5.0. DATA AND INVENTORY MANAGEMENT

5.1. REPOSITORY RECEIPT AND INVENTORY OF NEW SPECIMENS

5.1.1. SWAN Clinic Sites Ship Frozen Samples to the Repository

According to the standard protocol (see Section 4), all seven SWAN clinic sites ship newly collected serum, plasma and urine samples to the Repository (located at Precision Bioservices) on dry ice using FedEx overnight services.

5.1.2. Repository Facility Receives and Inventories New Specimens

The Repository facility, Precision Bioservices, receives the shipments and follows procedures found in proprietary Standard Operating Procedures (SOPs) of Precision, specifically SOP25220 (Receipt of Incoming Frozen Samples) and SOP25330 (SWAN Study Specific Information).

Generally, shipments are received and placed in temporary frozen storage (-80 °C) and a confirmation email is sent to the shipping site. In SWAN I-IV, the Specimen Collection Record (SCR) forms were sent as paper copies along with the samples, serving as the shipping manifest, and were entered by the Repository into a Forms database using double data entry. In SWAN V (Visit 15), the SCR data is provided electronically to approved Precision personnel

after the clinic sites entered the data into a secure database hosted by the SWAN Coordinating Center. This is typically done within 5 business days of receipt of a shipment.

The SCR data serves as the manifest for the Inventory Scan. The frozen samples, shipped in bags and boxes, are scanned into the Inventory database (the BSI-II), examined visually (for color, vial integrity, volume confirmation), assigned a location, and placed into long-term storage boxes.

Any discrepancies found in this process are included in a Discrepancy Report and sent to the clinic site. Examples of common discrepancies include: samples in the shipment with no forms; missing samples; empty vials; samples received which are intended for assay at the CLASS lab; vials cracked or frozen sideways or upside down.

5.1.3. Samples are Committed into Repository Inventory

When all discrepancies are resolved and all corrections entered into the database, samples are placed into long-term storage. Finally, a 5% location verification is performed for QC purposes.

5.2. INVENTORY MANAGEMENT ACTIVITIES

5.2.1. Inventory Investigations

5.2.1.1. Purpose and Scope

Beginning in 2009 and concluding in 2013, inventory investigations were conducted on stored Repository specimen collections from Baseline through Visit 10. The purpose of these investigations was to examine the accuracy of recorded material types and vial volumes. While the time and financial burden involved in these vial-by-vial investigations was considerable, the SRO and NIA agreed the efforts were warranted to have a firm understanding of available inventory and to be able to accurately promote the specimens to the scientific community.

The extensiveness of each visit year's investigation ranged from 100% of specimens from earlier visits to 5% from later visits, as clinic and repository protocols became more standardized and regulated, and fewer errors were found. The table below shows the percentage of each visit years' collections which were investigated.

Visit	% Inventoried
V00	100%
V01	100%
V02	100%
V03	100%
V04	100%
V05	10%
V06	5%
V07	5%
V08	5%
V09	5%

V10	5%

5.2.1.2. Results

This 5-year investigation resulted in reliably-recorded material types in the inventory database. It also highlighted specific visits, and sites, where vial volumes were consistently accurate, and areas which will require additional volume verification before release. With this knowledge, the Repository ended the collection-wide investigations and updated protocols to perform any additional volume verification work only on vials being requested and pulled for an approved study. This effort shifts the burden of 100% volume accuracy to the end-user investigators, and related costs can be included in Repository recharge (i.e., cost-recovery) rates, in line with industry standards.

5.2.2. DNA Renewal Activities

5.2.2.1. Project and Purpose

A molecular project to renew the SWAN Repository's DNA collection was approved and funded in the Repository III renewal/supplement. The goals of this molecular work were to:

- Renew and replenish the Repository's supply of extracted DNA, a frequently requested specimen type;
- Document/assure that the immortalized lymphocyte cell lines remain viable (frozen in LN2 for 7+ years);
- Document/assure that all immortalized lymphocyte cell lines are free of cross-contamination; and
- Expand the pool of cell lines in anticipation of increasingly more demand (proteomics, metabolomics, and selected gene expression studies).

5.2.2.2. Tasks Involved

The major tasks involved in the project were expanding currently frozen immortalized (EBV-transformed) cell lines, extracting DNA, and performing SNP analysis on 13 previously genotyped SNPs. All tasks were completed at Precision Bioservices.

The project was divided into two phases: Phase 1 included 828 of the 1538 women (roughly half) with DNA available. These 828 were chosen based on menopausal status - having "clean" FMPs at the time Phase 1 began (early 2012). Phase 2 began after Phase 1 showed successful results, and included 403 women who were not in Phase 1 and had since been classified as 'clean post" OR had 2 or fewer vials of extracted DNA remaining in stock. A total of 1231 cells (80%) were included in the project.

5.2.2.3. Results

Precision Bioservices attempted the expansion of all Phase 1 (828) and Phase 2 (403) previously frozen EBV transformed cell lines, with a 97% success rate.

Cell Line Expansion Results: Approximately 97% of cell lines were successfully expanded.

Total Phase 1 and 2 Cells to undergo expansion	**1231**	
EBV Transformed cell lines successfully expanded	1192	97%
Number of EBV cell lines that failed	39	3%

All vials were screened for *Mycoplasma* contamination and sterility, and found to be clean. For each cell line, a portion of the newly expanded cells was used to create new stock of frozen material with the remainder being used for DNA extraction, QC testing of the DNA, and aliquoting.

Following DNA extraction, one sample from each woman was genotyped using 13 off-the-shelf SNPs which had been previously analyzed. Match rates for re-genotyped SNPs from the sex steroid pathway were 94%-100% for the 13 SNPs analyzed.

New Repository inventory/yields:

- 3 Dry cell pellets (each 10 million cells/mL/vial)
    - 1 of these 3 pellets was immediately used to:
        - Create 3 new working stock DNA vials (ready to distribute);
        - Create 1 master stock ; and
        - Genotype the 13 SNPs.
    - 2 remaining pellets stored for future DNA extraction.
- AND 2 vials of Viable Cells (also 10 million cells/ml/vial) – to be used for future expansions.

5.3. REPOSITORY DATA MANAGEMENT AND REPORTING

5.3.1. IMS Services

The SWAN Repository subcontracts inventory management services to Information Management Services (IMS), who work closely with Precision Bioservices. IMS is the developer of Biological Systems Inventory (BSI-II), one of the major repository inventory management and control systems which fully meet Federal IT requirements. IMS was initially responsible for building a custom inventory database, using the BSI-II, to transfer and house the SWAN Repository collections. IMS maintains and updates the database and all electronic resources necessary for tracking and managing the SWAN Repository specimen inventories. IMS provides updated inventory files monthly, via an automated transfer to UM, occurring on the first of each month.

For a list of IMS key personnel and contact information, see Section 2 of this manual.

5.3.2. Inventory Management at UM

The monthly inventory files, transferred from the BSI-II database, are received by email to the Repository Manager (Merillat) on the 1st of each month. The text files (txt.gz format) contain the entire SWAN Inventory, divided into tables by material type: Serum, Plasma, Urine, DNA, and Other (containing genetic materials other than DNA). These inventory tables are used, as needed, to replace existing tables when new inquiries require sample size estimates, embargo or pull lists need to be created.

5.3.3. Quarterly Reports

5.3.3.1. Quarterly Reports from Precision to UM

Precision provides a quarterly report to the UM Repository team, reporting on all activities performed, including incoming shipments received, vial investigations or database updates performed, outgoing shipments released, and other special project tasks. Equipment maintenance and repair performed on the SWAN freezers is also reported and any equipment recommendations are given. An electronic table of new specimens received that quarter accompanies the report.

5.3.3.2. Quarterly Reports from UM to SWAN Sites

The UM Repository Manager produces a quarterly report for the 7 SWAN Clinic Sites in times of new specimen collection. This report shows all shipments received from the sites, plus any deficiencies or problems with the shipments, and looks at the number and volume of vials collected at each clinic, helping to correct any collection or shipping issues in a timely fashion.

5.4. SWAN STUDY DATA MANAGEMENT AT THE REPOSITORY

The SWAN Repository receives copies of clean, frozen datasets from each SWAN study visit, as well as analyses datasets, from the Coordinating Center (CC). The variables in these datasets are indexed in the publicly-available SWAN Data Warehouse (see section 8.1.2). Limited, encrypted datasets are individually created from these data for each approved Repository study (see section 6.3.3).