Ensuring the quality of a test system using the principles of Good In Vitro Method Practices (GIVIMP): A case study of cryopreserved human precision-cut lung slices

A. Ulrey, M. Marimuthu, J. Alvarez, V. Patel, A. Wahab, K. Battle, J. Hughes, H. Behrsing and M. Gaydosh
Institute for In Vitro Sciences, Inc. Gaithersburg, MD

ABSTRACT

Human precision-cut lung slices (hPCLS) are a highly relevant 3-dimensional model of the lung. They offer native architecture and cells of the lung tissue including respiratory parenchyma, small airways, and immune competent cells involved in inflammatory and sensitization processes. The scarcity of human lung tissue available for research and the inability to conduct larger scale testing has limited the use of hPCLS as a test system for routine, high-throughput testing. To overcome this barrier, IVS has refined the methodology behind the cryopreservation, storage, thaw and post-thaw maintenance of human lung slices. As primary tissues have varied quality and responsiveness, a standardized performance characterization (PC) is conducted on all donor batches. To establish credibility for the approach, the principles of the OECD guidance document (No. 286), “Good In Vitro Method Practices (GIVIMP),” were applied. Documentation for 1) Donor batches created (including blinded donor demographics/medical data), 2) hPCLS physical and functional characteristics (e.g., PC data) and storage conditions, 3) recommended thaw and culture protocol, and 4) chain of custody documents relevant to the distribution of hPCLS to other laboratories are maintained. The quality principles of GIVIMP are crucial to the hPCLS serving as a reliable test system for use in repeatable research and regulatory toxicology. With improvements in slice creation, storage, culture conditions, and the quality framework surrounding all of these efforts, the IVS hPCLS can be confidently used for larger scale testing, tissue banking, and repeat donor experimentation while retaining tissue integrity and functionality, both in a research and regulatory context.

STANDARDIZATION AND DOCUMENTATION

In vitro test systems must reliably perform as expected when used in studies. GIVIMP recommends standardizing procedures (Chapter 7), training to the standards (Chapter 2), and documenting that the standards have been followed (Chapter 10). GIVIMP also provides guidance on consideration when optimizing the procedures during the later stages of standardization. IVS meets the recommendations in GIVIMP for cryopreservation of hPCLS activities.

• Step-by-step procedures from procurement of the lung, through preparation of slices and their assessment and cryopreservation, to shipment of the test system to the purchaser are documented in management approved Standard Operating Procedures (SOPs).
• Batch records are available for each lot of tissue that attribute each procedural step to trained individuals and provide traceability to media and equipment used. ALCOA + principles are followed with all paper and electronic based documentation.
• Personal training is standardized and documented in training records.
• Several manuscripts and posters have been published describing the optimization of the precision cut lung slice procedure.

INFORMATION PROVIDED TO PURCHASERS

GIVIMP chapter 1 discusses the responsibility in vitro test system providers have to share information on test system characterization, authenticity, and safe transport, use, and disposal. IVS provides a package of this information to test system purchasers to satisfy the GIVIMP requirements of test system providers.

• Donor information including blinded donor demographics/medical data
• hPCLS physical and functional characteristics of the batch of PCLS (PC data)
• A shipment inventory sheet traceable to the IVS processing batch records
• Training and general culture instructions for the hPCLS
• A shipping checklist to assure all required information is included and serving as a chain of custody document

TEST SYSTEM CHARACTERIZATION AND CONTROLS

Chapters 5 and 2 of GIVIMP discuss measures to improve the quality of the test systems used in in vitro testing. Some of these topics include: cell and tissue sourcing, handling and maintenance of the test system, cryopreservation and storage, contaminant screening, and quality control of test systems. The documentation and procedures in place at IVS surrounding the preparation of hPCLS tissues was assessed against the applicable GIVIMP recommendations. Select points are discussed and examples given below.

• Lungs are ethically sourced through Organ Procurement Organizations. These groups assure donor consent in accordance with federal and state laws through the Organ Procurement Agencies.
• Specific characteristics for the batches of tissues are requested and documented prior to receive of the lungs for processing (see figure below for example).

REFERENCES


