A.S.P.E.N. Sustain Home Parenteral Nutrition Project

February 5, 2014

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1. AMERICAN SOCIETY FOR PARENTERAL AND ENTERAL NUTRITION (A.S.P.E.N.)

1.1. VISION

A.S.P.E.N. envisions an environment in which every patient receives safe, efficacious, and high quality nutrition care. A.S.P.E.N. Website

1.2. MISSION

A.S.P.E.N.'s mission is to improve patient care by advancing the science and practice of clinical nutrition and metabolism.

1.3. HISTORY

In 1968, parenteral (intravenous) nutrition–an innovative therapy to nourish individuals during illness and starvation–was introduced. This therapy provided an option for healthcare providers concerned with their patients' nutritional status. This newly developed therapy led to the establishment of the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) when, in 1975, 35 professionals met in Chicago to create this interdisciplinary association. A.S.P.E.N. was founded to provide optimal nutrition for all people, under all conditions at all times. A.S.P.E.N.'s pioneers recognized the importance of research, clinical practice, advocacy, education, and an interdisciplinary approach to nutrition support therapy.

The first A.S.P.E.N. president was Dr. Stanley Dudrick, a clinical researcher who defined and demonstrated the effectiveness of total parenteral nutrition. Dr. Jonathan E. Rhoads, known as a surgical nutritionist, was another important leader of the Society. He not only provided critical research and programmatic guidance, but he also mentored many physicians and other healthcare professionals and served as a senior scientist in the development of parenteral nutrition.

The Society began publishing a scientific journal in 1977–the *Journal of Parenteral and Enteral Nutrition*–and a clinical practice journal in 1985–*Nutrition in Clinical Practice.* Both journals are indexed by the National Library of Medicine. The A.S.P.E.N. Rhoads Research Foundation was established in 1992 to honor Dr. Rhoads, and it continues to fund basic and clinical nutrition research. Today, A.S.P.E.N. has more than 6,000 members and continues a tradition of championing the best evidence-based nutrition support for our patients.

1.4. GOVERNANCE

1.4.1. Directors

A.S.P.E.N. has a 12-person Board of Directors. All Board members are expected to participate fully in developing and honing the Society's strategic priorities. Additionally, all Board members are expected

to participate in all Board meetings and other activities, including monthly conference calls and three in-person meetings each year. Board members do not receive any compensation for Board participation.

1.4.2. Criteria for Selecting Board Members

The A.S.P.E.N. Board of Directors uses a competency-based governance model. Under this model, the Nominations Committee uses pre-defined competencies to assist in selecting new Board members. It is not expected that any single member of the Board of Directors will have all competencies, but rather, that the Board as a governing body will have all of them. The identified competencies are:

- *Clinical Practice:* Conversant with clinical practice at a variety of levels
- *Research:* Conversant with the research process and funding mechanisms; well respected in the research community
- *Education:* Conversant with educational program planning and delivery mechanisms for educational activities
- *Public Policy:* Conversant with public policy issues affecting A.S.P.E.N. members and their patients
- *External Relations:* Involvement and connections with organizations related to A.S.P.E.N.'s mission, including international organizations
- *A.S.P.E.N. Knowledge:* Knowledge of A.S.P.E.N. goals and activities
- *Finance:* Experience in reading and interpreting financial reports
- *Leadership:* Demonstrated leadership role within A.S.P.E.N. or in other professional organizations

1.5. MEMBERSHIP

A.S.P.E.N. is an international, interdisciplinary organization whose members are involved in the provision of clinical nutrition therapies, including parenteral and enteral nutrition. A.S.P.E.N.'s 6,000 members form a community of dietitians, nurses, pharmacists, physicians, scientists, students and other health professionals from every facet of nutrition support. Members include individuals, institutions, and other group entities. The Society's members work in a variety of settings including hospitals, home care agencies, long-term care facilities, research facilities, and academia. Their specialties range from critical care to gastroenterology to pediatrics to surgery. The Society is a dynamic organization that offers its members opportunities to participate fully in research, education, and training to advance the profession. Most importantly, A.S.P.E.N. empowers its members to become champions of clinical nutrition. Membership Information is available on the A.S.P.E.N. website.

1.6. CLINICAL NUTRITION WEEK

Clinical Nutrition Week (CNW) is A.S.P.E.N.'s main educational and scientific meeting. CNW Information CNW, which occurs annually, brings together more than 2000 physicians, dietitians, nurses, pharmacists, nurse practitioners, physician assistants, educators, and researchers. Approximately 30% of attendees are from outside the United States.

CNW content spans the care continuum, age spectrum, as well as basic and advanced topics. A formal, peer-review process ensures that material presented at CNW is based on solid research. The

meeting seeks to challenge attendees to identify areas for new research and to work collaboratively to find answers to critical questions in nutrition support.

1.7. PROFESSIONAL STAFF

A.S.P.E.N. maintains a staff of approximately 20 professionals. The organizational leadership includes:

- Debra BenAvram, Chief Executive Officer
- Patrick McGary, Chief Operating Officer
- Peggi Guenter, PhD, RN, Senior Director of Clinical Practice, Advocacy and Research Affairs
- Joanne Kieffer, Senior Director of Finance

2. SUSTAIN REGISTRY: HPN PROJECT

2.1. DEFINITION OF HOME PARENTERAL NUTRITION

Parenteral nutrition is the intravenous administration of nutrients delivered into a large-diameter vein (usually the superior vena cava) or peripheral vein. Home parenteral nutrition (HPN) is indicated when the need for parenteral nutrition is greater than 2 weeks and the patient no longer requires hospitalization. HPN has provided patients with intestinal failure with a life-saving option. Some individuals have survived for over 30 years on this therapy.

2.2. DEFINITION OF A PATIENT REGISTRY

According to the Agency for Healthcare Research and Quality, a patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purpose(s). The registry database is the file (or files) derived from the registry. Although registries can serve diverse purposes, many focus on describing the natural history of disease, determining clinical effectiveness or cost effectiveness of health care products and services, measuring or monitoring safety and harm, and/or measuring quality of care.

2.3. RATIONALE FOR SUSTAIN

Currently in the United States, little is known about the utilization of HPN. Medicare, a large payer for home parenteral and enteral nutrition, does not generate specific reports on this patient population. The most recent published data are from 2002. At that time, it was estimated that 39,000 people received HPN. However, this estimate was based on one home care infusion therapy database, and was not representative of the U.S. population. HPN is a high-expenditure procedure, and was estimated to cost between $125,000 – $250,000 per year in 2010. In addition, this therapy is high risk because of its association with elevated morbidity and mortality. Patients requiring HPN may receive therapy for only a few months, or a lifetime. Yet, prior to Sustain, a U.S. national registry did not exist to record how many patients receive HPN, patient characteristics, diagnoses, or geographic patterns. This information would permit evaluation of the effectiveness and outcomes of this life-sustaining therapy.

2.4. HISTORY OF HPN PATIENT REGISTRIES

In 1976, and as part of the Organ Transplant Registry, the American College of Surgeons and the National Institutes of Health (NIH) funded a registry to collect data on the growing numbers of patients on HPN. Through this voluntary national registry, clinicians began contributing data for HPN patients. The Home TPN Registry was transferred to the New York Academy of Medicine in 1977. The registry was limited because it reported aggregate data, and not all patients discharged home on PN were included. In 1984, a second voluntary patient registry was developed to track longitudinal outcomes of a cohort of HPN patients in the United States and Canada. This registry, named OASIS (Oley–A.S.P.E.N. Information System), was a joint effort of the Oley Foundation and A.S.P.E.N., and it operated from 1985–1992. In 1992, the registry changed its name to the North American Home Parenteral and Enteral (HPEN) Patient Registry and was under the sole direction of the Oley Foundation. During the period that this registry collected data, the rate of HPN was 238 patients per million people in the United States. The data were provided voluntarily by clinicians, which led to variation in reporting and challenges with interpretation. The registry stopped collecting data because the paper-based data collection tools became too costly to maintain. The last data from this effort were published in 1994.

Once the North American HPEN Patient Registry ceased to collect data, there was a void in the scientific literature regarding HPN patient outcomes in the United States. Researchers began to look at outcomes from clinical databases used by home care providers or individual institutions in order to capture information to evaluate HPN patient outcomes. Although these reports provided retrospective glimpses of HPN care, little was known about the incidence, prevalence, and outcomes of HPN in the United States. Indeed, although researchers and clinicians in the United States played a pivotal role as leaders in the development of PN, the United States lags behind other countries in HPN tracking.

The Sustain Registry provides a national, Web-based approach that allows all providers of HPN to participate, thereby facilitating inclusion of patients from all regions and health systems. Given that that the United States is a major user of HPN, a systematic approach to capture data related to incidence, prevalence, and outcomes of this high-risk, high-cost therapy was needed. Development of Sustain - *JPEN* Article

2.5. SUSTAIN: OVERVIEW

Sustain is A.S.P.E.N.'s national patient registry for nutrition care. Sustain is a comprehensive, web-based tool that allows clinicians to enter patient data, measure and analyze results, benchmark outcomes against aggregate data, and use the information to publish findings. In its initial phase, Sustain will collect data on patients receiving HPN. Subsequent phases of this registry will allow expansion to other populations and therapies. The registry was launched in January 2011 and data entry for the current phase of Sustain began in August, 2011.

2.6. PROJECT GOALS

Sustain's overarching goal is to maintain a prospective, longitudinal nutrition therapy patient registry in order to improve patient outcomes. Other objectives include:

- Collect information regarding the patients and populations who require home parenteral nutrition in the U.S.
- Measure outcomes associated with home parenteral nutrition.
- Allow institutional benchmarking against the aggregate data; and
- Publish the findings in order to improve the quality of care for patients receiving home parenteral nutrition.

2.7. LEADERSHIP AND GOVERNANCE

The Sustain Registry is overseen by the Executive, Scientific, and Operations Advisory Councils. The Executive Council is mainly responsible for high level strategy and direction of the Sustain Registry. Responsibilities of the Scientific Advisory Council include reviewing the data collection tools, annual reports, IRB templates, quality improvement/benchmarking reports, scientific queries, research proposal reviews, and publications. The Operations Advisory Council has responsibility for ongoing site recruitment, ensuring data quality and integrity, statistical infrastructure, and user satisfaction. A number of characteristics were sought as Sustain crafted its leadership structure. These characteristics included:

- Subject matter: A registry must be designed so that it contains the appropriate data to meet its goals as well as the needs of its constituents.
- Registry science: Epidemiology and biostatistics expertise specific to the subtleties of patient registries is useful in the design, implementation, and analysis of registry data.
- Data collection and database management: The decision to include various data elements can be made in consultation with experts in this field to place “critical fields” in a prominent and logical position on the data form for both paper-based and electronic data collection tools.
- Legal/patient privacy: Legal and privacy expertise is needed to protect both patients and owners of the database by ensuring that the registry complies with all national and local laws applicable to patient information.
- Quality assurance: Expertise in quality assurance will help in planning a good registry. The goals for quality assurance should be established for each registry, and the efforts made and results achieved should be described.
- Project management: Project management will be needed to coordinate the components of the registry; to manage timelines, milestones, deliverables, and budgets; and to ensure communication with sites, stakeholders, oversight committees, and funding sources.

2.7.1. Executive Advisory Council

The Sustain Executive Council serves as an oversight and ultimate decision making body, answerable to the A.S.P.E.N. Board of Directors. The responsibilities of the group include major financial, administrative, legal/ethical, and scientific decisions that determine the direction of the registry. These decisions are made with appropriate input from legal, scientific, and administrative experts.

2.7.2. Scientific Advisory Council

Sustain’s scientific oversight is provided by the Scientific Advisory Council. This council has 8 members, including 2 members from the Executive Council. This group is responsible for a number of functions including: institutional and patient recruitment, institutional review board (IRB) material

development, data integrity, quality improvement/benchmarking reports, scientific queries, data and proposal requests, abstracts, and publications.

2.7.3. Operations Advisory Council

Sustain management is conducted by the Operations Advisory Council. This council also has 10 members, including 2 members from the Executive Council. This group is responsible for a number of registry functions including: fundraising, vendor and staff management, data safety, reports generation, IRB/ institutional management, marketing-communication, and meeting planning.

2.7.4. A.S.P.E.N. Staff

Two members of the A.S.P.E.N. staff are heavily involved in Sustain's operations.

- Peggi Guenter, PhD, RN, A.S.P.E.N.'s Senior Director of Clinical Practice, Advocacy and Research Affairs, provides scientific oversight for Sustain. In this role, she is responsible for promoting the mission of the Registry, ensuring that the data are of the highest quality, and promoting dissemination of research using the Registry's data resources.
- Katy Hanley, Sustain Registry Coordinator, provides day-to-day management of centralized registry operations. She is responsible for Administration of Sustain's day to day activities; training new Sustain users; communication with potential and enrolled sites to transition them to active sites; marketing of Sustain; development and distribution of Sustain benchmarking reports; provision of support to site users; maintenance of Sustain's financial records and coordination of Sustain Advisory Council meetings.

2.8. INTERFACE WITH CNW

Since its inception, Sustain has been an integral part of CNW. The meeting is used as a vehicle to teach clinicians about Sustain, to enroll field centers, and to present results. CNW offer an opportunity to gain buy-in from new clinician-collaborators, to hold annual meetings for users and to receive feedback on novel findings.

2.9. FIELD SITES

Sustain data are collected from field sites across the United States. These sites have access to, or care for patients with home PN. Field sites are often hospitals, but they can also be other organizations such as home infusion companies.

2.9.1. Enrolled Sites

An "enrolled site" is one that has expressed interest in working with the Sustain group and enrolling patients into the Registry. To initiate the enrollment process, sites provide information on a web-based enrollment form (see Appendix 1), which is then reviewed and acted upon by A.S.P.E.N. staff. The transition from enrolled status to active participation in Sustain requires that sites complete a Participation and Data Use Agreement (see Appendix 2) and compliance with the terms of this Agreement, including obtaining IRB approval. It should be noted that individual sites can negotiate

modification in the terms of their Data Use Agreements, but these changes must be approved by the Sustain Council. To help sites through the IRB process, Sustain provides an IRB protocol template that sites can use as part of their IRB applications (see Appendix 3).

2.9.2. Active Sites

An “active site” is one that has completed the Participation and Data use Agreement, obtained IRB approval, and completed all Sustain training requirements.

2.10. BENCHMARKING DATA

As part of its larger efforts to provide support and feedback to participating sites, Sustain generates periodic benchmarking reports that are delivered to each field center. These reports provide detailed data that are specific to each site, and they also provide aggregate data so that each site can understand its own characteristics relative to Sustain as a whole. These benchmarking reports contain information detailing how many patients have been enrolled at each site and across the Registry as a whole; the demographic and clinical characteristics of patients and rates of key events such as infections and hospitalizations. These reports provide Sustain with a vehicle to demonstrate the value of the Registry to participating sites, as well as to facilitate forward movement in HPN research as a whole. As with use of all Sustain data, a number of safeguards are in place to ensure confidentiality in these reports.

2.10.1. Field Center Use of Sustain Benchmarking Data

Appropriate use and dissemination of Sustain data are encouraged. To promote these activities, the Sustain Scientific Council developed a set of Publications Guidelines that provides a framework in which participating sites can use Sustain benchmarking data. These Guidelines can be found in Appendix 4. It is important to stress that sites are able to request specific information for approved research purposes, and that Sustain is committed to facilitating these activities because they are consistent with the overall goal of using the Registry to inform on policy and practice.

2.11. AVAILABILITY OF SUSTAIN DATA FOR OUTSIDE INVESTIGATORS

In addition to making Sustain data available to field centers and associated investigators, Sustain also encourages acquisition and use of Sustain data by investigators who are based at institutions and organizations that are outside of Registry operations. The availability of these data resources will help promote use and dissemination of Sustain by a wider pool of researchers. Sustain takes active steps to make the research community aware of the availability of its data resources using marketing materials such as those presented in Appendix 5.

2.12. CONTRACTORS

2.12.1. Global Vision Technologies

Global Vision Technologies (GVT) is a private company that provides web-based data management services. GBT is based in St. Louis, MO, and is the vendor selected by A.S.P.E.N. to develop, deploy and maintain the Sustain data management architecture. GVT's responsibilities are detailed later in this document.

2.12.2. Resnick, Chodorow, and Associates, LLC

Resnick, Chodorow, and Associates (RCA) is a consulting firm that provides technical support on a variety of topics related to clinical research. RCA is based in Silver Spring, MD, and is the vendor selected by A.S.P.E.N. to oversee a series of statistical and data management activities that occur "downstream" of GVT's responsibilities. RCA's responsibilities are detailed later in this document.

2.13. REGULATORY OVERSIGHT

2.13.1. Overview of Central and Local Administration

Regulatory oversight for Sustain is provided by both A.S.P.E.N. and each participating field site. A.S.P.E.N. is responsible for overall approvals concerning the Sustain Registry as a data collection entity, as well as HIPAA and other regulatory training for its employees and business associates. A.S.P.E.N. uses the New England IRB for its regulatory oversight.

2.13.2. New England IRB

The New England Institutional Review Board (NEIRB) provides regulatory oversight to A.S.P.E.N. for the Sustain Registry. It defines and regulates A.S.P.E.N.s responsibilities, defines the participation period, indicates if written consent is required and oversees any special requirements as appropriate for the Registry. In addition to providing A.S.P.E.N. with regulatory oversight, a number of Sustain's field sites also use NEIRB. These sites are typically not university-affiliated and therefore do not have an existing relationship with an institutional review board. A.S.P.E.N. facilitates a connection between these sites and the NEIRB. Most sites with available IRBs are solely responsible for securing the necessary approvals for their sites. NEIRB and A.S.P.E.N. does not have a role in those secondary relationships.

2.13.3. Eligible Participants

Eligibility for Sustain includes all children and adult patients who are on HPN, whether they are newly discharged or patients who have been on this therapy for some time. Patients in long term care facilities, rehabilitation facilities, prisoners, and patients on Intradialytic Parenteral Nutrition(IDPN) are not eligible entry into the Sustain Registry. The racial, gender, and ethnic characteristics of individuals who are eligible for participation generally reflect the demographics of patients receiving or seeking HPN at each field site.

2.13.4. Potential Risks

There are no risks of physical harm associated with participation in the Sustain registry. As with all studies that involve collection of patient information, participation involves potential risks associated with breach of confidentiality and issues related to data security. Further, after the data are entered at the field sites, they are transferred to GVT where that organization's staff has access to patient data. In addition, RCA, which is involved in post-GVT data management and analysis, also has access to Sustain patient data. Thus, risks associated with breach of confidentiality could be related to several points in the research process where data are being handled by various entities.

2.13.5. Intended Benefits for Patients

Patients who contribute data to the Sustain Registry through a participating field site may realize certain benefits. These include:

- Contributing to prospective outcomes data development in the field of parenteral nutrition.
- Helping to increase awareness of parenteral nutrition in the public realm through publications that will be facilitated by patient data.
- Providing data that will assist with benchmarking and outcomes research.
- Helping to improve clinical practice with the development and application of best practices derived from this registry.
- Improved care through the sites' receipt of periodic reports comparing their performance to aggregate data.

2.13.6. Human Subjects Protections

Most of the risk associated with involvement in Sustain pertains to data security. Accordingly, protections are focused primarily in this area. Risks are minimized by (1) removing participant identifiers (i.e., names, medical record numbers) from information stored in the registry such that the registry contains only a "limited data set" as defined by HIPAA; (2) securing, in a separate location at the participating site, and limiting access to information that connects study ID numbers with direct participant identifiers; and (3) limiting access to information contained within the registry to the primary investigators, site users and Sustain staff and investigators. Further, additional safeguards are in place at both GVT and RCA. Data are only delivered using encrypted files, and all contractor computers are password protected.

2.13.7. Data Safety Monitoring Plan

Sustain's data and safety monitoring plan is outlined in Sustain's IRB template, located in Appendix 3. This plan involves quarterly monitoring by Sustain's Operations Advisory Council of the (1) removal of identifiers from information contained in the registry, (2) documentation of investigator access to the registry, (3) security of the database linking registry study codes with patient identifiers and documentation of investigator access to this database, and (4) any conditions that may adversely impact the confidentiality of information contained within the registry.

2.13.8. Informed Consent

Participating sites have full responsibility for obtaining all internal approvals necessary for participation in the Sustain Registry. Most sites use their institutional IRBs but a small number use the NEIRB as their IRB of record. Sites that use the NEIRB come under Sustain's institutional umbrella. Consistent with routine practice, local IRBs determine whether informed consent is necessary, or whether a waiver of consent is acceptable. If the IRB determines that informed consent is not necessary, sites must provide each enrolled patient with a waiver of informed consent information sheet that explains the meaning of waiving consent. Copies of a sample informed consent and assent forms as well as a waiver of consent are provided in Appendices 6, 7, and 8

2.13.9. HIPAA and Security Policies and Procedures

Sustain complies with numerous policies related to the Health Insurance Portability and Accountability Act of 1996 as well as additional policies related to data security as required by the Health Information Technology for Economic and Clinical Health Act (HITECH) which was signed into law February 2010. This included significant changes to HIPAA, with most going into effect on September 23, 2013. These policies are listed below.

2.13.9.1. HIPAA Policies

1. General HIPAA Policy and Documentation
2. Cooperation with HHS Investigations
3. Anti-Retaliation and Intimidation Policy
4. Business Associate Contact Requirements
5. Breach of Unsecured Protected Health Information
6. Minimum Necessary Use and Disclosure of Protected Health Information
7. De-Identification of Protected Health Information
8. Uses and Disclosures of PHI
9. Uses and Disclosures of Protected Health Information to Personal Representatives
10. Right to Request Access to Protected Health Information
11. Amendment of Protected Health Information
12. Accounting of Disclosures
13. Privacy Officer and Complaint Process
14. Privacy Training Policy
15. Administrative, Physical and Technical Safeguards to Protect PHI
16. Disposal of Protected Health Information
17. Sanction Policies and Procedures for HIPAA Violations

2.13.9.2. Information and Data Security Policies

1. Risk Analysis and Security Official
2. Risk Management
3. Sanction
4. Information System Activity Review
5. Workforce Security
6. Information Access Management

7. Security Awareness and Training
8. Protection from Malicious Software
9. Password management
10. Security Incidents
11. Contingency Plan
12. Business Associate Agreement
13. Facility Access Controls
14. Workstation Use and Security
15. Device and Media Controls
16. Disposal of ePHI
17. Technical Access Control
18. Integrity and Authentication
19. Person or Entity Authorization
20. Transmissions Security

2.13.10. HIPAA and Security Training

A.S.P.E.N. is responsible for HIPAA training for its employees and business associates. This training is in the form of a PowerPoint presentation that all relevant personnel are required to watch and for which they are responsible. After watching the presentation, relevant personnel are required to sign a form and return it to the Sustain Coordinator to certify that this training was completed. Re-training on HIPAA and security policies is required annually of all relevant A.S.P.E.N. staff and business associates. All Sustain sites, including those that use the NEIRB, are responsible for HIPAA training in a manner that is consistent with local institutional requirements.

3. SUSTAIN HPN PROJECT DATA SYSTEM AND ARCHITECTURE

3.1. OVERVIEW OF CONTRACTING ORGANIZATION

Global Vision Technologies, Inc., (GVT) is a private firm founded in 1997. GVT assists with the information needs of healthcare, pharmaceutical, and human service professionals. GVT helps organizations with secure web-based information management systems for the collection and analysis of their patient and client-related data, as well as child welfare case management. GVT has partnered with large pharmaceutical firms, bio-tech firms, universities and non-profit organizations to build, manage, and scale patient registries. GVT provides both ready-made and custom IT solutions with a focus in three areas: Child welfare/human services case management, clinical patient registries and E-learning management.

3.1.1. Scope of Work

GVT's role in this project is to develop and maintain a web-based patient outcome registry that prospectively collects data on patients receiving HPN. Data collection includes a series of forms that comprise data capture from "baseline" as well as a series of subsequent forms that capture follow-up episodic entries. The Registry has a number of purposes: Direct patient data collection; administrative tools for patient management; observation of trends; identification of new events and monitoring and

measurement of outcomes. GVT also works with RCA to facilitate the process by which Sustain data are transferred from the GVT data system for eventual use in research-oriented data analysis.

3.2. SITE REGISTRATION

Institutions or home infusion companies ("sites") that join Sustain all utilize the same data entry processes and access the same website for the Registry. Each site has its own account and may have up to 10 users entering data on the same or different patients. The system begins with a clinician enrollment form that allows sites to register as participants in the Sustain Registry. As each site registers to participate in the Registry, the Sustain Coordinator receives an email notification. The Sustain Coordinator can log into the system to review all "applicants." After sites complete the approval process, training and when they transition to active status, the Sustain Coordinator provides users at each site with individual user accounts. GVT's Vision Server (the platform that drives registry solutions), contains all of necessary security and HIPAA settings to set up different roles for different users in the system. In addition, the Sustain Coordinator has a master control panel to view all users at each location. She can set permissions, mirror sessions, lock-out users, and change passwords settings as needed.

3.3. FORM CONFIGURATION AND FUNCTIONALITY

The baseline and follow up forms have been tailored to specifications including workflow. Each patient is automatically assigned a serial number that is tied to the site that is treating them. Typically, a site will have an ID number such as: 0001005. In this example, the ID number refers to patient #5 from facility #1. When a physician or study coordinator is logged into their site – they would click the "add new patient" button and the system would automatically assign the next available patient number to use for their site upon saving the new patient's baseline form. Searching for patients can be done through the patient search tool. Each record has editing capabilities until the record has been saved with the site user's signature.

3.4. REPORTING

Each facility that has entered complete data into the registry is provided a set of pre-determined tables, graphs and charts such as patient enrollment, breakdown of patients via race, gender, , diagnoses, catheter type, food and diet, medications, diagnoses, etc. For both cross-sectional and longitudinal reports, comparisons are made between the individual site's aggregate data and the Sustain aggregate data by pediatrics, adults and combined (both pediatrics and adults.) This provides the facility to get a better understanding of their patient population and the data can be used for benchmarking.

Cross-sectional graphs are based on the Sustain aggregate data (pediatric and adult patients combined). While the longitudinal graphs compare aggregated site data to aggregated Sustain data separately for pediatric, adult patients and the combined group of pediatric and adult patients if this site has all types of patients. Catheter infection rates per 1000 PN days, Thrombosis/occlusion rates per 1000 PN days, and Re-hospitalization rates per 1000 PN days are the graphic comparisons made in the longitudinal section of the report.

3.5. ADMINISTRATOR FUNCTIONALITY

The Sustain data system allows automated emails to be sent to participating sites. The system utilizes a workflow scheduler that can tailor an "action" to happen based on a certain event or series of events. The system includes a set of emails for different reasons that are programmed to be sent based on certain events or timeframes. Email reminders for no data or incomplete records and/or that help to identify potential duplicate records go to the Sustain Registry Coordinator who notifies the two sites to adjudicate the duplicative record. All data can be exported into various formats, such as EXCEL, CSV, PDF. The system permits queries for missing or duplicative data within patient entry. The system provides an automated flag to data manager when a duplicate record has been identified via an email alert. The system is compatible with Internet Explorer 10 and above, Firefox, Chrome, and Safari.

3.6. SYSTEM INFRASTRUCTURE AND SPECIFICATIONS

3.6.1. Visions Server/ClinicalPURSUIT Architecture

This proprietary software handles all the .NET calls within the applications and provides the framework. It is the development platform for the ClinicalPURSUIT/ Sustain HPN application used in the Sustain Registry. The Visions Foundation was originally developed to track clinical trials data, which required tight, integrated security, as well as a tamper resistant data design. This technology was adapted to the current platform that resides on a web server. It is a web-based application that utilizes HTTP and HTTPS for data transmission and a browser for client access to the application. The only software required to access the system is a standard web browser.

3.6.2. The Visions Server

The server is designed around n-tiered architecture. It supports multiple protocols and standards for inter-system communications (e.g., HTTP, HTTPS, SSL, VPN, TCP/IP, XML, SOAP). It can be scaled from hundreds of users to ten thousand or more and its scalability based on server capacity and bandwidth.

3.6.3. System Architecture

The basic GVT architecture, including the Sustain system, contains 4 distinct layers as shown in the diagram below. In this this architecture, the application (Visions Server) and reports layer are between the web layer and the data. This provides a level of security that is often not found in other web applications. Requests come in via the browser to the web server, and the Visions Connector (using .NET architecture) queues requests to a common "pool" that the application servers (running Visions Server services) process. The application servers (which contain a meshed presentation layer along with the programming logic) perform the required database operations and send output streams back to the Visions Connector. These are then sent back to the browser (or other requestor, which can be another portal or application). Security is handled at the application server, which is why it generally is between the reports process and web layer. Administration of the web layer is performed using standard IIS tools and administration of the database layer is performed using standardized tools that generally come with the DBMS (such as SQL Management Studio). System level administration of the

application layer (Vision Server software) is performed using GVT-supplied tuning tools, as well as normal network administration functionality. Application level administration is performed using front end forms that are supplied with the system. These include: navigation, security, and business logic. Although the reports layer is architecturally administered the same way, third party reporting tools (such as Microsoft Access, Crystal Reports, SQL Reporting Services or other reporting mechanisms implemented) generally come with their own tools.

3.6.4. Server Configuration

The following server configuration is designed to support approximately 1,000 users and allow for future expansion. The "BASE DESIGN" is a starting point for the hosting environment, and "EXPANSION DESIGN" shows approaches for growing the system as necessary.

3.6.4.1. Base Design

- The system's firewall is a Sonic Wall Pro or comparable firewall.

- System backup is achieved through several means. These include: DLT 35/70 GB with autoloader; controller card for DLT autoloader; backup Exec Enterprise (or comparable) for controlling and storing to DLT autoloader; SQL server agents that backup the SQL server while the database is being used, and remote server agents for each Application or WWW server)

- The network attached storage consists of backup for controlling and storing to the DLT Autoloader, SQL server agents that backup the SQL server while the database is being used, and remote server agents for each application or WWW server.

- The data server consists of a dual Xeon 2.4GHz, 2 GB RAM, RAID 5 Controller, 4 X 36GB SCSI Hard Drives (4 for RAID with hot spare), Gigabit NIC, Windows 2003/2008 Server, and it uses SQL 2008 database software.

- The application server consists of several elements including: a dual Xeon 2.4 GHz Processor, 2GB RAM, 36GB SCSI Hard Drive, Gigabit NIC, Windows 2003/2008 Server 5 user license; Davinci Graphics Handler; Codestone SMTP Client; Chartdirector Charting Handler; VB6 Runtimes and .NET Framework 1.1 if needed.

- The web server consists of a single Xeon 2.4 GHz Processor, 2GB RAM, 36GB SCSI Hard Drive, Gigabit NIC, Windows 2003/2008 Server 5 user license and .NET Framework 2.0 if .ASPX queuing is enabled.

3.6.4.2. Expansion Design

- In the data server, additional servers can be added to the environment via Microsoft SQL Clustering. Elements include: 4 X 72GB SCSI HD (or more), 3 GB RAM (or more) and Quad Xeon 2.4 (or more).
- In the application server, additional servers can be added to the environment for load balancing and failover. There is no practical limitation to the number of application servers and the reports server software can run on any application server.

- For web servers, additional servers can be added to the environment, and these require Windows Load Balancing (or equivalent).

3.7. DATA VALIDATION

Data validation in ClinicalPURSUIT is achieved through use of fields with values that are chosen from an established list, formatted date & time fields, elements in the Server Data Dictionary and alerts that are coded into data entry forms. The Server Data Dictionary can be used via the front-end by system administrators and site administrators to select what type of data may be entered into open fields as well as designating field(s) to be required entry prior to saving a record. JavaScript is also used to help users comply with logic rules related to entering data in a particular order, setting data point "outliers", enforcing dependencies between different data elements, as well as showing and hiding fields based on the way other fields are filled in.

3.8. DATA SECURITY

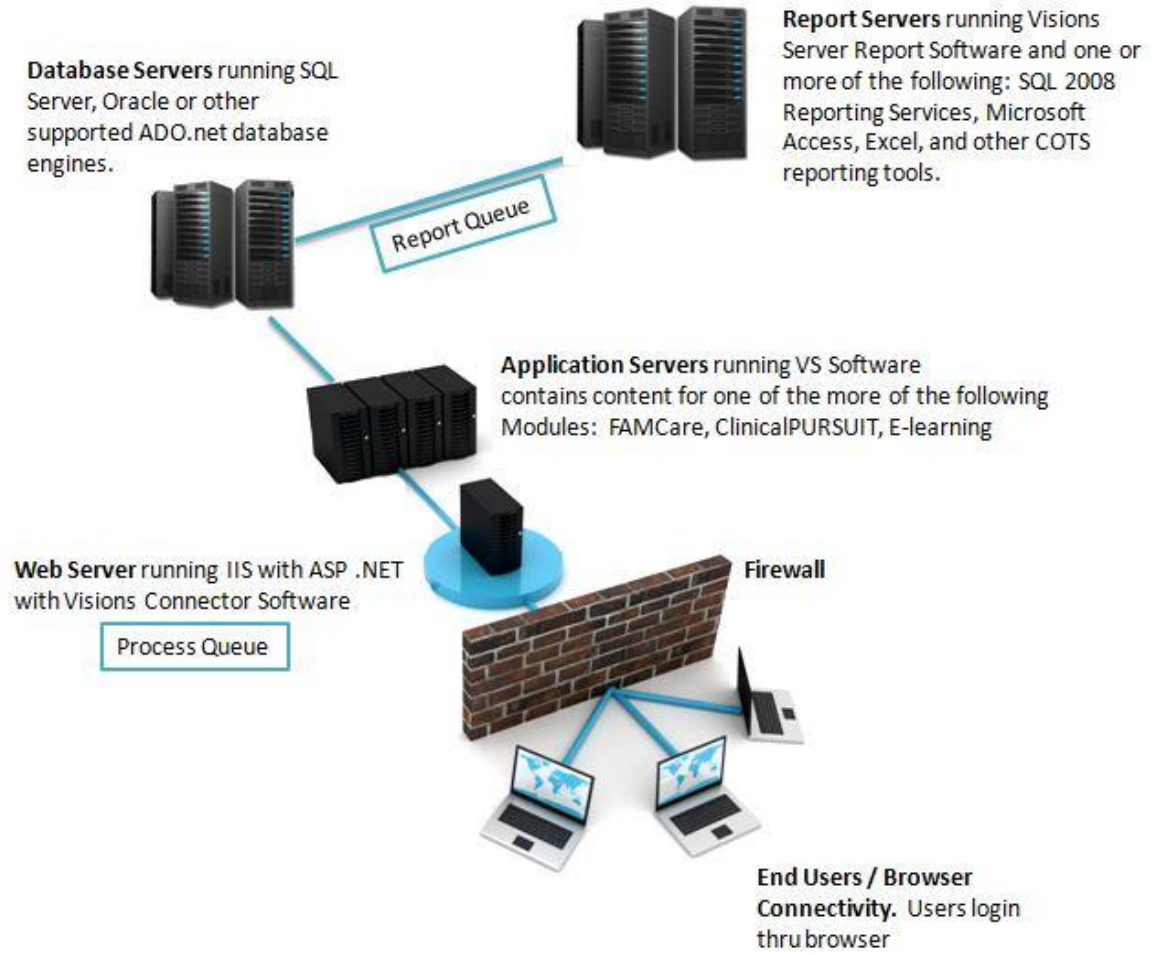
The Visions Server utilizes a flexible multidimensional security model. Users are assigned to groups that define functional duties, including levels of access for each form in the system. Users are also assigned to logical "organizations" that define access roles for each individual. This is a hierarchical structure that the Visions Server automatically maintains to ensure users can only access cases they are allowed to view. GVT maintains both in-house staff and external relationships to enable HIPAA compliance regarding security. The Visions Server automatically tracks all changes with full audit records for each form and it automatically tracks all accesses to data as required by HIPAA guidelines. There is also individual field level encryption, which is done at the platform level to ensure confidentiality of the most sensitive data. The architecture uses https protocol (built into IIS) and there is also separation of the data servers from the web servers. This means all data access from browsers must go through the application platform, effectively disconnecting the data server directly from the Internet.

The software is secured via username/password. Users are put into groups (based on their role at the site) to handle security. Security is also tied to form access. Reports follow the same security hierarchy. Different access levels to data forms include read access only, read/write/edit, unlimited, etc. The password protocol is 8 characters – which includes 2 capital letters and 2 numbers. GVT forces password changes every 90 days. SSL certificates are used to encrypt transport from the user to the server. GVT uses Sonicwall firewalls that are set to block all traffic except for traffic that is absolutely necessary. GVT's software has a dedicated web server that speaks a proprietary language to the database server.

A number of other measures provide additional security. Physical Security is provided such that the hosting partner hosts our applications in a state-of-the-art facility that is camera and escort monitored, locked cabinets and biometric scanning. Authentication and password security features are in place as is anti-virus software. Additional security features include firewalls, VPNs, logging and auditing, timed access control and the fact that the software and hardware are not available to the public.

3.9. DATA ARCHIVING AND STORAGE

Test recoveries are performed every 6 months and backups are taken once a day. In the event of a disaster involving a single server, the recovery process takes around 3 hours. If the disaster was to the entire data center, the recovery point would be greater than a day. GVT ships full/encrypted archives offsite once per month. The max recovery point is one month if the data center were completely destroyed. Restoration of service after catastrophic events such as fires, storms, earthquakes, or accidental damage is on an around-the-clock basis. GVTs data center capabilities also include redundant Internet lines, redundant power lines, generators, servers with RAID5 hard drives, daily Acronis TrueImage images of servers, monthly offsite storage of encrypted backups, and mirroring of data to the secondary data center.



3.10. CONTACT INFORMATION FOR PROJECT STAFF

Christopher Ettere (Client services and support) - chris.ettere@globalvisiontech.com

George Ritacco (Director, Client Services) - George.ritacco@globalvisiontech.com

Ray Scott (Chief A.S.P.E.N. registry developer and technical support) - ray.scott@globalvisiontech.com

4. SUSTAIN HPN PROJECT FIELD CENTERS

4.1. OVERVIEW OF PROJECT ACTIVITIES AND EXPECTATIONS

Sustain's national network of field sites is the core of Registry activities. As part of the enrollment process (see Appendix 1), each site agrees to several provisions. These include:

IRB Approval

- Sites have sole responsibility for obtaining all necessary approvals for participation in the Registry. Sustain provides a template of the Sustain Registry protocol (see Appendix 3) to facilitate local IRB submission.

Contribution of Data

- Sites agree to contribute the data elements contained in the data collection forms (see Appendix 2) established by Sustain, and according to procedures outlined in the IRB-approved Sustain protocol. Sites agree to follow instructions regarding elimination of patient identifiers such that the data constitutes no more than a "Limited Data Set" as defined by HIPAA. Sites agree to be responsible for complete, accurate, and timely submission of participant data to the Registry.

Identification of Leadership and Access Controls

- Sites agree to identify one individual to act as the "Site Investigator." This person often acts as the primary contact for communications with Sustain regarding Registry activities. Sites are responsible for ensuring that Site Investigators respond promptly to Registry-related communications and requests. Sites also agree to comply with access control policies established by Sustain related to user IDs, passwords, and software.

Provision of License to Use Data

- Sites must be legally authorized to submit data to the Registry. Participant data will be de-identified and aggregated with data contributed by other sites. Accordingly, sites must give Sustain license to use participant data for the purpose of aggregating it with other participants' data and using the Aggregated Registry Data for research, public health, and/or health care operations.

4.2. LIST OF ACTIVE SITES

An up-to-date List of Active Sites can be found on the Sustain website. At the present time, there are 29 active sites in the Sustain network. It is anticipated that additional sites will continue to be added to the registry.

4.3. FIELD CENTER TRAINING PROGRAM

After a field site has completed and delivered all of its regulatory/IRB paperwork and signed Participation and Data Use Agreement to the Sustain Coordinator, the site is eligible to participate in Sustain training. These trainings are administered by the Sustain Coordinator and consist of an online meeting with the field site staff members who will be enrolling patients, entering data and/or overseeing the site's participation in Sustain. This training session includes educating the participants on the following:

- Logging into the Sustain database, resetting the passcode and completing security questions
- Searching and locating a patient in the site patient list
- The importance of keeping a secure log to Sustain patient id number for future reference when entering follow-up data
- Entering baseline and follow-up data
- How often follow-up data should be entered
- Resources for questions and help

As part of this training, a Sustain Site User Manual is emailed to all approved site personnel. A copy of this manual is available on the Sustain website.

4.3.1. Certification Requirements

Other than completion of, and compliance with local IRB and HIPAA regulations, Sustain does not have formal certification requirements for field sites or individual staff. The training that is conducted by the Sustain Coordinator functions as a gatekeeping mechanism for quality control purposes.

4.3.2. Re-training

In addition to the initial training described above, Sustain is instituting an annual re-training requirement for all field site personnel who input data. The rationale for this change in procedure is associated with the change in data forms that was implemented in the February, 2014. These form modifications resulted in a sufficient level of changes to the data system that re-training was warranted. Further, Sustain staff wished to implement a re-training requirement in order to enhance quality control efforts for the Registry as a whole.

4.4. SITE RECRUITMENT

Efforts to raise awareness of the Sustain registry and to recruit new sites include advertising in the *Journal of Enteral and Parenteral Nutrition*, the Program Guide and Onsite book that is distributed at A.S.P.E.N.'s Clinical Nutrition Week, building and maintaining a Registry website

(www.nutritioncare.org/sustain), ongoing email communications with A.S.P.E.N. members, provision of updates in A.S.P.E.N.'s general email communications, exhibiting at meetings (CNW, the Oley Foundation, Academy of Nutrition and Dietetics, Infusion Nurses Society, Society of Hospital Medicine), and distribution of press releases. In addition, marketing and recruitment documents are distributed at speaking engagements, they are sent to Chapters for their events, they are distributed at CNW, as well as at other industry events/exhibit booths. Finally Sustain newsletters are sent to current users, potential sites and advisory council members.

4.4.1. Health Professional Recruitment

A key to securing new sites for the Sustain Registry is securing the interest of one or more health professionals at a potential new site. A.S.P.E.N. staff and others reach out directly to key decision-makers at potential sites with letters that outline the purpose and goals of Sustain (see Appendix 9)

4.5. SITE RETENTION AND SOLICITATION OF FEEDBACK

Each year Sustain sites are asked for feedback prior to CNW. This is implemented via and email survey, and results are tabulated at A.S.P.E.N. and distributed to the Sustain Users group and the Councils at CNW. Examples of some of the questions that are posed to the sites include:

- How long is it taking you to complete baseline entry for one patient?
- On average, how often are you entering follow-up data for each patient?
- What percent of the data collections forms are you completing for baseline?
- What percent of the critical elements are you completing for the baseline forms?
- What elements would you eliminate from the data collection forms?
- What other modifications would you make to the data collection forms?
- What modifications would you make to the Site Reports?
- What positive gains are you receiving or expecting to receive from this project?
- What barriers and challenges you have encountered along the way?

In addition to these annual surveys, when quarterly reports are emailed to active sites, the cover letter contains a request for feedback on the report as well as any other feedback or information regarding content that the site would like to appear in future reports. Beyond these structured retention activities, A.S.P.E.N. staff strive to maintain open lines of communication with the sites, so that the sites are comfortable offering suggestions, and A.S.P.E.N. staff also try to connect with key personnel from each site during training sessions and at CNW. A.S.P.E.N. also publishes a periodic newsletter that is sent to all approved personnel at each site.

In addition to activities that aim to retain existing sites, A.S.P.E.N. also has strategies in place to respond to sites that are under-performing, both in terms of enrollment or follow-up. For example, a survey was recently sent to under-participating sites to understand challenges that were preventing the site from entering data. When A.S.P.E.N. can understand these challenges the Sustain Coordinator can often assist with troubleshooting and problem resolution.

4.6. PATIENT RECRUITMENT, SCREENING AND CONSENTING

Potential Sustain Registry patients are recruited locally at approved sites once they have received IRB approval. Although various strategies are used for recruitment, the most common approach is direct contact between field personnel and potential Registry participants. In addition to direct contact, some sites post information about Sustain that includes contact information for the local coordinator, and the Oley Foundation also provides information for potential participants in its newsletter. When a potential patient is identified, field-staff assess patient eligibility and if the patient is eligible for enrollment, he or she is consented and enrolled in the system. To assist the sites, Sustain staff have provided sample consent form templates. These can be found in Appendices 6-8.

4.7. WEB-BASED DATA COLLECTION FORMS

Patient data are entered into the Sustain Registry using a secure web-based data entry system. As noted above, data collection for this phase of Sustain began in August, 2011. In February of 2014, a number of changes were implemented to the forms, and accompanying changes were made to training and other materials describing the Registry. As a result, the current phase of Sustain has used two sets of certain materials, including the data collection forms. These are referred to as the first version (August 2011 through February 2014) and the second version, which was implemented in February 2014. Although data are collected on separate forms for adults and children, many variables are shared between the two patient populations. Both versions of the data collection forms can be found on the Sustain website.

4.7.1. Baseline forms

The baseline data collection forms include information that was current at the time patients are enrolled into the Sustain Registry. Many of the variables that are collected in these forms are used to categorize patients in various ways, and they are therefore important for many analyses that are conducted with Sustain data.

- Adult (Version 1)

    1. Patient Information
    2. Baseline Nutritional Status
    3. Baseline PN Formula/Medication/Nutrient Intake
    4. Baseline Psychosocial
    5. Baseline Functional Status

- Pediatric (Version 1)

    1. Patient Information
    2. Baseline Nutritional Status
    3. Baseline PN Formula/Medication/Nutrient Intake
    4. Baseline Psychosocial
    5. Baseline Functional Status

- Adult and Pediatric (Version 2)

    1. Baseline form is the same for both adults and children.

4.7.2. Follow-up forms

The Sustain protocol stipulates that after a patient is enrolled into the Sustain Registry, s/he is followed over time and data are entered periodically during follow-up. Ideally, follow-up data are collected at least every quarter for patients new to HPN up to a year, and every six months for patients established HPN. The follow-up data include information such as updates on medications and diagnoses as well as key outcomes such as catheter infections and hospitalizations. When linked with the baseline data, follow-up data allow analysts to explore "risk factor-outcome" relationships in the field of HPN. The analytic capacity that is permitted by Sustain is a key strength of the Registry. Similar to the baseline forms, the follow-up data collection forms were also revised approximately 2 years after data collection began. Thus, there are two versions of the follow-up forms for adults and two versions for children.

- Adult (Version 1)

    1. Follow-up Demographics
    2. Current Nutritional Status
    3. Current PN Formula
    4. Morbidity
    5. Mortality
    6. Current Psychosocial
    7. Current Functional Status

- Pediatric (Version 1)

    1. Follow-up Demographics
    2. Current Nutritional Status
    3. Current PN Formula
    4. Morbidity
    5. Mortality
    6. Current Psychosocial
    7. Current Functional Status

- Adult and Pediatric (Version 2)

    1. Follow-up form is the same for both adults and children

5. SUSTAIN HPN PROJECT STATISTICAL SUPPORT

5.1. CONTRACTING ORGANIZATION

Resnick, Chodorow and Associates (RCA), a research consulting firm located in Silver Spring, MD has been retained by A.S.P.E.N. to provide targeted statistical and data management support for Sustain.

5.2. SCOPE OF WORK

Under its agreement with A.S.P.E.N., RCA serves a number of technical support functions. These include:

- Documentation and implementation of data collection and delivery protocols
- Formal documentation of raw and derived variables and variable definitions
- Production of a research-oriented data dictionary
- Enhancing regulatory oversight and re-configuration of field center training
- Production of fully documented, analysis-ready datasets
- Oversight of quality control and archiving of data and documentation
- Production of a data analysis plan to guide study-level Sustain analyses
- Implementation of the analysis plan and delivery of results
- Analytic support for Clinical Nutrition Week and the Sustain Steering Committee
- Provision of manuscript support for external investigators

5.3. CONTACT INFORMATION FOR PROJECT STAFF

Helaine Resnick, PhD, MPH (Project Lead) – heresnick@gmail.com

Kathy Poneleit, BSEE, MPH, MPhil (Statistics/Data Management) – poneleit@hotmail.com

5.4. DATA DICTIONARY

A data dictionary is a document that lists all variables that are available for use in the Sustain analysis data sets, as well as information about these variables. The data dictionary is a critical tool without which analysts could not utilize Sustain data for research purposes. This document is available to analysts who wish to use the Sustain data set for approved research topics.

5.5. DATA ANALYSIS PLAN

5.5.1. Development and Rationale

A project-level Data Analysis Plan was developed to guide statistical analysis of Sustain HPN data. This plan can be found in Appendix 10. The purpose of this Plan is to ensure that the most important, global questions related to HPN are answered. The Plan was developed from a series of research questions that were developed and approved by Sustain's Scientific Committee. These questions are:

- Who are the HPN patients in the Sustain registry?
- What are the rates of key outcomes among HPN patients in the Sustain registry?
- Do rates of key outcomes differ by clinical characteristics?
- Is there an association between duration of HPN and specific patient diagnoses?

5.5.2. Frequency and Format of Analyses

The project-level data analyses will occur twice each year. The analyses will be presented as a series of tables that flow down from the research questions listed above. The tables that summarize data

addressing the research questions will be supplemented by text that will help the reader interpret findings. It is important to note that because the Sustain data continue to "grow," the project level data analyses will be run on larger data sets each time they are conducted.

5.6. DOCUMENTATION PROCEDURES

The purpose of documentation for statistical activities is to record the relevant steps in standard and unique processes, to preserve the output of such processes, to preserve the computer programs and other materials used to develop products and tabulations, and to establish a knowledge base to which will provide a road map information necessary for the performance of the project now or in the future. To the maximum extent possible, documentation should be an integrated by-product of the production process.

Documentation includes computer programs, data files, spreadsheets, reports, resource materials such as key references, etc. These are generally provided in an electronic format. Detailed source tabulations that support summary report tables and charts are also provided in electronic format.

5.7. SAS/STATA PROGRAMS

Statistical programs are used to analyze complex data and data relationships. There are two distinct aspects to programming: Data management and data analysis. Data management is a process required such that the data are ready for analysis. This involves a number of steps including obtaining the data, ensuring it is of sufficient quality to begin analysis, providing summary descriptive information, header documentation, and updating filename paths, macros and variables. Data analysis is structured programming, documentation within the programming, and review of and presentation of results. The first data management step involves downloading baseline and follow-up CSV files from the GVT query system. These files are used to create SAS datasets. A SAS program is then used to convert the CSV file to a SAS dataset. A SAS QC/validation program will then be run against all new CSV downloads to ensure the quality of the data for analysis. If problems are found, they are documented and adjudicated. Once the QC is completed, there are some additional tasks before analysis can begin. The first step is to add a SAS program header for documenting specifics of the project. This header will include:

- Purpose of the program
- Filename
- A list of related file names such as macros, labels, formats, etc., needed to run the program
- Programmer name
- Date of creation
- Date of last modification
- Contact information for the programmer

Another task is to update any filenames paths and SAS macro variables such as dates that are used in the analysis program. Actual analysis requires that good structured SAS programming practices. These practices include sufficient use of comments so that the program is well documented and variable names that are easily understandable. SAS log files will be reviewed to make sure the

program(s) ran correctly without error with the number of anticipated patients for each dataset/subset analyzed. Outlier values will be reviewed and documented. The documentation will state the reason they are acceptable or what is needed to resolve problem, and results will be reviewed to ensure that they are plausible. Results are verified against known values within the registry such as number of patients, frequency of events, etc., and from outside sources such as publications and input from A.S.P.E.N. staff. Periodic delivery of information is provided to ASPEN. This package includes SAS programs, SAS labels and formats, spreadsheets, and other resource materials along, with a statistical analysis report. The report contents will conform to the requirements outlined in the analysis plan provided in Appendix 10.

Once the data management is complete, a PROC CONTENTS, A PROC UNIVARIATE, PROC MEANS and PROC FREQ will be run for the CSV download and will be included as part of the periodic data delivery. This SAS QC program can be provided with the data delivery for the purpose of quality improvement review. All of the above steps also apply if STATA is used instead of SAS.

5.7.1. Spreadsheets

Spreadsheets are often used as part of data analysis. They are helpful for viewing and manipulating data, and protocols have been developed to manage these documents. The first workbook in the spreadsheet should have descriptive information that should include the following:

- Purpose of the spreadsheet
- Filename
- A list of related files needed to understand the program
- Programmer name
- Date of creation
- Date of last modification
- A list of related files needed to understand the program
- programmer contact information for the programmer

Spreadsheet analyses will have an accompanying document that defines the derived variables and explains the results. Filename, version number if multiple versions, printed date, name of spreadsheet "owner" and page numbers are included in the print menu.

5.7.2. Word Documents

Word documents are frequently used to summarize results, for memos and for a variety of other purposes. Protocols have been developed to manage these documents. Descriptive header information is provided in the beginning of the document. This should include the following:

- Purpose of the document
- brief description of major edits and/or major version changes if there have been many changes or versions
- Author
- Date of creation
- Date of last modification

- Date printed
- A list of related files needed to understand the document
- Author contact information

Good writing practices will be used such as use of clear and concise plain language, use of white space, indenting/bullets/numbered lists, page numbers (page number of x number of pages), and summaries of key points. Font types and size match throughout the document unless intentionally modified to be different. Sources such as books, peer reviewed literature, grey literature, etc., will be clearly documented. Reports of statistical results and findings will be written, to the extent possible, such that a lay person can understand the information.

Interpretation of the results will be accompanied by tables and materials needed to make the point when needed.

5.7.3. Reports

A periodic delivery of information is provided to A.S.P.E.N. This includes information describing the SAS dataset (PROC CONTENTS, PROC UNIVARIATE, PROC MEANS and PROC FREQ), SAS import program, SAS labels and formats, spreadsheets and results from the statistical analyses. The periodic data delivery will include the statistical analysis report. The report contents will conform to the requirements outlined in the Project Level Data Analysis Plan, which can be found in Appendix 10.

5.8. PROCESS FOR REQUESTING CHANGES TO DATA SYSTEM

Changes for programming, spreadsheets, query and reporting must go through the Project Director for review and approval/denial/postpone. The request must have a description of the change(s) requested, why the request is being made (fix a problem, enhancement, decrease amount of time, etc.) and proposed solutions. For complex requests, a discussion with the Project Coordinator and/or GVT may be needed prior to formally submitting the request for the change.

5.8.1. Data Validation and Quality Control

Validation is the process of identifying data that are inconsistent, incomplete, inaccurate, and/or missing/unknown. The process is used to ensure that the data are consistent with desired values. Checks include evaluation of control totals, allowed characters and values, consistency of variable value frequencies with previous spreadsheets, cross-variable consistency, totals for variables across spreadsheets are consistent, data type, format type, absence of variables, range checks, spelling and grammar, unique IDs, and table look up checks. These types of checks will be done by running a SAS program for each new spreadsheet delivery from GVT. The data will be further screened against previously known problems and anticipated problems so that they can be identified and corrected prior to data analysis. New problems will be reported to the Project Coordinator for resolution. The SAS program will be repeated once the changes have been made to ensure that the problem(s) have been resolved and no additional problems have resulted from the changes.

5.9. DATA/DOCUMENT DELIVERY, ARCHIVING AND STORAGE

A critical element of the Sustain Registry is its ability to track and share project data and documentation. Document sharing not only helps ensure transparency, but it also facilitates dissemination of research using the Sustain Registry by making it easy for outside investigators to use Registry data. Because Sustain uses outside vendors for data collection and data management, there is a process for archiving materials that are produced by these outside vendors. That protocol can be found in Appendix 11.

5.10. DATA SECURITY

Data security is a process to ensure that appropriate administrative, physical and technical safeguards are incorporated in project work. Many of these safeguards are outlined in HIPAA documents and in GVTs security features. In addition to these elements, project computers or other electronic systems that will be used to access or transmit project documents have up-to-date anti-virus software. Computers that have project files such as data programs, documents and other electronic materials also have online incremental backup systems that store project files to prevent loss. Passwords are used on all computers with project data and they are set to periodically timeout. Standard software packages are used to prevent security breaches via malware or viruses. All electronically transmitted data and files that could violate HIPAA or in any way allow for a breach of patient confidentially are encrypted prior to transmission and all transmissions follow A.S.P.E.N.'s HIPAA compliance requirements.

5.11. PROTOCOL FOR DATA ANALYSIS AND PUBLICATIONS FOR EXTERNAL REQUESTS

To promote dissemination of Sustain data, investigators and interested groups and individuals outside of the immediate Sustain research group are invited to request access to Sustain data for approved analyses and publications. The process for use and acquisition of Sustain data is detailed in Appendix 5.

APPENDICES

APPENDIX 1: ENROLLMENT FORM

SustainTM, LLC Participant Enrollment Form

Completion of this form allows SustainTM staff to begin processing your application to participate in the registry. Full participation requires completion of a participant agreement and approval by an Institutional Review Board.

Site Information

Site Name:_____(Institution/company etc.)

Address:_____

City: _____State:_____ Zip:_____

Telephone:_____

Web site:_____

Are you part of a healthcare system or multisite company? Yes___ No___ If yes: Company/System Name:_____

Describe your institution/company_____

PN Patients

Inpatient bed size of institution (if applicable) _____

Approximate total number of Home PN Patients per year_____

Approximate number of NEW Home PN Patients per year_____

Does your group/company/or institution have access to an Institutional Review Board? Yes___No___

Primary Investigator (Primary manager)

Name:_____

Title:_____

Email:_____

Telephone:_____

Mailing Address (if different from above):_____

City: _____State:_____ Zip:_____

S

Primary Contact Information (Day to day clinician)

Name:_____

Title:_____

Email:_____

Telephone:_____

Mailing Address (if different from above):_____

City: _____State:_____ Zip:_____

Secondary Contact Information (Back-up day to day clinician)

Name:_____

Title:_____

Email:_____

Telephone:_____

Mailing Address (if different from above):_____

City: _____State:_____ Zip:_____

APPENDIX 2: DATA USE AGREEMENT

THIS PARTICIPATION AGREEMENT (the "Agreement") is made and entered into by and between SustainTM, LLC, an Illinois limited liability company that is a wholly owned affiliate of the American Society for Parenteral and Enteral Nutrition ("Sustain"), and the individual or entity identified below ("Participant").

WHEREAS, A.S.P.E.N. is a not-for-profit, tax-exempt association whose purpose includes the improvement of patient care by advancing the science and practice of nutrition support therapy; and

WHEREAS, A.S.P.E.N. has established and owns Sustain, LLC, a national nutrition care registry to gather data to maintain a prospective, longitudinal nutrition therapy patient registry for the purpose of improving patient outcomes. ("Registry"); and

WHEREAS, the first phase of the Registry will collect information regarding patients and populations who require home parenteral nutrition in the U.S. to measure outcomes, to allow institutional benchmarking against aggregated data, and publish findings; and

WHEREAS, Participant is a medical center, hospital, home infusion provider, medical group, or other health care entity that desires to contribute data to the Registry.

In consideration of the mutual covenants and premises herein contained, the parties agree as follows:

TERM AND TERMINATION

Term of Agreement. This Agreement will begin on later of the signature dates indicated in the signature blocks below and will continue for an initial period of one (1) year (the "Initial Term"); this Agreement shall automatically renew for additional periods of one (1) year (each, a "Renewal Term") and will continue until terminated, as provided herein.

Termination. Sustain may terminate this Agreement upon termination of the Registry program or upon thirty (30) days written notice to Participant. Participant may terminate this Agreement on thirty (30) days written notice to Sustain.

DATA CONTRIBUTION.

IRB Approval. Upon execution of this Agreement, Sustain will provide a copy of the registry protocol established by Sustain for the Registry project (the "Protocol"). Participant acknowledges and agrees that it shall have sole responsibility to obtain any internal approvals necessary for participation in the

Registry, including Institutional Review Board ("IRB") approval or waiver, as may be required under the policies and procedures of the Participant. To the extent applicable, Participant will be solely responsible for obtaining any necessary informed consent documents that may be required by Participant's IRB.

Participant's Contribution of Data. Participant agrees to contribute the data elements, described in the "Data Collection Tool" established by Sustain from time to time (the "Data"), to the Registry. Participant shall follow the Protocol's instructions regarding blinding of patient identifiers such that the Data constitutes no more than a "Limited Data Set" as defined by the Health Insurance Portability and Accountability Act of 1996, as amended ("HIPAA"). Sustain may revise data elements, including their format, and the frequency of required contributions from time to time, provided that the Registry will remain a Limited Data Set. Sustain will provide reasonable advance notice of any revisions to all Registry participants through updates to the Registry website or other direct communication to participants. Participant agrees that it is solely responsible for the complete, accurate, and timely submission of Participant's Data to the Registry.

Leadership; Access Controls. Participant agrees to identify one individual to act as the "Site Investigator," who will be the primary contact person for communications with Sustain regarding the Registry. Participant will ensure that the Site Investigator promptly responds to all reasonable communications and requests from SUSTAIN related to the Registry. Participant agrees to comply with any access control policies established by Sustain and communicated to Participant with respect to user IDs, passwords, and software, which may be revised or updated by Sustain from time to time.

License to Use Data. Participant represents and warrants that Participant is legally authorized to submit the Data to the Registry. Participant's Data will be de-identified as to Participant's identity and aggregated with data contributed by other participants to create an aggregated database, which will be used to create benchmarking data and facilitate collaborative research. Accordingly, Participant grants to SUSTAIN a continuous, irrevocable, non-exclusive license to use Participant's Data for the purpose of aggregating it with other participants' data ("Aggregated Registry Data") and using the Aggregated Registry Data for research, public health, and/or health care operations.

Registry and Aggregated Data. Notwithstanding the ownership rights of Participant in Participant's own Data, SUSTAIN owns all right, title and interest in and to the Registry and the Aggregated Registry Data contained therein, including all associated intellectual property rights. SUSTAIN grants a non-exclusive, revocable, non-transferable license to Participant to use the Registry to obtain the summaries and benchmarking data provided to Participant in connection with the Registry. Participant's license to use the Aggregated Registry Data and the Registry shall terminate concurrent with termination of this Agreement.

Limitations. Except for the license rights expressly granted herein, no express or implied license, right or interest in or to any intellectual property of Sustain is conferred by this Agreement. Participant shall not remove any proprietary rights notice from the Registry or any deliverable or product provided to Participant by Sustain or the Registry. Any portion of the Registry or its content merged into or used in conjunction with other material will continue to be the property of Sustain and subject to the terms and conditions of this Agreement. Any use of the Registry not expressly permitted by this Agreement is prohibited. Without limiting the foregoing, Participant shall not, except as otherwise provided herein, (a) install or configure the Registry other than in accordance with Sustain's specifications; (b) reverse

assemble, reverse compile, reverse engineer or otherwise attempt to write the source code of the Registry; (c) modify, enhance or create derivatives of the Registry; (d) lease, sublease, sublicense, sell, distribute, transfer possession, rent, or grant other rights in the Registry.

REPORTS PROVIDED BY SUSTAIN

Benchmarking Reports. From time to time, but no less than on a quarterly basis, Sustain will create and make available to Participant certain benchmarking reports based on an analysis of Participant's individual Data compared to the Aggregated Registry Data ("Benchmarking Reports"). The Benchmarking Reports will be in a format developed by Sustain from time to time. Participant shall have access to the Registry and Benchmarking Reports only during the Term of this Agreement and only so long as Participant has contributed Data to the Registry in connection with Data collection protocols and timeframes established by Sustain. If Participant fails to submit complete Data in a timely fashion, Sustain will not release Benchmarking Reports to Participant and may terminate this Agreement as provided herein.

Additional Reports. Participant may request unique reports from Sustain and Sustain will evaluate such requests and, if feasible, provide them to Participant in exchange for a reasonable fee as agreed to by the parties.

PUBLICATIONS

Publications. Participant agrees that Sustain may publicize its name along with lists of Participants in the Registry. Participant may use Sustain's name and the name of the Registry only in connection with a general internal or external statement publicizing Participant's participation in the Registry. Any other press release, advertising, promotional sales literature or other promotional written statements or promotional oral statements to the public in connection with or alluding to the Registry or the relationship between the parties created by this Agreement that has or contains any reference to Participant, Sustain, the Registry, the name of any member of Sustain's staff or the name of Participant is prohibited without the prior written approval of the other party.

Use of Benchmarking Reports. Participant agrees to comply with all publishing or use guidelines established by Sustain from time to time regarding permitted uses and disclosures of Benchmarking Reports. In general, Participant shall only use reports for appropriate internal and external purposes in a manner that is accurate and not misleading.

CONFIDENTIALITY

Confidentiality of Participant Identity. Sustain will not release or disclose Participant's Data in any format that identifies Participant as the contributor of any specific data except as required by legal process, or as requested by the Participant. If any legal demand for the Participant's Data is made upon Sustain, Sustain will, to the extent allowed by law, promptly notify Participant so that Participant may, at its option, challenge the validity of the legal process. The data elements collected will include demographic information identifying Participant. These data elements will be maintained by Sustain only for purposes of administration of Participant's participation in the Registry. All identifying information will be removed prior to contribution to the Registry and replaced by a random ID number. The key that matches the ID number to the Participants will be maintained by the Sustain executive

director and his or her direct staff, who shall hold it in strict confidence and not disclose it to any third party or use it for any purpose other than as specifically permitted by this Section.

HIPAA Data Use Provisions.

Limited Data Set. The parties acknowledge that certain data elements requested as part of the Protocol and stored in the Registry may constitute Protected Health Information protected under HIPAA, including specifically, elements of dates. The parties acknowledge that the data elements exclude direct identifiers of the patient and therefore comprise a limited data set under HIPAA ("Limited Data Set"). Participant agrees to provide the Limited Data Set to Sustain for purposes of health care operations and research ("Authorized Purposes"). Sustain agrees that it will only use or disclose Participant's Data for the limited purposes described in this Agreement.

Uses and Disclosures by Sustain. Sustain agrees to use and disclose the Limited Data Set to assist Participating Site in quality improvement and other health care operations, including benchmarking and reporting as described in the Protocol. Sustain may also use and disclose de-identified data contained in the Registry to conduct research, as defined by HIPAA. Sustain will not use or further disclose the information maintained in a Limited Data Set except as permitted by this Agreement or as otherwise required by law. Sustain agrees not to use the Limited Data Set in such a way as to identify or contact any individual whose data is included in the Limited Data Set. Sustain shall limit the use or receipt of the Limited Data Set to the individuals employed or engaged by Sustain who need the Limited Data Set for the performance of the Authorized Purposes.

Safeguards. Sustain will use appropriate safeguards to prevent the use or disclosure of the Limited Data Set provided by Participant, other than as permitted under this Agreement or as required by law.

Reporting. Sustain will report to Participant any use or disclosure of the Limited Data Set not provided for by this Agreement of which Sustain becomes aware.

Agents and Subcontractors. Sustain will ensure that any agents, including a subcontractor, to whom Sustain provides the Limited Data Set agrees to the same restrictions and conditions that apply to Sustain with respect to such information. Participating Site acknowledges that Sustain has engaged a third party vendor to house the Registry and Sustain represents that such vendor has agreed to the required restrictions and conditions as described in this Agreement.

De-Identified Information. Participating Site hereby grants Sustain permission to de-identify data contained in the Registry in conformance with HIPAA and to use or disclose such information in Sustain's discretion.

FEES

No Fees for Preliminary Stage. In exchange for Participant's assistance with the development of the Registry, Sustain will provide Benchmarking Reports at no fee to Participant, except for reasonable fees related to additional unique reports as agreed to by the parties.

Future Fees. The parties acknowledge and agree that Sustain may institute a reasonable participation fee in the future and Participant shall have the right to terminate this Agreement if Participant does not wish to continue under a fee-based program.

NO WARRANTY; LIMITATION OF LIABILITY

DISCLAIMER OF WARRANTY.

TO THE MAXIMUM EXTENT PERMITTED BY APPLICABLE LAW, THE REGISTRY AND ANY AND ALL MATERIALS DEVELOPED BY SUSTAIN UNDER THIS AGREEMENT ("SUSTAIN MATERIALS") ARE PROVIDED "AS IS" WITH ALL FAULTS, AND SUSTAIN DISCLAIMS ANY AND ALL EXPRESS OR IMPLIED REPRESENTATIONS AND WARRANTIES WITH RESPECT TO THE REGISTRY AND SUSTAIN MATERIALS DEVELOPED HEREUNDER, INCLUDING ANY EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, ACCURACY, NON-INFRINGEMENT, OR THAT THE REGISTRY AND SUSTAIN MATERIALS DEVELOPED HEREUNDER WILL OPERATE ERROR FREE, UNINTERRUPTED OR BE FREE OF VIRUSES. THE ENTIRE RISK AS TO THE SELECTION, SATISFACTION QUALITY AND PERFORMANCE AND USE OF THE REGISTRY SHALL BE WITH THE PARTICIPANT.

LIMITATION OF LIABILITY.

TO THE MAXIMUM EXTENT PERMITTED BY APPLICABLE LAW, IN NO EVENT SHALL SUSTAIN BE LIABLE FOR ANY INDIRECT, SPECIAL, INCIDENTAL, CONSEQUENTIAL, PUNITIVE, OR EXEMPLARY DAMAGES (INCLUDING DAMAGES RELATED TO DELAYS, LOSS OF DATA, INTERRUPTION OF SERVICE OR LOSS OF USE, BUSINESS, REVENUE, OR PROFITS) IN CONNECTION WITH THIS AGREEMENT, USE OR INABILITY TO USE THE REGISTRY, UNDER ANY LEGAL THEORY, EVEN IF SUSTAIN HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. IN NO EVENT SHALL SUSTAIN BE LIABLE FOR ANY THIRD PARTY CLAIM. LIABILITY FOR DAMAGES SHALL BE LIMITED AND/OR EXCLUDED AS PROVIDED IN THIS AGREEMENT, EVEN IF ANY EXCLUSIVE REMEDY PROVIDED FOR IN THIS AGREEMENT FAILS OF ITS ESSENTIAL PURPOSE.

ADDITIONAL TERMS

Amendment. Any amendment to this Agreement must be in writing and signed by each of the parties. The parties agree to amend this Agreement from time to time as necessary for the parties to comply with the requirements of applicable law. Provided, however, that Sustain may make changes to the Protocol, the Registry, and Data collected from time to time by giving notice to all Registry Participants as soon as is practicable prior to their implementation and any such changes will not be considered an amendment to this Agreement.

Assignment. Neither party may, without the written consent of the other, assign, delegate or otherwise transfer this Agreement or any of its rights or obligations under this Agreement.

Severability. If any part of this Agreement is determined to be invalid, illegal or unenforceable, the parties will modify such part, if possible, to conform to the law, and the remaining parts will be fully effective and operative insofar as reasonably possible.

Entire Agreement. This Agreement, including its attachments and exhibits if any, constitutes the entire understanding and agreement between the parties concerning the subject matter of this Agreement, and supersedes all prior negotiations, agreements and understandings between the parties, whether oral or in writing, concerning its subject matter.

Jurisdiction. This Agreement is governed by the laws of the State of Illinois and venue for resolution of any disputes shall reside in the Federal or State courts in Cook County, Illinois. Each party consents to the personal jurisdiction of the Federal and State courts located in Cook County, Illinois.

Third Party Beneficiaries. The parties do not intend to create any third party beneficiaries to this Agreement.

Waiver. No provision of this Agreement may be waived except by an agreement in writing signed by the waiving party. A waiver of any term or provision shall not be construed as a waiver of any other term or provision.

Relationship of the Parties. The parties are independent contractors of each other. Nothing in this Agreement shall be construed to create a fiduciary relationship, partnership, employer/employee, joint venture, agency or other similar relationship between the parties. Neither party shall have the right to exercise control or direction over the business of the other party.

Authority. The undersigned represent and warrant that they are authorized to enter into this Agreement on behalf of the party he or she represents, and that this Agreement will be binding on such party, and its officers, directors, agents, and employees.

Notices. Any notices required pursuant to this Agreement shall be in writing and sent by US Mail, personal delivery, next-day express mail, or by facsimile addressed as identified below:

If to Sustain:

8630 Fenton Street, Suite 412,

Silver Spring, MD 20910

Fax: 301-587-2365

If to Participant:

_____

_____

_____

Fax: _____

Survival. All provisions of this Agreement relating to warranties, confidentiality, non-disclosure, proprietary rights, and limitation of liability, indemnification obligations and payment obligations shall survive the termination or expiration of this Agreement.

IN WITNESS WHEREOF, the parties have each executed this Agreement by their duly authorized representatives on the date(s) shown below.

SUSTAIN, LLC	PARTICIPANT
_____	[Print Company Name]
By:	By: _____
Title	Title:
Date: _____	Date: _____

APPENDIX 3: SAMPLE IRB TEMPLATE

SustainTM, LLC: American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)'s National Patient Registry for Nutrition Care

Version 1. March 15, 2011

Registry Protocol (For IRB use)

Objective and Specific Aims:

The specific goals of SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care ("The SustainTM Registry") are to:

1. Collect information regarding the patients and populations who require home parenteral nutrition in the U.S.,
2. Measure outcomes associated with home parenteral nutrition,
3. Allow institutional benchmarking against the aggregate data, and
4. Publish the findings in order to improve the quality of care for patients receiving home parenteral nutrition.

This will be done by collecting and performing analyses of a limited data set (as defined by federal HIPAA regulations) of the medical record information of qualifying patients seen by the Site Investigators which will be contributed to The SustainTM Registry.

Background and Significance:

The Site Investigator's institution will enter into a participation and data use agreement with SustainTM, LLC. In accordance with Federal regulations, the collection and use of a limited data set for research purposes does not require the prior authorization of the respective patients-subjects. If required by this IRB or institutional policies, patients seen at the participating institution or home care company will be asked to provide their written informed consent to allow the institution to contribute a limited data set containing certain data elements from their medical record related to their home parenteral nutrition (HPN) to The SustainTM Registry for the purpose of facilitating research studies directed at home parenteral nutrition outcomes.

Research Design and Methods:

Participation in The SustainTM Registry is limited to placement of a limited data set derived from each eligible patient's written medical record related to their home parenteral nutrition into an aggregated research database. The information derived from each institution will be aggregated with that of other participating institutions and will be used for quality assurance activities related to the health care operations of each participating institution, in addition to research directed at home parenteral nutrition patient outcomes.

1. If required by the applicable IRB, patients seen by the Site Investigator will be asked to provide their written informed consent to allow a limited data set derived from their written medical record information related to their HPN to be placed in The SustainTM Registry. The medical record information that will be placed in the SustainTM Registry will be limited to certain specific data elements developed by The SustainTM Registry related directly to the patient's HPN therapy as well as records related to concurrent medical conditions and treatments (i.e., not related directly to HPN) that may impact substantially the patient's HPN outcome.

2. A limited data set of the participant medical information will be transmitted electronically to The SustainTM Registry. Patient names, social security numbers, medical record numbers, and other identifiers described at 45 CFR 164.514(e) will not be entered into the registry. The Site Investigator will create a linkage code number for each participant. This linkage code will remain with the institution and will not be transmitted to The SustainTM Registry. Access to participant medical information contained within The SustainTM Registry will be restricted to the Site investigators and SustainTM staff.

a) Information linking the linkage codes to the participants' names will be stored in a secure location by the Site Investigator and will not be entered into The SustainTM Registry. Access to the information linking the linkage codes with participant identifiers shall be documented by the Site Investigator and will not be shared with or otherwise contributed to Sustain, LLC.

b) The limited data set information transmitted to The SustainTM Registry will be maintained for an indefinite period of time and will be aggregated with data contributed by other participating institutions.

3. The Scientific Advisory Board of The SustainTM Registry must approve all research studies being conducted by Sustain investigators using the limited data set contained within the SustainTM Registry. Such approvals shall be obtained prior to providing investigator access to the registry information; shall be based upon considerations of scientific quality and validity; shall be granted only for research studies related to the specific HPN patient outcomes that qualify as "Research" as defined at 45 CFR 164.501 . All researchers will be required to sign a data use agreement consistent with the participation agreement executed between the [institution] and SustainTM, LLC. All research projects approved by the Scientific Advisory Board of The SustainTM Registry and all access to the Registry by third parties for the purpose of performing research analyses shall be documented by SustainTM.

4. SustainTM may provide a de-identified dataset derived from The SustainTM Registry to secondary research investigators (i.e., research investigators who are not affiliated with Sustain). All such data shall be completely de-identified consistent with 45 CFR 164.502(d). The Scientific Advisory Board of

SustainTM, LLC shall require secondary investigators to obtain IRB approval of an “exempt” research application prior its provision of de-identified information to the secondary investigator.

5. Participants will not be informed directly by investigators or study personnel of the results of research studies involving the use of the limited data set of their medical record information contained within The SustainTM Registry.

Human Subjects:

Individual records to be included in The SustainTM Registry will include all adult (age > 18 years old) patients or parents/legal guardians of children who are receiving or seeking medical care at [institution]. Infants to 18 year old children may only participate pending the permission of their parent or legally authorized representative. Due to the complexity of state and federal requirements governing the participation of prisoners in research, information regarding prisoners shall not be contributed to The SustainTM Registry. Women of childbearing potential will not be excluded. There are no additional inclusion/exclusion criteria. The racial, gender and ethnic characteristics of the individuals whose information is contributed to The SustainTM Registry shall reflect the demographics of patients receiving or seeking medical care at the participating institution or home care company. No individuals shall be excluded from The SustainTM Registry based on race, ethnicity, gender or HIV status.

Recruitment Procedures (Applicable if the IRB Requires Written Consent):

If required by the IRB, all patients who are receiving or seeking medical care at the participating institution or home care company who will be discharged on HPN or who are currently on HPN will be invited to participate in the Registry. Potential participants will be approached by a member of the staff providing HPN care and will be asked to review a copy of the informed consent form prior to being seen by a Site Investigator. The Site Investigator will review the informed consent form with potential participants and address any questions or concerns prior to obtaining written informed consent for Registry participation. The Site Investigator will also address any future questions or concerns of Registry participants. If written informed consent is required, only the medical record information of patients who have provided directly their written informed consent for Registry participation will be placed in The SustainTM Registry. The participation of patients who are mentally incapacitated (e.g., comatose, unresponsive) will not be sought (i.e., during the period in which they are mentally incapacitated). With this type of registry research, there is not a power analysis and sample size calculations. All patients on this therapy will be potentially enrolled in the registry. Data will be collected at least quarterly and data collection will continue on each patient as long as they remain on HPN and do not withdraw from this registry.

Potential Risks of Research Registry Participation:

There are no risks of physical harm associated with participation The SustainTM Registry. Participation in this Registry does involve the potential risks of a breach of confidentiality of the limited data set of medical record information and associated privacy of the participants. Such risks will be minimized by 1) contributing only a limited data set that does not contain any direct participant identifiers (i.e., names,

social security numbers, medical record numbers) from information stored in the Registry; 2) securing, in a separate locked location, and limiting access to information linking codes (i.e., linkage codes) assigned to the Registry information with direct participant identifiers; and 3) limiting access to information contained within the Registry to the site investigators and SustainTM LLC staff.

The data and safety monitoring plan for The SustainTM Registry will involve routine (i.e., quarterly) monitoring by the Sustain Executive Board of 1) the removal of direct identifiers from information contained with the Registry; 2) the documentation of investigator access to the Registry; 3) the security of the database linking the Registry linkage codes with participant identifiers and the documentation of investigator access to this database; and 4) any conditions that may negatively impact the confidentiality of information contained within the Registry. As specified previously, the Sustain Scientific Advisory Board must provide approval for a site investigator to access the registry for studies involving the use of registry information. At the time of annual renewal, a list of studies conducted using the registry will be submitted to the IRB. In addition, any unauthorized access to any individually identifiable medical record information contained within The SustainTM Registry or to the database linking the Registry information to participant direct identifiers shall be reported to the IRB. Serious adverse events are not associated with this type of research and the reporting of serious adverse events will not occur with this registry.

Potential Benefits of Research Registry Participation:

There are no direct benefits associated with participation in SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care. The use of information contained within this Registry for research analyses may be of future benefit to patients receiving HPN.

Costs and Payments:

All costs associated with the implementation and maintenance of the SustainTM Registry shall be supported by SustainTM, LLC. No costs will be incurred by Registry participants or their health care providers. SustainTM, LLC patients will not be remunerated for their participation in the Registry.

APPENDIX 4: PUBLICATIONS GUIDELINES

Based on the following section of the Sustain Participation and Data Use Agreement, the Sustain Scientific Council has developed guidelines regarding the use of the data from the Benchmarking Reports.

Use of Benchmarking Reports. Participant agrees to comply with all publishing or use guidelines established by Sustain from time to time regarding permitted uses and disclosures of Benchmarking Reports. In general, Participant shall only use reports for appropriate internal and external purposes in a manner that is accurate and not misleading.

Guidelines on use of Sustain Data. Sustain Participants and Participating Sites engage in the process of collecting Sustain data and utilization of registry-derived information for the purpose of local and national improvement in the quality of Home PN care. This Guideline provides information on the specific and accepted professional use of this data and registry-derived information from Sustain.

Participant use of their own site's data. The participating site will be able use your own site's data in any way that your site wants including publication of such data.

Participant use of the Sustain benchmarking data. The benchmarking data is the site's data as compared to the aggregate Sustain data. Any information from the benchmarking report can be used internally for quality assurance and educational purposes. Such internal utilization may satisfy institution quality assurance requirements such as mortality and morbidity review and confidential service conference discussions. Process improvement within an institution may be monitored for continuous quality improvement impact, using the data and outcomes as reported for and by the Sustain Registry. The benchmarking reports and any data contained therein cannot be disclosed outside of the Participant for any reason, including but not limited to, for marketing or to promote the site's program as compared to others. Participant is prohibited from publishing the benchmarking reports. Data contained within the benchmarking reports cannot be used for publication or research unless all requirements set forth in #3 below in this document are met.

1. Use of Sustain benchmarking and aggregate data for research purposes

Individual Participant-specific site data and aggregate data may be used for clinical research by that Participant if reviewed and approved by the Sustain Scientific Council for scientific merit and ethical propriety. Clinical research on aggregated national data may be used to produce one or more of the

following forms for reporting and dissemination of information: abstract, scientific meeting presentation, or manuscript for publication in the medical literature under the following conditions:

1. Participants can only publish aggregate data after permission is received by the Sustain Scientific Council.

2. Any abstract, scientific meeting presentation, or manuscript for publication in the literature must have the “Sustain” name in the title or text or presentation materials.

3. Any scientific meeting presentation, or manuscript for publication in the literature must acknowledge the “Sustain” funding support using the following language:

Sustain is supported, in part, by unrestricted scientific grants from Baxter Healthcare Corporation and the A.S.P.E.N. Rhoads Research Foundation.

Note: Check the Sustain website periodically for additional supporters and include those as well.

Process for Obtaining Permission to Publish

Participants may submit requests to Sustain for scientific queries using either the benchmarking reports provided or requiring access to raw de-identified patient data from the Sustain Registry. Request for permission should include a full research proposal. All such requests for data queries and publication permissions shall be subject to prior approval by the Sustain Scientific Council who shall give due consideration to scientific merit, the funds and other resources available to address queries and other pertinent factors. As a part of its efforts to promote the use of the Sustain Registry as a tool for the development of beneficial scientific information, Sustain will provide reasonable assistance to the Participant in refining Participant’s requests for queries so as to enhance their potential for approval. Participant may be required to enter into an agreement regarding the use of the data.

The Sustain Scientific Advisory Committee retains the right to update this document on a periodic basis. Check the SUSTAIN website (www.nutritioncare.org/sustain) for the latest publication guidelines.

Adopted by the Sustain Executive Council Chairperson November 2012.

APPENDIX 5: PROMOTION OF SUSTAIN DATA UTILIZATION

Sustain Data Sets to Use for Scientific or Policy Analysis

Sustain™, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care is a longitudinal home parenteral nutrition (HPN) patient registry whose goal is to improve patient outcomes through clinical research. In an effort to encourage widespread use and dissemination of data from this important project, Sustain is making de-identified data sets available to interested users.

What is included in Sustain's public-use data sets?

- *Analysis-ready data sets* that contain both cross-sectional and longitudinal data describing Sustain participants, their health profiles, and outcomes
- A *data dictionary* that describes variables in the data sets
- A *study binder* that contains information about Sustain, including the Registry's rationale, operations, protocols, and regulatory considerations

Who can acquire Sustain's public-use data sets?

- Students
- Faculty
- For-profit and non-academic, not-for-profit organizations

What can Sustain's public-use data sets be used for?

- Hypothesis generation and hypothesis testing in the area of HPN
- Training tool for students
    - Manuscript preparation
    - Preliminary data for grant applications

How do I obtain Sustain's public-use data sets?

- Go to www.nutritioncare.org/sustain

- Go to Sustain Scientific Query Protocol and click on link
- Complete Sustain Registry Data Query Application
- Email to Katy Hanley (katyh@nutritioncare.org)
- This application will be reviewed by the Scientific Council
- If your application is approved, you will need to sign a data-use agreement

What do Sustain's public-use data sets cost?

- **Free** for students and faculty at institutions that participate in the Sustain registry
- $250 for students at non-participating institutions
- $1,000 for faculty at non-participating institutions
- A.S.P.E.N. will negotiate a fee associated with collaboration with non-academic institutions

Sustain's public-use data sets will be available in March, 2014.

Contact Katy Hanley (katyh@nutritioncare.org; 301-920-9133) for more information.

APPENDIX 6: SAMPLE INFORMED CONSENT

INFORMED CONSENT DOCUMENT

CONSENT TO ACT AS A PARTICIPANT IN A REGISTRY

TITLE: SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care

PRINCIPAL SITE INVESTIGATOR: (Name/Institutional Address/Contact Information)

SITE CO-INVESTIGATORS: (Names and Contact Information)

SOURCE OF SUPPORT: SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care

What is the purpose of this Registry?

Many advancements in medicine have resulted from research involving the collection and

comparison of the medical record information of patients with a certain disease or condition.

Because you or your family member are receiving Home Parenteral Nutrition (HPN), we are asking for your permission to allow us to place non-identifiable information (no one will know it is yours) from your past, current and future medical record information into a national data registry operated by SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care. The SustainTM Registry will collect data from many areas such as hospitals or home care companies into a national computer database. By placing the medical record information of many patients such as you or your family member into this registry, researchers will be able to conduct research studies directed at increasing our knowledge about home parenteral nutrition patients and their health condition. The mission of the SustainTM Nutrition Care Registry is to maintain a prospective, longitudinal (real time and long term) nutrition therapy patient registry in order to improve patient outcomes. The first phase of this registry will be to describe typical HPN patients.

The specific goals of this phase of the SustainTM ,LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care are to:

1. Collect information regarding the patients and populations who require home parenteral nutrition in the U.S.,
2. Measure outcomes associated with home parenteral nutrition,

3. Allow hospitals or home infusion companies to compare findings against like groups and against the total HPN patient population so that hospitals, physicians and home care agencies can see how they are doing compared to similar institutions, and
4. Publish the findings in order to improve the quality of care for patients receiving home parenteral nutrition.

Who is being asked to participate in this Registry?

All patients who are being discharged from the hospital and going home on home parenteral nutrition are being asked to participate in this Registry.

What will my participation in this Registry involve?

If you agree to participate in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, certain facts related to your past, current and future medical record information will be placed into the registry. This will permit research studies to be conducted on the medical record information contained within the registry. The data elements to be included in the registry will not identify you. That is, you or your child's name, address, phone number, e-mail address, social security number, medical record number, and other data that could be used to directly identify you or your child will not be shared with the Registry. The only potentially identifiable information included in the registry are dates and patient ages.

What are the possible risks of my participation in this Registry?

There are no risks of physical injury associated with you or your child's participation in the SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care. In order to preserve patient confidentiality and protect against the risk that information about you or your child's health might become known to individuals outside of the Registry, we will assign a special code number to your medical record information. This code will remain confidential with your hospital, physician, or home care organization and will not be transmitted to the SustainTM Registry. No information that could be used to directly identify you will be contributed to the Registry. Once contributed, your non-identifiable data will be combined with data on many other individuals. The Registry will control access to the aggregated database.

What are the possible benefits of my participation in the Registry?

It is unlikely that you will receive any direct benefit as a result of your participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care. However, the medical data contained within the Registry will be used for research studies directed at improving our knowledge and treatment of patients receiving HPN and this knowledge may benefit patients on HPN in the future.

Will I or my insurance provider be charged for my participation in the Registry?

There will be no costs to you or your insurance provider to participate in this Registry.

Will I be paid for my participation in the Registry?

No, you will not receive any payment for participating in this Registry.

Who will know about my participation in this Registry?

Any information from you or your child's medical records that is placed into SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care will not identify you by name, address, or any other direct identifiable. All information will be kept as confidential (private) as possible. You will not be identified by name or any other direct identifying characteristic in any publication of the results of research studies involving the use of your medical record information.

What is the nature of my medical record information that will be placed into the Registry?

Certain non-identifying facts related to you or your child's past, current and future medical record information will be recorded into the Registry. Examples of these might be diagnosis, type of IV catheter, hospitalizations, or type of HPN solutions. The researchers may review your medical records, including medical information related to any of your medical conditions and treatments, even if they do not directly relate to you or your child's HPN. This information will be collected from your hospital, home care and office visit records.

Who will have access to my identifiable medical record information contained in the Registry?

Only the site investigators associated with your hospital or home care company and their research staffs will have access to your full medical record. A current, complete listing of these individuals will be provided to you upon your written request (or these can be listed here____).

For how long will my medical record information continue to be placed in the Registry and for how long will this information be used for research purposes?

We will continue to place your medical record information into SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care until 1) you are no longer living; or 2) you withdraw your permission for participation in the Registry. Your non-identified medical record information contributed to the Registry will be used for research purposes for an indefinite period of time.

Is my participation in the Registry voluntary?

Your participation in the SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, to include the use of your medical record information for the research purposes described above, is completely voluntary. Whether or not you provide your permission for participation in this Registry will have no effect on your current or future medical care.

May I withdraw, at a future date, my consent for participation in this Registry?

You may withdraw, at any time, your consent for participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, to include the additional collection of your medical record information and its further use for the research purposes described above. However, any research use of your medical record information prior to the date that you formally withdraw your permission will not be destroyed. Further, any data from your medical record that was contributed to the Registry and combined with other information will remain in the combined database. To formally withdraw your permission for participation in the Registry you should provide a written and dated notice of this decision to the principal site investigator of the registry at the address listed on the first page of this consent form.

****

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of my participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care at any time, and that such future questions will be answered by the site investigators associated with this registry. I understand that a copy of this consent form will be given to me. I understand that any questions which I have about my rights as a participant in the registry will be answered by the site investigator at [insert name/contact information].

By signing below, I agree to participate in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care.

_____ _____

Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care to the above-named individual, and I have discussed the possible

risks and potential benefits of participation in this Registry. Any questions the individual has about this Registry have been answered, and the physicians and research staff associated with SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care will be available to address future questions as they arise.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

APPENDIX 7: SAMPLE ASSENT FORM

Child Assent to Participate in a Research Project

Committee # Name of Study volunteer

SustainTM LLC: American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)'s National Patient Registry for Nutrition Care - Home Parenteral Nutrition (HPN)

This assent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home a copy of this assent form to think about or discuss with family or friends before making your decision.

Will you be a part of this research study?

We are inviting you and many other children and adults receiving home parenteral nutrition (HPN) to give us information to place in a research registry (database). The purpose of the study is to collect information about the number of people who need HPN, how long they need it, their medical conditions, and how well they do on HPN. Since you are on HPN, you know that it is a special liquid food given into the blood through an intravenous (IV) catheter (needle in the vein) because your stomach or bowel is not able to digest or absorb enough food.

The name of the research registry is SustainTM. The information will be collected and safely kept by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). The goal of the registry is to include 100% of HPN patients in the United States.

In order to be a part of this study, you and your parent (or legal guardian) must listen to someone from your doctor's office explain this information about the study. You should ask any questions that you have. For you to start the study, your parent or your legal guardian must agree, in writing, that you will take part. Also, we are asking you to agree to take part, and you can do this by signing your name on the parents' form. If you decide to take part in this study and then change your mind, you may choose to stop at any time.

Do you need to be in this study to be treated?

Being in this study is your choice and the choice of your parent or legal guardian. You do not have to be in this study to receive your HPN. You will continue to receive the same care and monitoring of your HPN whether you are in the study or not. If you take part in this study you will not be asked to do anything other than to allow information from your medical record to be collected in an anonymous and confidential (private) manner.

What kinds of things will you do if you take part in this study?

If you take part in this study you will allow information from your medical record to be collected in a confidential (private) manner. The information being collected will include: date of birth, medical condition, height and weight, laboratory tests, parenteral nutrition solution, type of catheter,

medications, diet or other feedings, psychosocial status, activity, patient/caregiver teaching, hospital admissions, complications of therapy, and reason for ending HPN.

A code number will be used for your information. The only link to you and the code number will be with the study staff at this institution. Information will be collected and placed into the SustainTM registry while you receive HPN. Only information that is available in your medical record as part of your routine monitoring and care will be included. This information will be used indefinitely for research purposes.

Will you feel uncomfortable during the study?

There is no discomfort or side effects to you. Your medical care will not be different if you are in this study.

Who will see this information?

Your doctor and study staff will keep your medical information confidential (private). Your name will not appear on any of the information that your doctor shares with the SustainTM registry.

When will the study end?

The study will last as long as you receive HPN unless you change your mind or decide not to stay in the study, but all of the information already shared with the SustainM registry will be used indefinitely for research purposes.

APPENDIX 8: SAMPLE WAIVER OF CONSENT FORM

IRB Protocol #:_____

Approval Date: ___/____/_____

Renewal Date: ___/____/_____

SustainTM , LLC: American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)'s National Patient Registry for Nutrition Care

WAIVER OF INFORMED CONSENT DOCUMENT

PATIENT INFORMATION

TITLE: SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care

PRINCIPAL SITE INVESTIGATOR: (Name/Institutional Address/Contact Information)

SITE CO-INVESTIGATORS: (Names and Contact Information)

SOURCE OF SUPPORT: SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care

What is the purpose of this Registry?

Many advancements in medicine have resulted from research involving the collection and

comparison of the medical record information of patients with a certain disease or condition.

Because you or your family member are receiving Home Parenteral Nutrition (HPN), we are placing non-identifiable information (no one will know it is yours) from your past, current and future medical record information into a national data registry operated by SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care. The SustainTM Registry will collect data from many areas such as hospitals or home care companies into a national computer database. By placing the medical record information of many patients such as you or your family member into this registry, researchers will be able to conduct research studies directed at increasing our knowledge about home parenteral nutrition patients and their health condition. The mission of the SustainTM Nutrition Care Registry is to maintain

a prospective, longitudinal (real time and long term) nutrition therapy patient registry in order to improve patient outcomes. The first phase of this registry will be to describe typical HPN patients.

The specific goals of this phase of the SustainTM ,LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care are to:

1. Collect information regarding the patients and populations who require home parenteral nutrition in the U.S.,
2. Measure outcomes associated with home parenteral nutrition,
3. Allow hospitals or home infusion companies to compare findings against like groups and against the total HPN patient population so that hospitals, physicians and home care agencies can see how they are doing compared to similar institutions, and
4. Publish the findings in order to improve the quality of care for patients receiving home parenteral nutrition.

Who is being asked to participate in this Registry?

All patients who are being discharged from the hospital and going home on home parenteral nutrition or who are already on home parenteral nutrition are being asked to participate in this Registry.

What will my participation in this Registry involve?

If you agree to participate in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, certain facts related to your past, current and future medical record information will be placed into the registry. This will permit research studies to be conducted on the medical record information contained within the registry. The data elements to be included in the registry will not identify you. That is, you or your child's name, address, phone number, e-mail address, social security number, medical record number, and other data that could be used to directly identify you or your child will not be shared with the Registry. The only potentially identifiable information included in the registry are dates and patient ages.

What are the possible risks of my participation in this Registry?

There are no risks of physical injury associated with you or your child's participation in the SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care. In order to preserve patient confidentiality and protect against the risk that information about you or your child's health might become known to individuals outside of the Registry, we will assign a special code number to your medical record information. This code will remain confidential with your hospital, physician, or home care organization and will not be transmitted to the SustainTM Registry. No information that could be used to directly identify you will be contributed to the Registry. Once contributed, your non-identifiable data will be combined with data on many other individuals. The Registry will control access to the aggregated database.

What are the possible benefits of my participation in the Registry?

It is unlikely that you will receive any direct benefit as a result of your participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care. However, the medical data contained within the Registry will be used for research studies directed at improving our knowledge and treatment of patients receiving HPN and this knowledge may benefit patients on HPN in the future.

Will I or my insurance provider be charged for my participation in the Registry?

There will be no costs to you or your insurance provider to participate in this Registry.

Will I be paid for my participation in the Registry?

No, you will not receive any payment for participating in this Registry.

Who will know about my participation in this Registry?

Any information from you or your child's medical records that is placed into SustainTM , LLC A.S.P.E.N.'s National Patient Registry for Nutrition Care will not identify you by name, address, or any other direct identifiable. All information will be kept as confidential (private) as possible. You will not be identified by name or any other direct identifying characteristic in any publication of the results of research studies involving the use of your medical record information.

What is the nature of my medical record information that will be placed into the Registry?

Certain non-identifying facts related to you or your child's past, current and future medical record information will be recorded into the Registry. Examples of these might be diagnosis, type of IV catheter, hospitalizations, or type of HPN solutions. The researchers may review your medical records, including medical information related to any of your medical conditions and treatments, even if they do not directly relate to you or your child's HPN. This information will be collected from your hospital, home care and office visit records.

Who will have access to my identifiable medical record information contained in the Registry?

Only the site investigators associated with your hospital or home care company and their research staffs will have access to your full medical record. A current, complete listing of these individuals will be provided to you upon your written request (or these can be listed here____).

For how long will my medical record information continue to be placed in the Registry and for how long will this information be used for research purposes?

We will continue to place your medical record information into SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care until 1) you are no longer living; or 2) you withdraw your permission for participation in the Registry. Your non-identified medical record information contributed to the Registry will be used for research purposes for an indefinite period of time.

Is my participation in the Registry voluntary?

Your participation in the SustainTM, LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, to include the use of your medical record information for the research purposes described above, is completely voluntary. Whether or not you provide your permission for participation in this Registry will have no effect on your current or future medical care.

May I withdraw, at a future date, my consent for participation in this Registry?

You may withdraw, at any time, your consent for participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care, to include the additional collection of your medical record information and its further use for the research purposes described above. However, any research use of your medical record information prior to the date that you formally withdraw your permission will not be destroyed. Further, any data from your medical record that was contributed to the Registry and combined with other information will remain in the combined database. To formally withdraw your permission for participation in the Registry you should provide a written and dated notice of this decision to the principal site investigator of the registry at the address listed on the first page of this consent form.

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Waiver of Informed Consent

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of my participation in SustainTM , LLC: A.S.P.E.N.'s National Patient Registry for Nutrition Care at any time, and that such future questions will be answered by the site investigators associated with this registry. I understand that a copy of this consent form will be given to me. I understand that any questions which I have about my rights as a participant in the registry will be answered by the site investigator at my institution or home infusion company or I may call the Sustain study number at 1-800-727-4567, ext. 133.

APPENDIX 9: PHYSICIAN LETTER

October 14, 2011

«First_Name» «Last_Name», «Designation»

«Address_Line_1»

«Address_Line_2»

«City», «StateTerritory» «Postal_Code»

RE: Get your organization enrolled in Sustain today!

Dear Dr. «Last_Name»,

I am writing to you today to invite you to participate in SustainTM, A.S.P.E.N.'s National Patient Registry for Nutrition Care. Sustain is a web based tool that allows clinicians to enter patient data, review and analyze results, benchmark outcomes against the national aggregate, post research questions and publish clinical research based on registry findings. Currently, the registry is focused on collecting data on new and existing Home PN patients, who require this high cost, high complication therapy. We now have 20 sites enrolled, comprised of medical centers, hospitals, and home infusion agencies, and data collection has begun, with over 100 patients entered into the Registry thus far.

The goal is to capture data on 100% of the HPN population in the US. That does not necessarily mean we need all data on each patient, but the registry will be more helpful with every HPN patient. We have identified critical elements such as diagnoses, reason for PN, and type of catheter to be completed.

Who Can Participate

Any clinician who discharges HPN patients from the hospital or who cares for them in the home is eligible. Sites must successfully complete the enrollment process which includes Institutional Review Board (IRB) approval and signing of a Participant Agreement. After patient data is submitted, each site will be allowed to analyze and publish their own series and benchmark against the total pooled data.

Why Participate?

Registry data will ultimately help your organization make better-informed patient treatment decisions, support the appropriate use of nutrition support therapy, justify the need for nutrition support clinicians, and help translate results into improved patient outcomes. Please note, unlike many other registries, there will be no charge to your practice or institution to participate.

For more information, go to our Sustain website, www.nutritioncare.org/Sustain, or contact Katy Hanley, at katyh@aspen.nutr.org , phone: 1-800-727-4567, ext. 133 or Peggi Guenter, RN, PhD at peggig@aspen.nutr.org.

Sincerely,

Lawrence Robinson, PharmD

Sustain Executive Council Chair

APPENDIX 10: PROJECT-LEVEL DATA ANALYSIS PLAN

Statistical Plan for Addressing Project Level Research Questions
Sustain HPN Project

Overview

Sustain's Scientific Council defined four overarching clinical research questions that will be explored twice each year. These questions will be answered by conducting a series of statistical analyses that will (1) answer the research questions; (2) serve as a foundation for manuscript preparation; (3) provide information that can be used for advocacy and (4) secure external support for Sustain's continued operations.

As noted in the Study Binder, the research questions that were articulated by the Scientific Council were:

- Who are the HPN patients in the Sustain registry?
- What are the rates of key outcomes among HPN patients in the Sustain registry?
- Do rates of key outcomes differ by clinical characteristics?
- Is there an association between duration of HPN and specific patient diagnoses?

The analyses that will be conducted for each of these questions are described below. It is important to note that A.S.P.E.N. staff use the Sustain data system reporting infrastructure to run a series of descriptive analyses on a regular basis. The analyses that will be run as part of the project-level analysis plan will not replicate those analyses. Rather, they will provide supplementary information on cross-sectional aspects of the Registry that are not included in the automated system infrastructure as well as longitudinal analyses that can't be conducted with existing Registry tools. In this document, we provide a description of each research question, followed by "table shells" that provide a visual tool to help understand how the data will be presented in the bi-annual reports.

1. Who are the HPN patients in the Sustain registry?

This cross-sectional question involves a series of descriptive statistics that will provide insight into the Sustain population. Importantly, because the GVT data system generates descriptive statistics on Sustain participants, the focus of these analyses will be on understanding how demographic and clinical characteristics differ by participant age and duration of HPN therapy. As noted above, we anticipate that the results that will be generated by these analyses will shift somewhat over time because the data set upon which they are based will increase in size.

Table 1: Sustain Study Population: Demographic and Clinical Characteristics as of {Date here}

Characteristic	**N={total}**		
Demographic Variables {here}			
Clinical variables {here}			

Statistical notes: Table 1 will show summary statistics on the Sustain population at the "as of" date, the date at which the data will be "pulled down for analysis. Most data will consist of categorical variables that will be expressed as percents, while a smaller number of variables will be expressed as mean+/- s.d.

Table 2: Demographic and Clinical Characteristics of the Sustain Study Population, By Age, as of {Date here}

Characteristic	N={total}	<18			>=18			
		N={all}	<=12 months	1=<18 years	N={all}	18-44	45-64	65+
Demographic Variables here								
Clinical Variables here								

Statistical notes: Table 2 will focus on age and show summary statistics on the Sustain population at the "as of" date, the date at which the data will be "pulled down for analysis. One column will repeat the data from Table 1 for reference, and within the pediatric and adult sections, there will be an "all" category as well as smaller categories. As with Table 1, most data will consist of categorical variables that will be expressed as percents, while a smaller number of variables will be expressed as mean+/- s.d. In Table 2, there is interest in understanding differences within each age group (e.g. tests for differences between 18-44 year olds and those 45-64) as well as differences between pediatrics and adults as a whole. Further, there is interest in understanding the distribution of both row and column percents.

Table 3: Demographic and Clinical Characteristics of the Sustain Study Population, By HPN Duration, as of {Date here}

Characteristic	N={total}	New Patients				Existing Patients			
		N={all}	PN days	HPN<1 yr	HPN >=1yr	N={all}	PN days	HPN<2.5 yr	HPN>=2.5 yr
Demographic Variables here									
Clinical variables here									

Statistical notes: Table 3 will focus on HPN duration and show summary statistics on the Sustain population at the "as of" date, the date at which the data will be "pulled down for analysis. One column will repeat the data from Table 1 for reference, and within the duration sections, there will be an "all" category as well as smaller categories, as appropriate. As with Table 1, most data will consist of categorical variables that will be expressed as percents, while a smaller number of variables will be expressed as mean+/- s.d. Because we will have follow-up data when these analyses are done, we may be able to stratify new patients by subcategories of HPN duration. Similar to Table 2, there is

interest in understanding within- and between stratum differences, as well as distributions by row and by column.

Tables 1-3 will involve descriptive statistics, stratified analyses, and significance testing of the potential cross-sectional associations between both age and HPN duration and the distribution of demographic and clinical variables. We anticipate that significance testing will involve t-tests for differences in means between two groups, ANOVA for differences in means in more than two groups, and chi-square tests for differences in proportions of categorical variables. There are a number of ways that significance testing can be approached, all of which are heavily influenced by missing data and ascertainment bias. These issues will be covered in analysis notes that will accompany the results.

2. What are the rates of key outcomes among HPN patients in the Sustain registry?

This question is at the heart of the Sustain Registry's long term goals: To inform on HPN outcomes and drive best practices. This question involves use of the "outcome" data that are collected on follow-up forms. In particular, the outcomes are based on rates which are calculated using follow-up time and the number of events that occur after the participant entered the Registry. Follow-up time is the number of days from enrollment into the registry to the last reported information on the patient which include outpatient, hospitalized, laboratory values, died, etc. All of this information is collected after baseline, and is therefore dependent on the frequency of follow-up on the part of the field centers. For this question, we will summarize rates of key outcomes by describing follow-up time, counts of key events, and how these numbers work together to produce event rates.

Table 4: HPN event counts and rates of key outcomes, as of {date here}

Outcome	Event count*	Follow-up time	Number of follow-ups	Rate (per 1000 PN days)
All-cause mortality				
HPN related mortality				
Hospital admission				
Re-hospitalization due to catheter issue				
Catheter infection				
Catheter thrombosis				
Liver failure				
Metabolic bone disease				

*With the exception of death, a single individual could have more than one event within each event category.

Statistical Notes: Table 4 provides counts and unadjusted event rates for the Sustain population. This table shows data for ALL events, as opposed to "first events" after entry into the Registry. Event rates will be examined using calculated variables that are provided by the GVT data system. The calculation is simple: [(event count/PN days)*1000]. Although these data have been examined carefully for quality

control, cautious interpretation of event rate data are in order. The field centers engage in varied practices with regard to patient follow-up, and this has direct implications for interpretation of event rates. Further, loss to follow-up, if differential across field centers also has the ability to introduce bias into data interpretation. With these cautions, calculation and reporting of event rates from Sustain represent the first reporting of this type of information from a large data collection effort, and are therefore important as a springboard for future activities in this area. As an extension of Table 4, a related table could be produced that has events for all patients, patients with only one event and patients with more than one event.

Table 5: HPN event counts and rates of first outcomes, as of {date here}

Outcome	Event count*	Follow-up time	Rate (per 1000 PN days)
All-cause mortality			
HPN related mortality			
Hospital admission			
Re-hospitalization due to catheter issue			
Catheter infection			
Catheter thrombosis			
Liver failure			
Metabolic bone disease			

*With the exception of death, a single individual could have more than one event within each event category.

Statistical Notes: Table 5 provides counts and unadjusted event rates for FIRST events the Sustain population. Thus, Table 5 shows data for a subset of events in Table 4, which shows event rates for all events after entry into the Registry. Event rates will be examined using calculated variables that are provided by the GVT data system. The calculation is simple: [(event count/PN days)*1000]. Although these data have been examined carefully for quality control, cautious interpretation of event rate data are in order. The field centers engage in varied practices with regard to patient follow-up, and this has direct implications for interpretation of event rates. Further, loss to follow-up, if differential across field centers also has the ability to introduce bias into data interpretation. With these cautions, calculation and reporting of event rates from Sustain represent the first reporting of this type of information from a large data collection effort, and are therefore important as a springboard for future activities in this area. It should be stressed that this table provides rates of “first” events occurring after enrollment into the Registry, as they are defined in the Sustain Registry. That is, existing patients may well have had events of interest prior to their entry into the Registry.

3. Do outcomes rates differ by selected demographic and clinical characteristics?

This question extends findings from Question #2 by exploring whether key variables that are postulated to impact event rates are actually associated with differences in these rates. These analyses will generally follow the same approach-stratification by categories of the demographic or clinical variable of interest. Because of the potential problem of small event counts within categories of some variables, we anticipate focusing these analyses on total event counts, rather than first events.

In the table below, we use all-cause mortality as a sample outcome and age and HPN duration as sample demographic and clinical variables to illustrate how this series of tables will be presented. We anticipate a separate table for each outcome (for a total of 8 tables in this series), with the rows organized in a manner similar to what is presented here.

Table 6: All-Cause Mortality Among Sustain Participants, by Selected Demographic and Clinical Variables, as of {date here}

Outcome	Event count	Follow-up time	Rate (per 1000 PN days)	p-value
Demographic Variables				
Age				
All				
<1 year				
1 to <18				
18-44				
45-64 65+				
[etc]				
Clinical Variables				
Type of catheter				
PICC				
Port				
Tunneled				
Other				
[etc]				

Statistical Notes: Table 6 and the other outcomes tables that are organized in this way would show data for the following variables, which would be stratified into logical categories: Age, race/ethnicity, insurance status, reason for PN or diagnoses, co-morbidities, goals of PN, PN duration, new or existing patients, nutritional status, sole source PN vs. combination therapy, medications, type of catheter.

Event rates will be examined using calculated variables that are provided by the GVT data system. The calculation is simple: [(event count/PN days)*1000]. Although these data have been examined carefully for quality control, cautious interpretation of event rate data are in order. The field centers engage in varied practices with regard to patient follow-up, and this has direct implications for interpretation of event rates. Further, loss to follow-up, if differential across field centers also has the ability to introduce bias into data interpretation. With these cautions, calculation and reporting of event rates from Sustain represent the first reporting of this type of information from a large data collection effort, and are therefore important as a springboard for future activities in this area.

If hypothesis testing is desired, this can be done within each independent variable category, with the p-value presented on the far right of the table. This would reflect the statistical significance associated with a question such as, “Does the rate of all-cause mortality among Sustain participants differ by age group?” This analysis could be done with Cox regression. It is important to note that as the number of categories (rows) increases for any given variable of interest, the data will become sparser and less reliable. As a result, when the analyses are actually implemented, it may become necessary to collapse some of these categories. Sparse cells could also result in non-significant findings for contrasts across categories of independent variables because of limited statistical power.

Table 7: Selected Demographic and Clinical Variables, Stratified by All-Cause Mortality as of {date here}

Demographic Variables	Dead		Not Dead		P
	N	%	N	%	
Age					
All					
<1 year					
1 to <18					
18-44					
45-64 65+					
[etc]					
Clinical					

Variables					
Type of catheter					
PICC					
Port					
Tunneled					
Other					
[etc]					

Statistical Notes: Table 7 Shows potential risk factors in relation to a binary outcome reflecting all-cause mortality. Similar tables will be constructed for the other outcomes of interest. Significance testing will be conducted to begin to identify which variables may be of interest for inclusion in the multivariable models described below.

4. Is there an association between duration of HPN and specific underlying patient diagnoses?

This question explores the relationship between underlying diagnoses and whether these conditions are associated with the likelihood of being a new, or existing patient.

Table 8: Frequency of underlying diagnoses according to HPN duration, as of {date here}

Diagnoses	All	New			Existing			p-value
		N={all}	HPN<1yr	HPN>=1yr	N={all}	HPN<2.5yr	HPN>=2.5yr	
listed here								

Statistical Notes: Table 8 shows distributions of diagnoses in relation to HPN duration. These are expressed as percents. Significance testing could be conducted to contrast new and existing patients with regard to the frequency of individual diagnoses, and similar testing could be done (if meaningful) within the new and existing groups according to a meaningful sub-category of duration such as the sample scheme provided here.

Regression Analyses Based on Synthesis of Descriptive Data

Synthesizing the information from the above tables, the last step in the analyses will be to build multivariable models for each of the 8 outcomes in an effort to identify and quantify the independent effects of specific risk factors on event rates. It is anticipated that the first step in this process is to understand what variables were associated with increased risk of each outcome-many of those analyses will have been conducted in Table 7 and other tables that stratify the data on the outcomes of interest. Variables that differed significantly in these analyses will be considered for inclusion in multivariable models whose goal is to quantify the adjusted contributions of individual risk factors to each outcome. It is anticipated that the models will differ according to outcome, and that modest event rates for some outcomes may result in modeling challenges.

APPENDIX 11: DATA ARCHIVING PROTOCOL

Background and Rationale:

A key element of responsible stewardship of Sustain data involves a structured and predictable approach to archiving the data and related documentation.

Overview:

Sustain data are input by trained field staff into a distributed data system that is managed by an external vendor. That vendor, GVT, stores the data and calculates several variables based on fields that are included on the data collection forms. Each month, a second vendor, Resnick, Chodorow and Associates (RCA), receives a data download from GVT. These downloads are used to produce data sets that are appropriate for research purposes. Because A.S.P.E.N. will administer external requests for access to the analytic data sets, the archiving of Sustain data occurs at the A.S.P.E.N. offices.

Process:

RCA downloads two data sets each month: the "baseline" data set and the "follow-up" data set. These downloads occur at the same time in order to ensure continuity across patients in terms of follow-up. A number of quality control procedures are run at the time of each download. These are described in greater detail in the "Sustain Study Binder." In brief, these quality control procedures are designed to catch issues with the data that may not have been captured by the data system or by GVT. Issues that are identified during this process are either addressed (when possible) or they are conveyed to the Sustain Coordinator who adjudicates them with individual sites. RCA logs these quality control issues and works with the Sustain Coordinator to ensure that the problems are resolved and/or that training is modified to reduce the appearance of these problems in the future.

Each month, RCA produces a CD that contains several files. These files include:

1. An updated baseline data set
2. An updated follow-up data set
3. An updated log of quality control issues
4. The most recent version of the Sustain Data Dictionary
5. Any other documentation that pertains to the most recent version of the data sets

These CDs are delivered to the A.S.P.E.N. offices where they are copied by the Sustain Coordinator onto the secure part of the network that contains Sustain data.

Network Organization:

Sustain data will be stored in a dedicated and secure part of the A.S.P.E.N. network. In this section, there will be one folder that is labeled for each month and year, starting with February, 2014. When the Sustain Coordinator receives the data delivery, she will copy the files into the folder that is designated for that month and year. CDs will be labeled by hand and stored in the A.S.P.E.N. offices in a locked cabinet.