic analyses.

The person in charge of quality should analyse the results, compare them with the usual ones from the laboratory and the reference values, evaluate the situation, detect trends and outliers, and determine

whether guidelines must be applied. If improvements are introduced, they should be described and registered, indicating when they will be implemented. After a specified period, the results should be verified, and it should be decided whether the adopted measures are appropriate (Deming cycle).

Biological safety and occupational risk recommendations

Biological security is defined as a set of technologies and preventive measures aimed at preventing exposure to biological agents and toxins or their involuntary release. All ART laboratory personnel must be familiar with the security policies and processes.

The recommendations listed below are based on European and international standards (*Asociación Española de Normalización, 2013*; *Castilla and Magán, 2003*; *European Directorate for the Quality of Medicines & HealthCare, 2022*; *Ferrer et al., 2021*; *Hughes, 2012*; Practice Committee of the American Society for Reproductive Medicine and Practice Committee of Society for Assisted Reproductive Technology, 2008):

- Ensure that the clothing of personnel entering the laboratory is appropriate for exclusive use. Use scrub suits, gowns, clogs with non-slipped soles, disposable hats and masks that cover the mouth and nasal mucosa.
- Do not wear hand accessories (watches, rings or bracelets).
- Avoid the use of contact lenses to be able to wash your eyes in case of splashes.
- Wash hands with liquid antimicrobial soap (VOC-free) on entering the laboratory, after removing gloves and on leaving the laboratory.
- Laboratory personnel should have appropriate primary containment barriers, such as PPE and BSC. These elements should be readily available, appropriately used, and controlled.
- Liquid nitrogen handling necessitates PPE, which includes gloves to protect against the cold, aprons, safety glasses and non-slip clogs without holes.
- Filled cryogenic containers should have liquid nitrogen transfer heads or a tilting trolley to avoid excessive effort.
- All laboratory personnel should be trained in handling liquid nitrogen.
- Offer laboratory personnel a hepatitis B vaccination plan and annual medical check-ups with serological testing.
- Prepare a safety manual and conduct other training activities to provide tools to avoid contagion, standard precautions for handling samples, and basic notions pertaining to the management of biological waste.

Facilities and equipment related to risk prevention

- Access of personnel to the laboratory should be restricted.
- All entrances to the laboratory should have biohazard signage and an alert for the appropriate use of clothing.
- Gas and liquid nitrogen rooms should have suffocation hazard signs and require the use of appropriate PPE.
- Ambient O_2 and CO_2 sensors with visual and audible alarms should be installed inside and outside the laboratory, with visual and audible alarms.
- Emergency equipment — specifically, first-aid kits and fire extinguishers — must be used to prevent fires.
- Faults detected in the equipment should be immediately reported to the laboratory director.
- Conditions of air-conditioning, noise (<65 dB), light and accessibility must be established for each work area, complying with the requirements for an ART laboratory. A temperature regulation system that allows temperatures of 19–26°C and warm adjustable light sources (2700–3000 K) must be ensured.
- Appropriate furniture should be provided for the correct ergonomics of workers in each job.

Recommendations regarding the management of biological material (*ESHRE Guideline Group on Good Practice in IVF Labs et al., 2016b*) are listed below:

- Treat all biological materials as potentially infectious and take adequate precautions to avoid contagion when handling blood or body fluids.
- Wear single-use non-toxic powder- and latex-free gloves for handling fluids and culture media. Do not reuse gloves or touch other equipment or furniture.
- Always use a pipetting device. Never pipette via the mouth.
- To avoid injury take special precautions when handling sharps or cut materials contaminated with blood or fluids. Never recap sharps and always dispose of materials in appropriate containers at the end of use.
- Disinfect work surfaces before and after handling biological samples. Use effective and non-embryotoxic disinfectants.
- Do not handle more than one sample (from different patients) within the same work area.
- Minimize the creation of droplets or aerosols during fluid handling processes.
- Handle samples under appropriate environmental conditions (according to current legislation) using an LFC or BSC.
- Screen all donor and patient tissues and fluids for infectious diseases. The type and periodicity of serological studies must comply with current regulations. Follow defined protocols for processing samples according to their serological status.

Action against accidental exposure to biological materials

An action protocol against accidental exposure to biological materials should exist and be accessible. Specific medical examinations and adequate working conditions should be provided to workers during pregnancy, the post-partum period and lactation to avoid accidents with biological materials (*Instituto Nacional de Seguridad y Salud en el Trabajo [INSST], 2011*).

Responsibilities related to the prevention of biological and occupational risks

A designated person should be placed in charge of an occupational risk prevention programme. The person responsible for biosecurity should undertake the following:

- Take all necessary actions to correct any security hazards that may exist.
- Ensure that personnel have appropriate clothing, PPE and primary containment barriers and that they are used.
- Ensure that workers receive training on safety procedures at work.
- Understand the protocol for action against accidental exposure to biological materials.

Worker responsibilities include the following:

- Communicating all accidents and damage to the laboratory director.
- Immediately reporting unsafe conditions and procedures to the laboratory director.
- Being aware of the dangers of day-to-day work and adopting all necessary measures to eliminate the risk of accidents.
- Wearing appropriate personal protective clothing and using the necessary equipment, ensuring that it is in a satisfactory condition.

Biosecurity

A person responsible for laboratory biosecurity should be appointed, and the necessary records should be established to guarantee the unequivocal location of the gametes and embryos cryopreserved at the centre from the time that they enter the laboratory until the end of their cryostorage or until their transfer to another centre. The identification of the dish or tube containing the gametes or embryos of a patient must be double-verified, making sure it corresponds with the identification on the cryopreservation security device, and that the samples stored in the cryobank are identified and located. In the case of the transfer of biological samples, custody is transferred to the receiving centre (*Ferrer et al., 2021*).

Transfer and transportation of biological samples

A protocol should be established for the transfer of biological samples between assisted human reproduction centres, and an agreement between authorized centres must be established to preserve the traceability of biological materials in accordance with current regulations (*Buch et al., 2020*). Patients should sign a transfer consent and authorization form at the issuing centre and should be informed of the risks associated with transport. It is recommended to use an authorized and certified company that can conduct the transport of biological materials in accordance with current regulations. For the transfer and transport of reproductive biological material to another centre, relevant information on the cycle must be provided, and current regulations must be followed (*Ferrer et al., 2021*).

CONCLUSIONS

This paper collates already published guidelines, recommendations and standards related to the operation of a human IVF laboratory in terms of minimum requirements, laboratory structure and equipment, taking into account the main and annexed areas, culture media and consumables, maintenance, cleaning and waste management, traceability and control of stocks and expiration, quality management, use of indicators for continuous quality improvement, biological safety and occupational risk recommendations, biosecurity and the transfer and transportation of biological samples.

Taken together, the key aspects covered aim to help IVF laboratories minimize risk and ensure the safety of gametes and embryos.

DATA AVAILABILITY

No data was used for the research described in the article.

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AUTHOR CONTRIBUTIONS

Conception and design of the work: C.O., E.V., L.S., E.F., N.O., A.M., M.F., L.M., M.L. L.R. and M.I. Systematic literature search, selection, and analysis: C.O., E.V., L.S., E. F., N.O., A.M., M.F., L.M., M.L.L.R. and M. I. Data review: C.O., E.V., L.S., E.F., N.O., A.M., M.F., L.M., M.L.L.R. and M.I. Manuscript and figure preparation: C.O., E.V., L.S., E.F., N.O., A.M., M.F., L.M., M.L. L.R. and M.I. Manuscript review: C.O., E. V., L.S., E.F., N.O., A.M., M.F., L.M., M.L.L. R. and M.I. All authors have agreed to the final version of the manuscript.

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