

## Aims

- Reduce variation in preanalytical factors to obtain high quality biospecimens for laboratory analyses
- Annotate specimens to adjust for variation in preanalytical variables in study analysis

## Abstract

Differences in preanalytical variables may alter molecular properties of a biospecimen, potentially influencing study results. Variation in preanalytical variables should be minimized to obtain high quality of biospecimens for downstream laboratory analyses. Specimens should be highly annotated to account for preanalytical variation in study analysis. The National Children's Study (NCS), a prospective cohort of 100,000 children and their parents, will examine the influence of several exposures (environmental, chemical, genetics, psychosocial) on priority health outcomes (birth defects, development, asthma, obesity, diabetes) in children. NCS presents unique challenges including collecting specimens in the home and at birth, including participants from over 100 sites across the U.S. A variety of mechanisms will reduce effects of preanalytical variables on NCS specimens. Variation in collection will be addressed by using specimen collection kits, creating standardized operating procedures, tracking participant fasting status and other participant variables, and requiring highly qualified and trained data collectors. Preanalytical variation in processing will be minimized by performing most processing centrally; using standardized operating procedures for processing and storage across study centers and at a central repository; establishing mandatory processing times of specimens and requiring frequent shipments to a central repository at appropriate temperatures. To reduce variability in storage conditions, specimens will be stored at a central repository in accordance with established guidelines and optimum temperatures. An automated system will be used to track specimens throughout the life cycle. To assess preanalytical variation, extensive annotation will accompany each biospecimen including recording timing of collection, processing (centrifugation, addition of preservatives) and storage as well as monitoring temperature during transport and shipping. Early testing of samples may be performed to assess quality of samples and stability testing modeling collection procedures is proposed. These measures will ensure that biological specimens collected for NCS will serve as an invaluable research resource for years to come.

## Overview National Children's Study (NCS)

- 100,000 children from before birth to age 21 and their parents
- Over 100 locations (urban to rural) across U.S.
- Home, clinic and hospital collections

## Table 1. NCS Priority Exposures and Outcomes

| Exposures  | Outcomes  |
|--|---|
| <ul style="list-style-type: none"> <li>• Physical (housing, community design)</li> <li>• Chemical (air, water, pesticides)</li> <li>• Biological (inflammation, infection)</li> <li>• Psychosocial (stress)</li> <li>• Genetics</li> </ul> | <ul style="list-style-type: none"> <li>• Pregnancy outcomes (preterm birth)</li> <li>• Neurodevelopment and Behavior (autism, cognitive development)</li> <li>• Injury</li> <li>• Asthma</li> <li>• Obesity and Physical Development</li> </ul> |

For more information (<http://www.nationalchildrensstudy.gov/>)

## Table 2. Summary of Biological Specimens by Person/Visit

| Pre-pregnancy Home   | 1st Trimester Home |            | 3rd Trimester Clinic | Birth          |            | 1 and 3 Months Home | 6 Months Home |        | 1 Year Home |
|----------------------|--------------------|------------|----------------------|----------------|------------|---------------------|---------------|--------|-------------|
|                      | Mother             | Father     | Mother               | Mother         | Child      | Mother              | Mother        | Father | Child       |
| Spot Urine           | Spot Urine         | Spot Urine | Spot Urine           | Umbilical Cord | Heel Stick |                     |               |        | Spot Urine  |
| Vaginal Swab         | Vaginal Swab       |            | Vaginal Swab         | Blood          | Cord Blood | Breast Milk         | Breast Milk   |        | Blood       |
| Hair                 | Hair               | Hair       | Hair                 | Blood          |            |                     |               |        | Hair        |
| Blood                | Blood              |            | Blood                | Saliva         |            | Saliva              | Saliva        |        | Blood       |
|                      | Saliva             |            | Saliva               | Placenta       |            |                     |               |        | Saliva      |
|                      |                    | Toenails   | Toenails             |                | Meconium   |                     |               |        |             |
| Pregnancy Test Urine |                    |            |                      |                |            |                     |               |        |             |

Planned specimen collection for NCS as of February 28, 2008. For more information and proposed analytes visit the website (<http://www.nationalchildrensstudy.gov/>). Saliva collection is for assessment of cortisol. Saliva for DNA will also be collected from participants who refuse blood draws.

Figure 1. NCS Collection, Processing and Storage Overview

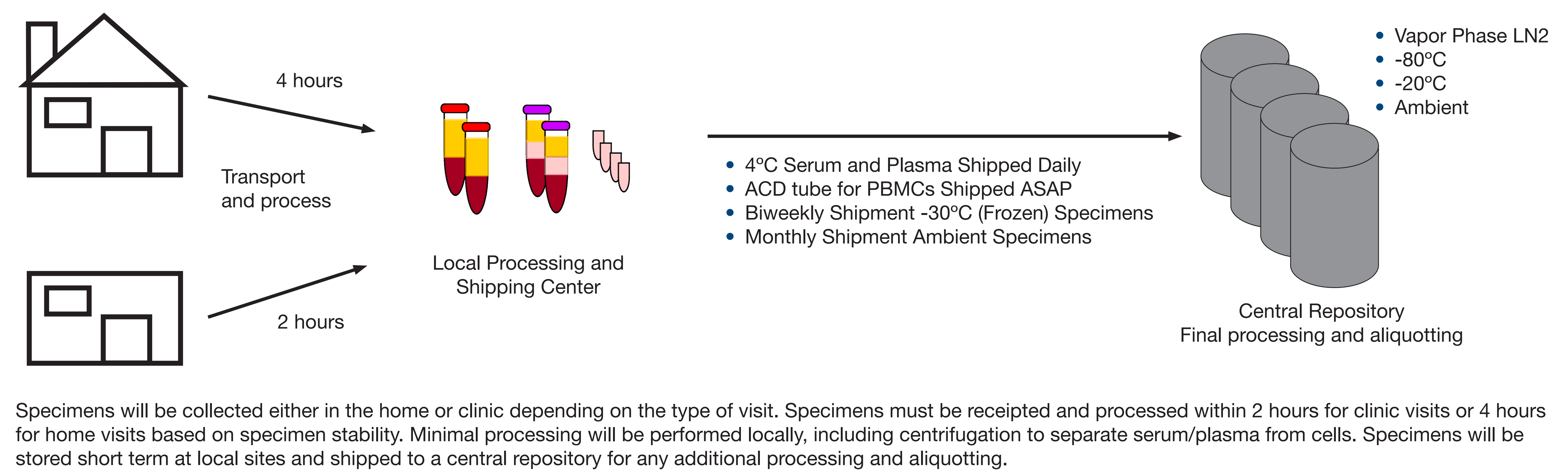


Table 3. Approach for Reduction of Variation of Preanalytical Variables

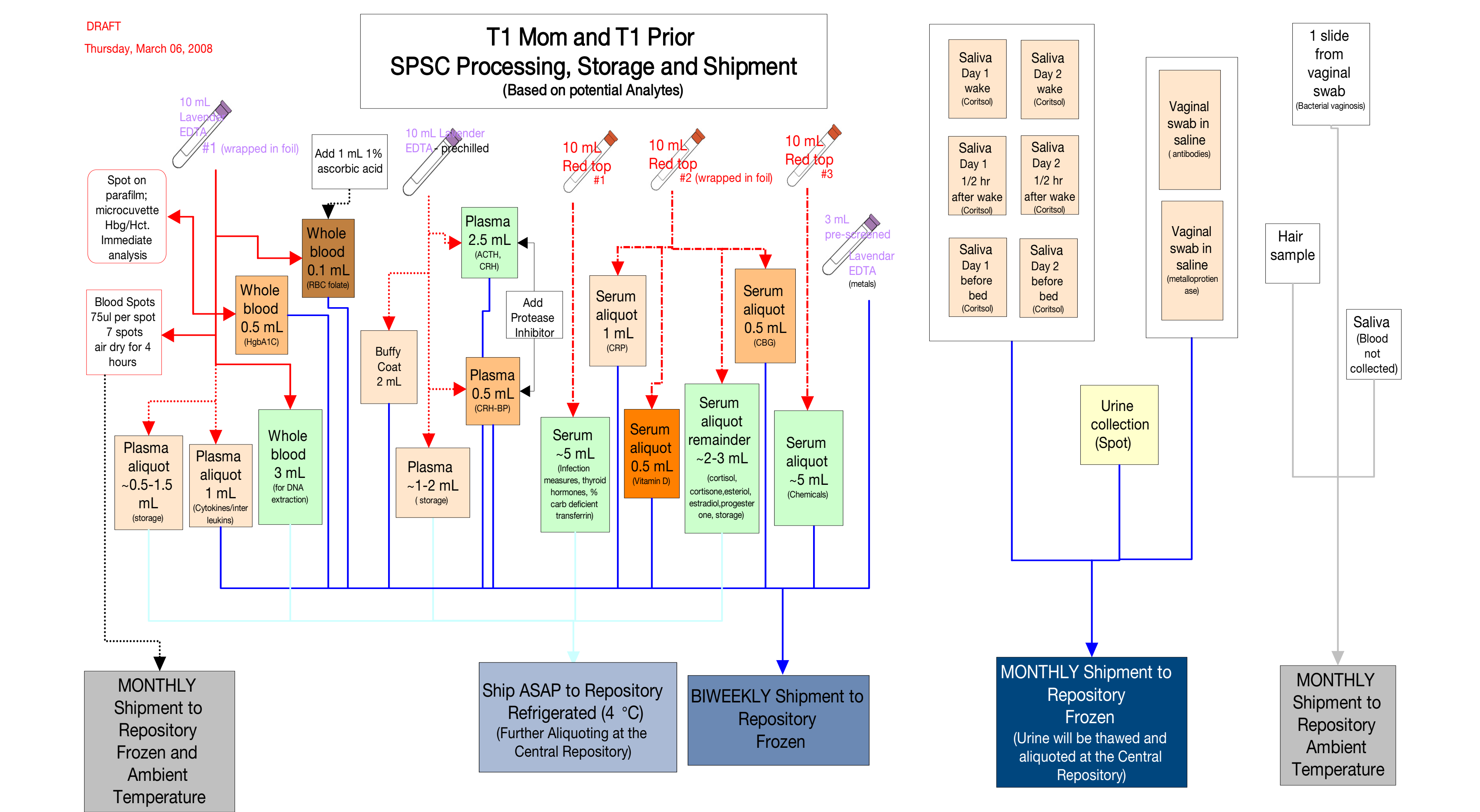
| Collection  | Processing   | Storage  |
|---|--|--|
| <ul style="list-style-type: none"> <li>• Standardized operating procedures</li> <li>• Specimen collection kits for each person- visit with pre-labeled containers</li> <li>• Tracking participant status (fasting, medications)</li> <li>• Highly qualified and trained data collectors (certifications, experience)</li> </ul> | <ul style="list-style-type: none"> <li>• Standardized operating procedures</li> <li>• Most processing will be performed centrally</li> <li>• Mandatory processing time</li> <li>• Frequent shipments at appropriate temperatures</li> <li>• Avoiding freeze-thaw cycles</li> <li>• Freezing specimens immediately for unstable analytes</li> </ul> | <ul style="list-style-type: none"> <li>• Standardized operating procedures</li> <li>• Store according to established guidelines</li> <li>• Optimal temperature based on specimen/ analyte stability</li> <li>• Store in small aliquot sizes to avoid freeze-thaw cycles</li> </ul> |

Table 4. Annotation of Specimens and Assessment of Preanalytical Variation

| Annotation   | Assessment  |
|--|---|
| <ul style="list-style-type: none"> <li>• Tracking specimens throughout their lifecycle using a web-based software application to capture data related to specimen receipt, processing, shipping, storage, and requisition</li> <li>• Recording time of collection, processing, and storage</li> <li>• Monitoring temperatures</li> </ul> | <ul style="list-style-type: none"> <li>• Quality assurance reports</li> <li>• Early quality control laboratory testing</li> <li>• Stability testing of processing delays and storage</li> </ul> |

Figure 2. NCS Local Processing Illustrative Example

This flowchart details proposed local processing procedures. The procedures were developed to minimize local processing steps, to avoid freeze thaw cycles, and to optimize stability of proposed NCS analytes.



## Conclusion

These measures will ensure that biological specimens collected for NCS will serve as an invaluable research resource for years to come.