

7. Incidental Findings and Reporting

7.1 Introduction

The PVDOMIC protocol is designed to lead to a comprehensive understanding of patients with pulmonary vascular disease based on phenotypes and endophenotypes. In order to conduct this study, patients, at risk cohort comparators and true controls will be enrolled amongst the centers. All five WHO groups of pulmonary hypertension patients will also be recruited.

Subjects will undergo many tests as part of the study protocol, including but not limited to, overnight sleep monitoring, complete PFTs, echocardiography, cardiac MRI, chest CT, blood work and ventilation perfusion scan. Although these tests are part of a research protocol, they may reveal abnormalities in study subjects. This manual of procedures is designed to discuss the process of the identification of abnormalities and the dissemination of the information so that the patient can be made aware and receive the appropriate clinical work-up and treatment by their clinical health care provider.

7.2 Incidental Findings Discovered at the Center

All subjects that are enrolled in PVDOMICS should identify a primary care provider or primary physician with contact information. This information should be kept in the study binder by the study coordinator. Testing conducted at the site may reveal an abnormality. The clinical site PI or his or her designee will notify the study subject within two weeks unless the finding is deemed critical by the PI, in which case it will be handled as described below. Findings will be highlighted and patients will be encouraged to check with their primary care providers regarding abnormalities. Findings deemed by the PI or designees to be clinically significant will be shared with the patient and primary care providers and other providers as designated by the patient. Critical abnormalities (such as severely abnormal blood tests) will be conveyed to the patient and primary care provider on an urgent basis (within 24 hours).. Although infrequent, an incidental finding may be found in a healthy control subject. The healthy subject will be notified and advised to check with their healthcare provider.

7.3 Incidental Findings Discovered at the DCC

Testing and samples collected at the clinical centers and sent to the DCC will be analyzed as outlined in the Manual of Procedures. Incidental findings that are discovered by Cores at the DCC of the PVDOMICS network will be reported (to the Principal Investigator and lead coordinator at the subject's site using only the subject's study ID. The PI or his or her designee will share this finding with the study subject at their clinical site. These findings will be highlighted and subjects will be encouraged to check with their primary care providers regarding the findings. Critical abnormalities (such as severely abnormal blood tests) will be conveyed to primary care providers on an urgent basis. During certain circumstances, primary care providers and other providers as designated by the patient will receive reports of significant abnormalities.

Results from genetic testing will only be reported if the subject agrees at the start of the study to have these findings reported. Only genetic results related to pulmonary hypertension risk or other clinically actionable genes (as defined by the American College of Medical Genetics) will be reported. The

central core laboratory that is doing genetic testing is a research facility and does not have the ability to provide genetic test results to the subjects. Therefore, the information will be conveyed to the site PI in general terms only. Site investigators will refer the subject to a genetic counselor to discuss options for clinical testing in a CLIA-approved laboratory. The cost of genetic counseling and clinical genetic testing is not covered under the research protocol.

The study site will provide acknowledgement to the DCC of their receipt of an incidental finding. The study site once notified by the DCC is responsible for the subject notification. We cannot forecast what incidental findings may be found on these tests or their clinical significance. That is why this information will be provided to the clinical center Principal Investigator who is familiar with the subject.

7.4 Placement in Medical Records

Many of the studies performed locally at a site will likely be placed into the subject's medical record, which means they would be available to the subjects and their healthcare providers. If an abnormality is found by a PVDOMICS core lab during research analyses, the results will not be placed into the subject's medical record.