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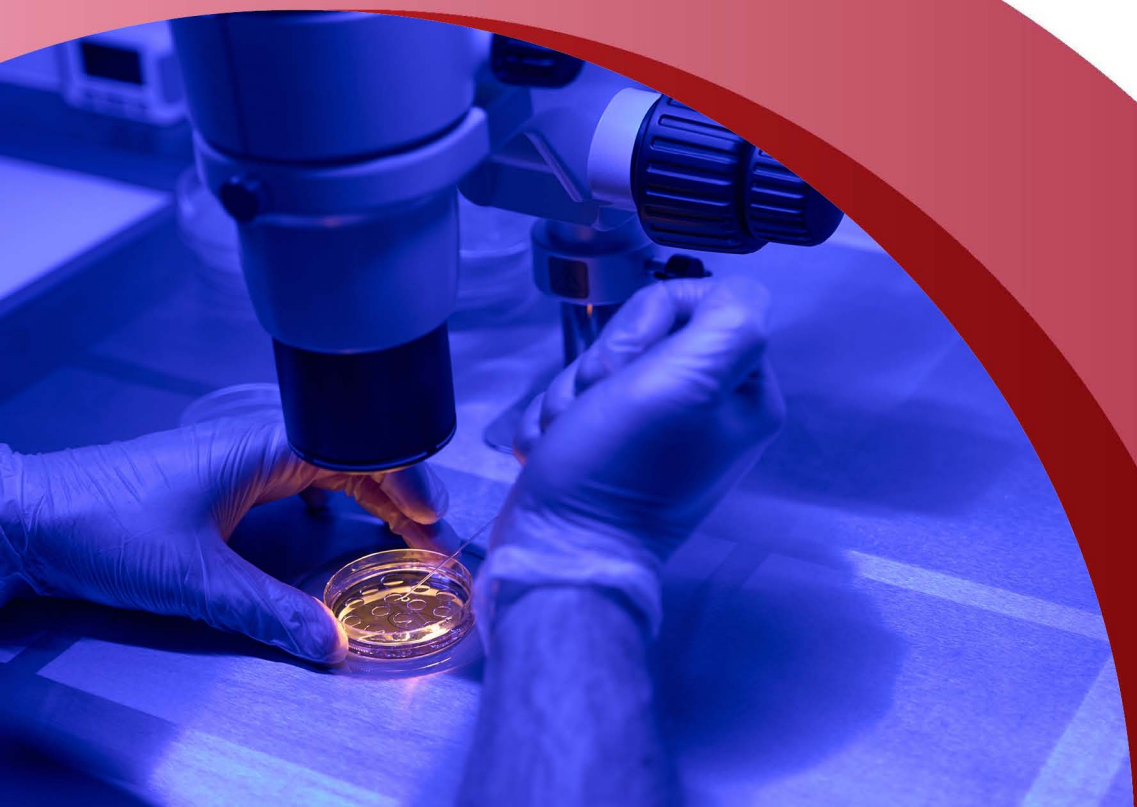
Quality Control in the Assisted Reproductive Technology Laboratory

Durai P



Quality Control in the Assisted Reproductive Technology Laboratory

This book provides an overview of quality control in ART laboratories. It explores frameworks and essential tools necessary for effective quality management. The fields of monitoring, equipment maintenance, and the intricate aspects of embryo care and cryopreservation are thoroughly examined. The significance of the ART lab witnessing system is highlighted, demonstrating the seamless integration of both manual and electronic witnessing tools. Readers will gain insights into the roles played by KPIs and SOPs. For aspiring embryologists, this guide offers an exploration of training techniques, addressing the inherent challenges of the field. Practical coping strategies are provided to help navigate these stressors successfully.

With real-world case studies and discussions on laboratory design, this resource serves as a guide to achieving excellence in ART. It emphasises the importance of balancing patient care, procedural accuracy, and practitioner well-being.

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Dedicated to patients who are bravely facing the challenges of infertility,

and to all the embryologists and clinicians who work

tirelessly to make patients' dreams come true.

Contents

Preface

The rapidly evolving field of assisted reproductive technology (ART) has been a beacon of hope and possibilities for countless couples struggling with infertility. The history of ART dates back to the birth of the first "test-tube baby," Louise Brown, in 1978, marking a milestone in the successful application of in vitro fertilisation (IVF). Since then, ART has undergone significant advancements, encompassing a range of techniques. As ART labs continue to innovate, maintaining high-quality standards and adhering to best practices becomes increasingly crucial.

Quality Control in Assisted Reproductive Technology Labs is a comprehensive guide designed to provide embryologists, clinicians, lab technicians, and other stakeholders with an in-depth understanding of the quality control measures required in IVF labs and practical guidance on their effective implementation.

Drawing on real-life case studies, examples of logs and SOPs, and lessons learned from mishaps in IVF labs around the world, this book highlights the importance of quality control and offers practical insights and strategies for enhancing the efficiency and overall performance of ART labs. By focusing on both the technical and human aspects of quality control, this guide aims to equip readers with the knowledge and tools needed to consistently deliver the highest standard of care.

The guide provides insights into the complex regulatory compliance landscape, with an overview of ART lab regulations from various countries. The diversity of legal frameworks and the challenges faced by professionals working in different regulatory environments are clearly laid out.

The content herein has been carefully curated to empower professionals in the ART field to provide exceptional care to their patients, continuously improve their practices, and drive the field of assisted reproduction forward.

In conclusion, I express my deepest gratitude to everyone who contributed to this project. My profound thanks go to Dr S Vyjayanthi for her instrumental guidance and Dr M. Prasad for generously sharing his scientific insights. I would like to extend my appreciation to the management of KIMS Hospital for their unwavering support. I sincerely thank Robert Peden, the commissioning editor, for his guidance throughout this journey.

I am grateful to my family for their support and encouragement. I also wish to acknowledge the resilience of all professionals and patients in the ART field, whose experiences have greatly enriched this book. Finally, thanks to the entire editorial and production team for their attention to detail, ensuring a high-quality final product.

This book is a testament to the power of collective knowledge and the relentless pursuit of excellence in the field of ART. As we move forward, I hope this resource serves as an essential tool, contributing to this field's continued success and evolution.

1

Introduction to QC in ART Labs

There are three principles in the field of assisted reproductive technology (ART), quality control (QC), quality assurance (QA), and good laboratory practices (GLPs), that serve as the pillars of laboratory operation. The foremost objective of QC is to ensure that laboratory processes and outcomes meet quality standards; this entails monitoring the performance of equipment, handling samples, and thorough testing of products to identify and resolve any potential issues.

On the other hand, QA focuses on maintaining the high quality benchmarks established by QC methods. Key components of QA include developing and implementing standard operating procedures (SOPs), conducting external audits, and regularly evaluating laboratory procedures to identify areas for improvement.

GLPs constitute a framework to ensure the reliability, repeatability, and accuracy of laboratory results. This is achieved through training of personnel, recording of data, and diligent maintenance of equipment. The synergy between QC, QA, and GLP creates a system that enhances accuracy in ART laboratories, strengthening the validation of results.

To ensure the integration of QC, QA, and GLP in ART facilities, it is essential to have defined goals and measurable standards for evaluating performance. The implementation of key performance indicators (KPIs) plays a role in achieving this. By monitoring and assessing KPIs, ART laboratories can pinpoint any issues and take the necessary actions to improve the effectiveness of their processes.

The interplay between QC, QA, and GLP within ART laboratories is crucial for maintaining a quality management system. QC primarily concentrates on monitoring equipment performance and managing sample handling processes to ensure consistency across parameters. Whenever any inconsistencies are detected, QA measures such as audits come into play, facilitating corrective actions to rectify the issues.

Standard operating procedures are the outcome of QA efforts and play a role in bringing uniformity to laboratory procedures. By establishing protocols, SOPs directly contribute to the accuracy and reproducibility of lab results.

GLP specifically emphasises personnel training, ensuring that laboratory staff possess the required skills for their designated roles. Moreover, GLP principles advocate for data documentation and practical storage systems, which ultimately promote accurate results recording.

In the context of ART laboratories, QC serves as an approach to inspecting and monitoring laboratory processes. Its primary objective is to achieve predictable results while minimising errors. The ultimate goal of QC in ART labs is to optimise the success rate of ART techniques and to enhance care. Any inconsistencies or deviations can have consequences for treatment outcomes, impacting the emotional and financial well-being of patients.

Internal quality control (IQC) and external quality control (EQC) play roles in monitoring and assessing laboratory processes. For example, environmental monitoring in ART labs involves checks on air quality, water quality, and surfaces to identify contaminants. Additionally, regular calibration of equipments, assessment of media quality evaluations of personnel competency, and quality control testing are components of QC in ART labs.

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1.1 Schematic Overview

To effectively understand and implement quality measures in an in vitro fertilisation (IVF) laboratory, it is essential to have a comprehensive understanding of the IVF lab process to help identify points and areas where errors may occur during operations.

This schematic approach does not assist in problem-solving; instead, it highlights areas that may require more attention or improvement. By providing a framework for examining the IVF process, it ensures that every step in the process is carefully considered and all possible concerns are adequately addressed (Figure 1.1).

The Role of QC: ART procedures such as in vito fertilisation (IVF), intracytoplasmic sperm injection (ICSI), and preimplantation genetic testing (PGT) are intricate and costly. Hence, a comprehensive QC programme is indispensable for ensuring safety and optimising treatment effectiveness. The key roles of QC in ART labs include safeguarding well-being, enhancing ART outcomes, adhering to regulations and standards, and providing reassurance to patients.

The importance of QC: The significance of QC in ART labs cannot be emphasised enough. Its contribution to achieving ART outcomes is paramount. QC monitors and documents physical and chemical parameters such as culture media to ensure the accuracy of equipment and enable prompt maintenance when necessary. Furthermore, QC plays a role in maintaining laboratory conditions, handling andrology procedures, conducting embryo culture, and selecting embryos for transfer. Adhering to procedure protocols is vital to ART procedures such as IVF and ICSI, where even minor deviations can have a substantial impact on success rates.

The implementation of total quality management systems (TQM) plays a role in an ART lab. TQMS embody an approach that prioritises quality and continuous improvement,

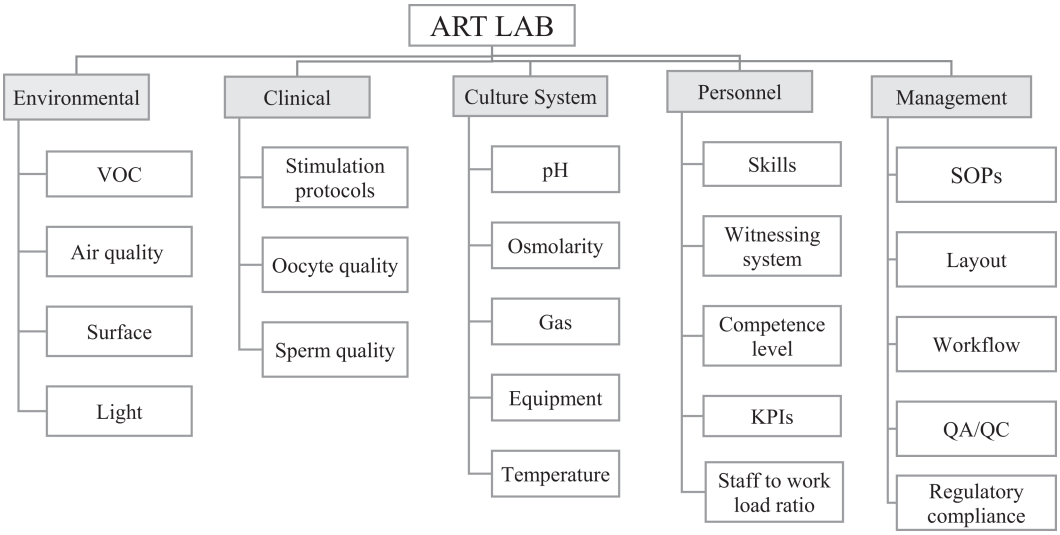

FIGURE 1.1
Schematic overview of ART lab.

involving all levels of the organisation. Within the realm of embryology, TQMS aim to optimise processes from oocyte retrieval to embryo transfer or freezing. This approach emphasises high quality standards, ultimately elevating the success rate of IVF procedures and enhancing satisfaction. Integrating TQMS within ART labs is not merely a luxury—it is an imperative. It guarantees the provision of high-quality services to patients, augmenting the likelihood of positive outcomes and upholding the long-term viability of lab operations.

1.2 Regulatory Overview: ART Labs and Embryologists Worldwide

The field of ART continuously offers advanced solutions to couples facing fertility challenges. However, it also raises social and ethical considerations that require careful examination. Key concerns revolve around the misuse or abuse of this technology, limited accessibility due to costs, and the safety implications for both individuals undergoing ART procedures and the children conceived through these methods.

The high expenses associated with ART procedures can lead to limited access to treatment, exacerbating the socioeconomic divide by creating disparities between those who can afford these advanced reproductive treatments and those who cannot. Consequently, the opportunity to conceive children with the help of ART is unevenly distributed among individuals. Furthermore, safety is a concern within the realm of ART, as it encompasses risks such as the occurrence of multiple pregnancies, premature births, and potential long-term health effects on the children conceived through ART.

Non-medical applications of ART, like gender selection or the prospect of creating 'designer babies', are topics of ongoing debate. The underlying concern arises from the possibility of prioritising certain traits over others, a shift that could fundamentally alter societal values and expectations.

It is crucial for the industry to prioritise enhancing the accessibility and affordability of ART while also preventing its medical misuse. When using donor gametes or embryos, it is important to handle considerations like informed consent, privacy protection, and the well-being of individuals who are conceived through donor-assisted procedures with care.

To address these concerns, regulatory agencies and professional organisations have set up guidelines for ART labs. While specific requirements may vary across regions, the overall commitment to maintaining practices and delivering top-quality care remains consistent across the board.

1.3 ART Regulations in the United States of America

The responsibility of overseeing ART in the United States of America (USA) primarily falls on the Food and Drug Administration (FDA). The FDA's role involves monitoring the handling of donor eggs, sperm, and embryos across ART labs and fertility clinics. The FDA's strict protocols aim to guarantee safe treatments. Non-compliance with these standards can lead to fines, licence suspensions, or other penalties, emphasising the FDA's role in upholding the integrity of ART practices.

In addition to the FDA, the Centers for Disease Control and Prevention (CDC) also plays a part in regulating ART in the United States. The CDC reports data related to ART practices nationwide through the National Assisted Reproductive Surveillance System (NASS). This comprehensive data allows the CDC to closely monitor and evaluate ART outcomes. The reports furnish insights into success rates, birth occurrences, and other important statistics. This robust evidence base enables evaluation of the safety and effectiveness of ART procedures. The Society for Assisted Reproductive Technology (SART) is another organisation involved in regulating ART within the community. SART upholds clinical standards by providing guidance to ART clinics and laboratories, thereby ensuring excellence in their practices.

Some places require insurance companies to include ART procedures in their coverage to guarantee that people can receive the treatments they need. Additionally, certain states have put regulations in place to ensure the safety of patients and donors when using donor eggs, embryos, and surrogates. However, the fact that regulations vary from state to state emphasises the need for policies that address insurance coverage for ART.

1.3.1 For Embryologists

In the United States, individuals aspiring to become embryologists typically pursue a bachelor's degree in biology or a related field as a foundation for acquiring the knowledge required for this profession. Specialised training in embryology further hones their skills and expertise. Professional bodies such as the American Board of Bioanalysis (ABB) and the American Association of Bioanalysts (AAB) offer certification programmes to enhance professionalism within the field.

However, regulatory standards for embryologists vary throughout the country, leading to disparities. For instance, states such as New York and Florida mandate that embryologists obtain a licence in order to practice, underscoring the need for regulations that ensure embryologists meet established qualifications and adhere to safety-focused guidelines.

1.4 ART Regulations in Brazil

In Brazil, there is a body called the Federal Council of Medicine (CFM) that provides guidelines for aspects of ART. These guidelines were initially established in 1992 and have been regularly updated to keep up with advances in technology. Clinics offering ART services in Brazil are required to obtain accreditation from the CFM, and it is mandatory for these clinics to adhere to the provided guidelines.

Embryologists in Brazil typically hold degrees in the sciences or medicine and then receive specialised training in embryology or human reproduction. To become certified embryologists, they must meet the requirements set out by the Brazilian Society of Assisted Reproduction (SBRA) or other professional organisations.

1.5 ART Regulations in Europe

Each country in Europe has its own set of rules and regulations for ART; this approach allows countries to adapt their regulations to fit local legal and ethical considerations.

By adopting country-specific regulations, European nations can address the perspectives and values within their societies, ensuring that ART practices are conducted in a way that respects and reflects the context of each nation.

In addition to regulations, pan-European organisations play a role in creating detailed guidelines and recommendations for ART facilities. These organisations are crucial in establishing and promoting procedures and best practices across Europe. They formulate guidelines that ensure the quality, safety, and ethical implementation of ART procedures. They also provide educational programmes and credentials for professionals in the field. Renowned institutions including the European Society of Human Reproduction and Embryology (ESHRE) and the European IVF Monitoring Consortium (EIM) contribute knowledge. It is crucial for ART clinics and practitioners to stay up to date on regulations in their countries to ensure compliance and provide safe and ethical ART services.

In the European Union, there are regulations governing the use of tissues and gametes in ART. The EU's Directive on Tissues and Cells (Directive 2004/23/EC) mandates that ART labs adhere to good manufacturing practices (GMPs) and GLPs. They are also required to maintain records and report any events. Additionally, the European Union stipulates that ART laboratories must comply with ISO 15189, which is a recognised standard for medical laboratories.

Furthermore, there are guidelines provided by organisations such as the European Society of Human Reproduction and Embryology. ESHRE is a body comprising ART clinics and practitioners offering guidance and recommendations for ART clinics and laboratories. It provides directives in areas such as donor gametes, preimplantation genetic testing, and managing stimulation in IVF cycles. It is worth noting that individual countries may have their own guidelines or regulations pertaining to ART practices alongside those provided by ESHRE.

1.6 ART Regulations in France

In France, the French Biomedicine Agency is responsible for overseeing the rules and regulations surrounding ART. They ensure that ART is implemented in accordance with the French Bioethics Law, which establishes guidelines for the use of gametes and embryos. To comply with these regulations, the agency sets standards for ART practitioners, including their training and certification. Quality control measures are also in place to monitor and report on ART procedures and their outcomes. It is worth noting that in France, gamete donations are kept anonymous, and donors are not allowed to make contact with their offspring.

In France, professionals working in the field of embryology usually hold a university degree in the sciences or a related field. Additionally, they undergo specialised training specifically focused on embryology, ensuring that they meet the laboratory standards set in the country.

1.7 ART Regulations in Spain

The Spanish Fertility Society (SEF) is responsible for formulating guidelines for ART applications in Spain.

In Spain, embryologists commonly have a background in biology, medicine, pharmacy, biochemistry, or biotechnology. They also undergo training in reproduction to become experts in this field. Additionally, they have the opportunity to obtain certification through the Spanish Association for the Study of Biology and Reproduction (Asociación para el Estudio de la Biología de la Reproducción; ASEBIR) to reflect their level of professional competence.

1.7.1 For Embryologists

In the United Kingdom, embryologists who work in ART clinics are required to register with the Human Fertilisation and Embryology Authority (HFEA), which serves as the body overseeing ART implementation. These embryologists follow the HFEA Code of Practice, which provides guidelines and standards to ensure quality control and optimal patient care in ART procedures. Typically, embryologists have specialised education and training in embryology. Many also hold a certificate from or are registered with the Association of Clinical Embryologists (ACE).

In Europe, embryologists are expected to have a degree in biology or a related field. ESHRE encourages professionals in the field to enhance their expertise by pursuing certifications. One such certification programme offered by ESHRE is the Certification for Clinical Embryologists (CCE). The CCE programme involves education and training followed by an examination, and it is recognised throughout Europe. This certification validates the competency of individuals working as embryologists. Moreover, ESHRE provides training opportunities to support the growth of embryologists and keep them updated with advancements in reproductive medicine.

1.8 ART Regulations in Australia

In Australia, the National Health and Medical Research Council (NHMRC), a government organisation, closely oversees the application of ART. The council plays a role in providing guidance, funding, and nationwide support for health and medical research.

To operate in Australia, ART clinics must obtain a licence from the Reproductive Technology Accreditation Committee (RTAC) and abide by the standards outlined in the NHMRC's Ethical Guidelines. These guidelines govern the use of ART in both practice and research. Specific regulations are in place regarding the use of donor gametes; these determine how many families a single donor can contribute to and allow donors to set conditions for their gametes' usage. Additionally, individuals conceived through donor gametes have the right to access identifying information about their donors once they reach adulthood.

Regarding surrogacy, Australia permits only those arrangements in which the surrogate receives compensation solely for expenses incurred. Before entering into such an arrangement, both the intended parents and the surrogate must undergo counselling.

ART clinics in Australia have an obligation to report data, including success rates, incidents, and other outcomes, to the Australian and New Zealand Assisted Reproduction Database (ANZARD).

1.8.1 For Embryologists

For those aspiring to be embryologists, it is important to know that embryologists and ART laboratories in Australia adhere to the guidelines of the National Health and Medical

Research Council and the Reproductive Technology Accreditation Committee. To pursue a career in embryology, individuals must hold qualifications in embryology, biotechnology, or a related life science field. Furthermore, they are required to undergo training in embryology, and they may need accreditation from organisations like the Fertility Society of Australia (FSA) or the Australian Association of Clinical Embryologists (AACE).

1.9 ART Regulations in China

The Chinese government has implemented regulations for ART due to the country's population and the challenges associated with infertility. The Ministry of Health and the National Health and Family Planning Commission are responsible for overseeing the practice of ART in China.

To operate in China, ART clinics are required to obtain a licence from the National Health Commission of the People's Republic of China. These clinics must also adhere to the standards and guidelines established by the Chinese Medical Association.

The qualifications for embryologists in China are rigorous. Typically, they are required to hold a degree in life sciences, biotechnology, or clinical embryology. Additionally, they must undergo training in embryology. They must obtain certification from the Chinese Society for Reproductive Medicine or a similar professional organisation.

1.10 ART Regulations in Japan

In Japan, the Japan Society of Obstetrics and Gynaecology (JSOG) plays a role in overseeing assisted technologies like in vitro fertilisation. This organisation establishes guidelines and regulations that clinics and practitioners must follow.

For clinics in Japan that provide ART services, it is necessary to obtain licences and accreditations from the Ministry of Health, Labour, and Welfare. These clinics are obligated to adhere to the guidelines provided by JSOG, which are also mandated by the government. Embryologists in Japan typically have a background in life sciences or medicine and undergo further training in embryology. Certification from JSOG or a similar professional organisation is often a requirement.

1.11 ART Regulations in India

In 2020 India introduced the ART Regulation Bill with the aim of governing ART procedures and the practice of surrogacy. This proposed legislation seeks to establish state boards that will ensure compliance with ART regulations. These boards will oversee ART practices across the country and focus on regulating ART within states.

Under the law, all ART clinics and practitioners are required to register with the national board and undergo inspections to guarantee they meet the standards. The legislation also provides guidelines for the storage and disposal of gametes and embryos, as

well as limiting the number of embryos that can be transferred during IVF treatments. Furthermore, it allows surrogacy for couples who face challenges with conception while strictly prohibiting any form of surrogacy that could lead to exploitation or harm to the women involved.

Furthermore, the ART bill proposes the establishment of a registry and accreditation authority for overseeing ART clinics and banks across the country. Per this law, the regulatory authority is obligated to create and manage a database that includes all ART clinics and banks operating throughout India. This law sets forth rules and regulations for conducting ART procedures in India. The primary objectives are to prioritise the safety and efficiency of these procedures while safeguarding the welfare and rights of both patients and donors engaged in these practices.

In compliance with the legislation governing ART and surrogacy, practitioners in this field must fulfil training criteria. They should hold a degree in embryology, biotechnology, or life sciences. They must also receive training related to ART procedures at clinics that adhere to Level 2 standards; this ensures that these professionals possess the expertise and capabilities to carry out ART procedures with safety and effectiveness.

1.12 The Impact of the ART Bill 2020

The ART Bill 2020 aims to enhance care and minimise risks associated with assisted technologies. A key aspect of this bill is the creation of a database for ART clinics, which ensures consistency in practices and safeguards patient rights.

Quality assurance measures: The bill brings about advancements in the regulation of ART clinics. It sets out requirements that ART clinics must adhere to, such as employing healthcare professionals like medical practitioners, embryologists, and counsellors. Additionally, it emphasises the need for facilities and adherence to safety protocols. By implementing quality assurance checks, ART clinics strive to improve the reliability, accuracy, and safety of their procedures. These measures include monitoring the environment, calibrating equipment, and following maintenance protocols to uphold the standards of ART practices.

Record-keeping obligations: Another important provision in the bill is the requirement for ART clinics to maintain records for a minimum of 10 years. This ensures accountability and transparency, allowing for the traceability of procedures. The bill gives the national authority the ability to inspect these records to ensure compliance and quality control, ultimately safeguarding the rights of patients and donors.

Enhanced accountability for ART clinics: The new legislation places an emphasis on accountability by establishing a board for ART clinics. This regulatory body will oversee the implementation of the law and evaluate the operations of ART clinics nationwide. Its purpose is to promote accountability and ensure that clinics comply with the standards, thus leading to improved patient outcomes.

Patients' rights: One crucial aspect of this bill is the protection of patients' rights. It guarantees that patients have access to counselling services, where they receive information about the outcomes and risks associated with the procedures. The bill

also necessitates consent, ensuring that individuals fully comprehend the implications of the treatments before making a decision. Additionally, it establishes a framework to safeguard the rights and wellbeing of children born through ART procedures.

By encouraging clinics to adhere to regulations, this bill works towards instilling trust in the safety and effectiveness of ART procedures. With a focus on transparency and accountability, the ART Bill 2020 creates an environment where patients feel more assured about the quality of services they receive.

CHAPTER 1

SUMMARY

- Implementing quality control is integral to the operations of assisted reproductive technology laboratories, ensuring the reliability and precision of equipment, processes, and personnel. This commitment to QC helps identify and address potential issues as early as possible, thereby enhancing the overall success rate of ART procedures.
- The emphasis on QC measures contributes to improved treatment outcomes by maintaining stringent standards across all stages of the ART process. It facilitates the execution of each step accurately and efficiently, thus significantly improving success rates.
- A robust QC system is instrumental in building and maintaining patient trust. It guarantees the quality and safety of ART procedures, fostering confidence in the treatments provided.
- Compliance with QC protocols is a key determinant of the regulatory adherence of ART labs. This adherence varies with the jurisdiction and ensures that the labs operate within the bounds of the law.
- QC processes also foster a culture of continuous improvement, with ongoing evaluation and refinement of ART lab practices. This culture of improvement enhances the overall quality of ART procedures and contributes to advancements in patient care.
- Total quality management systems (TQMSs) are indispensable to ART labs, bolstering their quality and success rates. The focus of TQMS on continuous improvement, proficiency testing, and environmental monitoring creates a collaborative atmosphere conducive to the maintenance of high standards.
- The regulatory oversight of ART labs varies on a global scale, reflecting the diverse contexts within which these laboratories operate. The United States observes regulations from the CDC, SART, and CLIA and guidelines from the American Society for Reproductive Medicine (ASRM), while Europe follows guidelines and best practices developed by ESHRE. China's ART labs are governed by the NHC's guidelines, which emphasise personnel qualifications, laboratory conditions, equipment, and quality management systems.

- Australia's ART labs operate under the guidelines established by the FSA and RTAC, focusing on personnel qualifications, laboratory conditions, equipment, and the quality management system. They require proper accreditation for labs to operate.
- Regulatory compliance is paramount for ART labs. It ensures the maintenance of quality and safety standards in assisted reproductive procedures, minimises risks, improves patient outcomes, and fortifies trust among patients and the community.
- The process of regular inspections and evaluations is crucial to upholding high standards in ART labs, promoting a culture of transparency and accountability.
- Despite the differences in regulations for QC in ART labs across the world, the ultimate objective remains universal: to achieve and maintain the highest possible standards in ART procedures. This objective centres on promoting successful outcomes.

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