GpCRC

Gastroparesis
Clinical Research Consortium

Gastroparesis Registry 2

Standard Operating Procedures

Part I: Clinical Center Operations

3 April 2018

GpR 2 SOP Part I: Clinical Center Operations

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GpR 2 SOP Part I: Clinical Center Operations

1. Design overview

1.1. Design synopsis

Objectives

- To expand a registry of patients for the study of the epidemiology, etiology, and degree of morbidity associated with gastroparesis. The Gastroparesis Registry 2 (GpR 2) will enroll new patients and patients from the initial NIDDK Gastroparesis Clinical Research Consortium Gastroparesis Registry (GpR) of gastroparesis patients which was initiated in February 2007 and completed in March 2011.
- To continue to follow and expand the data collections of a well-characterized cohort to further define the natural history and clinical course of gastroparesis.
- To provide a reliable source for recruitment of well-characterized patients with gastroparesis for therapeutic clinical trials, pathophysiological, molecular, histopathologic, or other ancillary studies. These subsequent clinical trials or ancillary studies will be conducted under separate study protocols with separate consent processes.

Population

- Diabetic, idiopathic and post-Nissen fundoplication gastroparesis patients with delayed gastric emptying
- Patients with normal gastric emptying, but with symptoms of gastroparesis

Inclusion criteria

- Symptoms of gastroparesis of at least 12 weeks duration with varying degrees of nausea, vomiting, early satiety, postprandial fullness, and/or abdominal pain
- An etiology of either diabetic, idiopathic, or post-Nissen fundoplication gastroparesis
- Gastric emptying scintigraphy of solids and liquids using the 4 hour Egg Beaters® protocol within the last 6 months with either:
  - Abnormal gastric emptying rate defined as an abnormal 2 hour (>60% retention) and/or 4 hour (>10% retention) result based on a 4 hour scintigraphic low fat Egg Beaters® gastric emptying study performed at a GpCRC clinical center. (This group will comprise ~80% of patients in the registry.)
  - Patients with a normal gastric emptying rate, but who have symptoms of gastroparesis. (This group will comprise ~20% of patients in the registry.)
- Age at least 18 years at initial screening visit

Exclusion criteria

- Inability to comply with or complete the gastric emptying test by scintigraphy (including allergy to eggs)
- Presence of other conditions that could explain the patient's symptoms:
  - Pyloric or intestinal obstruction: by EGD, UGI, or Abdominal CT
  - Active inflammatory bowel disease

  - Known eosinophilic gastroenteritis
  - Primary neurological conditions that can cause nausea and vomiting such as increased intracranial pressure, space occupying or inflammatory/infectious lesions
  - Advanced liver disease
  - Chronic renal failure (serum creatinine >3 mg/dL) and/or on hemodialysis or peritoneal dialysis
  - Acute liver failure
  - Advanced liver disease (Child's B or C; a Child-Pugh-Turcotte (CPT) score of ?7)
  - Acute renal failure
- Total or subtotal (near complete) gastric resection, esophagogastrostomy, gastrojejunostomy, or gastric bypass. Note: patients with prior Nissen fundoplication will be eligible for enrollment.
- Any other condition, which in the opinion of the investigator, could explain the symptoms or interfere with study requirements
- Inability to obtain informed consent

Recruitment targets: A total of 750 patients are to be enrolled in the Gastroparesis Registry 2 (GpR 2): 400 new patients and 350 patients continuing from the first Gastroparesis Registry

Recruitment period: 24 months

Follow-up period: 48-192 weeks (1-4 years); up to 4 years follow-up depending on date of enrollment

Screening and Enrollment

- Enrollment must occur within 16 weeks of informed consent and registration
- Follow-up visits will occur at 24, 48, 72, 96, 120, 144, 168, and 192 weeks

Data Collection

- Baseline data collection includes demographic, socioeconomic characteristics and all measures listed below
- Follow-up data collection will include baseline measures and a repeat of certain procedures and laboratory tests as outlined in the data collection schedule (section 11.2)

Measures: Baseline (b) and Follow-up (f)

Scintigraphic gastric emptying test at (b) and 48 weeks (f) (percent retention at 1, 2 and 4 hours)

Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM)
Patient Assessment of Upper Gastrointestinal Disorders - Quality of Life (PAGI-QOL)
Rome III Diagnostic Questionnaire for Adult Functional GI Disorders
Health related quality of life (SF-36v2)
Brief pain inventory (BPI)
EGG and water load test
Beck Depression Inventory (BDI-II)
State Trait Anxiety Inventory (STAI)
Patient Health Questionnaire (PHQ-15)
Body mass index
HbA1c and glucose levels
Neuropathy Index using Neuropathy Total Symptom Score-6 (NTSS-6)
Block 2005 Food Frequency Questionnaire
Block Energy Expenditure Survey
Nausea Profile and Vomiting questionnaire
GpCRC abdominal pain questionnaire
Treatment histories for gastroparesis
Morbidity measures related to gastroparesis including mortality
Electrogastrography (EGG) with caloric meal and wireless motility capsule (SmartPill®) (Baseline only)

Sample size considerations

- Sample size for GpR 2: 750 patients
- For each publication or ancillary study proposed to the Steering Committee the following sample size considerations must be addressed:

  Specification of primary outcome measure for hypothesis
  Type I error <0.05 and power >0.80
  Specification of primary comparison groups and outcome measure
  Specification of minimum clinically meaningful effect size for the primary outcome
  Specification of methods for handling missing data
  Specification for multiplicity adjustments
  Method of analysis

1.2. Data collection schedule

	Screening visits	**Follow-up visits: Weeks from enrollment**							
	Screen and enroll	**24**	**48**	**72**	**96**	**120**	**144**	**168**	**192**
Consent, HIPAA authorization	X	.	.	.	.	.	.	.	.
Baseline medical history	X	.	.	.	.	.	.	.	.
Follow-up medical history	.	X	X	X	X	X	X	X	X
Upper gastrointestinal endoscopy	X	.	.	.	.	.	.	.	.
Gastric emptying scintigraphy[2]	X	.	X	.	.	.	.	.	.
PAGI-SYM questionnaire	X	X	X	X	X	X	X	X	X
PAGI-QOL questionnaire	X	X	X	X	X	X	X	X	X
Physical examination	X	X	X	X	X	X	X	X	X
EGG with SmartBar®, SmartPill®	X	.	.	.	.	.	.	.	.
Autonomic function testing with ECG	X	.	X	.	.	.	.	.	.
EGG and water load test	X	.	X	.	.	.	.	.	.
Rome III questionnaire	X	.	X	.	X	.	X	.	X
Eligibility confirmation	X	.	.	.	.	.	.	.	.
Neuropathy Total Symptom Score-6	X	X	X	X	X	X	X	X	X
Beck Depression Inventory	X	X	X	X	X	X	X	X	X
STAI: Self-evaluation questionnaire	X	X	X	X	X	X	X	X	X
Patient Health Questionnaire (PHQ-15)	X	X	X	X	X	X	X	X	X
Nausea Profile and vomiting questionnaire	X	X	X	X	X	X	X	X	X
Block 2005 Food Questionnaire	X	.	X	.	X	.	X	.	X
SF-36v2 Quality of Life	X	.	X	.	X	.	X	.	X
Block Energy Expenditure Survey	X	.	X	.	X	.	X	.	X
Brief Pain Inventory	X	.	X	.	X	.	X	.	X

	Screening visits	**Follow-up visits: Weeks from enrollment**							
	Screen and enroll	**24**	**48**	**72**	**96**	**120**	**144**	**168**	**192**
GpCRC abdominal pain questionnaire	X	.	X	.	X	.	X	.	X
Interim event form as needed (A)	.	A	A	A	A	A	A	A	A
Hematology (Complete Blood Count)	X	.	X	.	X	.	X	.	X
Comprehensive metabolic panel	X	.	X	.	X	.	X	.	X
Lipid panel, TSH, vitamin B12 & D levels	X	.	X	.	X	.	X	.	X
HbAlc†	X	X	X	X	X	X	X	X	X
ANA, hs-CRP, Sedimentation rate (ESR)*	X	.	.	.	.	.	.	.	.
Serum, plasma banking	X	.	X	.	X	.	X	.	X
DNA for banking*	X	.	.	.	.	.	.	.	.

Hematology (complete blood count): white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count

Comprehensive metabolic panel: sodium, potassium, chloride, carbon dioxide, calcium, BUN, creatinine, glucose, total protein albumin, and liver panel including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase

Lipid panel: total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, thyroid stimulating hormone (TSH), vitamin B12 and 25-hydroxy vitamin D levels

ANA= antinuclear antibody, hs-CRP= high sensitivity C-reactive protein, ESR= erythrocyte sedimentation rate

*Required only at screening

A= as needed

H HbA1c is required at each follow-up visit for diabetic patients only

2 The gastric emptying scintigraphy prior to enrollment is for solids and liquid emptying; whereas the gastric emptying test at 48 weeks will be quantitating gastric emptying of solids only

1.3. Blood collection schedule

	Study visits (weeks)					
Procedure	**screening/ enrollment**	**48**	**96**	**144**	**192**	**Total**
Hematology, metabolic/lipid panel, ANA, hs-CRP, ESR, TSH, vitamin B12 & D levels	25	.	.	.	.	**25**
HbA1c*	5	5	5	5	5	**25**
Fasting† plasma, serum banking	20	20	20	20	20	**100**
DNA banking	20	.	.	.	.	**20**
Total (mL)	**70**	**25**	**25**	**25**	**25**	**170**

Hematology: (complete blood count): white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count

Comprehensive metabolic panel: sodium, potassium, chloride, carbon dioxide, calcium, BUN, creatinine, glucose, total protein albumin, and liver panel including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase

Lipid panel: total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides

ANA= antinuclear antibody, hs-CRP= high sensitivity C- reactive protein, ESR= erythrocyte sedimentation rate, TSH= thyroid stimulating hormone, vitamin B12 and 25-hydroxy vitamin D levels

*HbA1c will be obtained at each follow-up visit (weeks 24, 48, 72, 96, 120, 144, 168, and 198) for diabetic patients only

†Fasting is defined as nothing by mouth except water in the 8 hours prior to blood draw. Fasting visits need to be scheduled for early morning and the patient must attend the visit after an overnight fast of at least 8 hours

1.4. Study population composition

Participants will be recruited predominantly from outpatient clinics either in gastroenterology, diabetes, or primary care settings. Inpatients (patients in the hospital) with the diagnosis of gastroparesis will also be invited to participate.

In GpR 2, the number of the participants with symptomatic nausea and vomiting with normal gastric emptying will be limited to 20% of the total participants enrolled. Participants with prior Nissen fundoplication will be eligible for enrollment and enrollment of participants with post-Nissen gastroparesis is limited to 20% of the participants with delayed gastric emptying. Assuming the goal of 750 participants are entered into GpR 2 and assuming similar types of enrollment as in the first registry this will result in the following types of participants: 300 idiopathic gastroparesis participants, 75 idiopathic participants with normal gastric emptying, 180 with diabetic gastroparesis, 45 diabetic participants with normal gastric emptying, 120 post-Nissen gastroparesis participants, and 30 post-Nissen participants with normal gastric emptying.

2. Eligibility and enrollment

2.1. Inclusion and exclusion criteria

Inclusion criteria

- Symptoms of gastroparesis of at least 12 weeks duration (do not have to be contiguous) with varying degrees of nausea, vomiting, early satiety, post-prandial fullness, and/or abdominal pain
- An etiology of either diabetic, idiopathic, or post-Nissen fundoplication gastroparesis
- Gastric emptying scintigraphy of solids and liquids test using 4 hours Egg Beaters® protocol within the last 6 months with either:
  - Abnormal gastric emptying rate defined as an abnormal 2 hour (>60% retention) and/or 4 hour (>10% retention) result based on a 4 hour scintigraphic low fat Egg Beaters® gastric emptying study performed at a GpCRC clinical center.
  - Patients with a normal gastric emptying rate but with symptoms of gastroparesis may be enrolled and classified as possible gastroparesis or gastroparesis like with normal gastric emptying
- Age at least 18 years at initial screening visit

Exclusion criteria

- Inability to comply with or complete the gastric emptying scintigraphy test (including allergy to eggs)
- Presence of other conditions that could explain the patient's symptoms:
  - Pyloric or intestinal obstruction as determined by endoscopy, upper GI series or abdominal CT scan
  - Active inflammatory bowel disease
  - Known eosinophilic gastroenteritis
  - Primary neurological conditions that could cause nausea and/or vomiting such as increased intracranial pressure, space occupying or inflammatory/infectious lesions
  - Acute liver failure
  - Advanced liver disease (Child's B or C; a Child-Pugh-Turcotte (CPT) score of ?7)
  - Acute renal failure
- Chronic renal failure (serum creatinine >3 mg/dL) and/or on hemodialysis or peritoneal dialysis
- Total or subtotal (near complete) gastric resection, esophagogastrostomy, gastrojejunostomy, or gastric bypass. Note: patients with prior fundoplication will be eligible for enrollment.
- Any other plausible structural or metabolic cause
- Any other condition, which in the opinion of the investigator would interfere with study requirements
- Inability to obtain informed consent

2.1. Inclusion and exclusion criteria

Clinical centers must be certified by the Scientific Data Research Center to start enrollment in the Gastroparesis Registry 2. Prior to implementation of this protocol, the principal investigator must have the protocol and consent form approved by the Institutional Review Board for Human Research (IRB) at his/her institution. Once a candidate for GpR 2 has been identified, study related details will be carefully discussed with the patient including the follow-up visit schedule and procedures. The patient will be asked to read and sign the consent form that was approved by the IRB. There will be a separate consent for the collection, storage, and use of DNA for genetic research.

2.2. Calculation of Child-Pugh-Turcotte score

Child-Pugh-Turcotte (CPT) score for severity of liver disease will be calculated as follows:

	Points
1. Serum albumin (g/dL; recorded on the LR form)	
greater than 3.5	1
2.8 – 3.5	2
less than 2.8	3
2. Serum total bilirubin (mg/dL; recorded on the LR form)	
less than 2.0	1
2.0 – 3.0	2
greater than 3.0	3
3. Prothrombin time (INR form)	
less than 1.7	1
1.7 – 2.3	2
greater than 2.3	3
4. Ascites: use all available information from all sources and best medical judgement	
None	1
Mild, easily managed	2
Severe, refractory	3
5. Encephalopathy: use all available information from all sources and best medical judgement	
None	1
Mild, easily managed	2
Severe, refractory	3

Child's stage A: 5-6 points
Child's stage B: 7-9 points
Child's stage C: 10-15 points

2.3. Rome III Diagnostic Questionnaire scoring algorithm

For Functional Dyspepsia (FD) Module

B1. Functional Dyspepsia

Diagnostic criteria*

Must include:

1. One or more of:
   a. Bothersome postprandial fullness
      Uncomfortably full after regular sized meal, more than 1 day/week (question 13>4)
      Onset more than 6 months ago (question 14=1)
   b. Early satiation
      Unable to finish regular sized meal, more than 1 day/week (question 15 >4)
      Onset more than 6 months ago. Yes. (question 16=1)
   c. Epigastric pain
      Pain or burning in middle of abdomen, at least 1 day/week (question 17>3)
      Onset more than 6 months ago. Yes. (question 18=1)
   d. Epigastric burning
      (This criterion is incorporated in the same question as epigastric pain)

AND

1. No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms
   No question.

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
   Yes. (question 18=1)

B1a: Postprandial Distress Syndrome

Diagnostic criteria*

Must include **one or both** of the following:

1. Bothersome postprandial fullness, occurring after ordinary-sized meals, at least several times per week

   Uncomfortably full after regular-sized meal, more than 1 day/week (question 13>4)

2. Early satiation that prevents finishing a regular meal, at least several times per week

   Unable to finish regular-sized meal more than 1 day/week (question 15>4)

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Requires a "Yes" to both. (question 14=1) & (question 16=1)

B1b: Epigastric Pain Syndrome

Diagnostic criteria*

Must include **all** of the following:

1. Pain or burning localized to the epigastrium, of at least moderate severity at least once per week

   Pain or burning in middle of abdomen, at least 1 day/week (question 17>3)

   Pain is at least moderate severity (question 20>2)

2. The pain is intermittent

   Pain or burning often disappears completely in the same day (question 19>1)

3. Not generalized or localized to other abdominal or chest regions

   Chest pain occurs once a month or less often (question 11 <3)

   Heartburn occurs once a month or less often (question 12 <3)

4. Not relieved by defecation or passage of flatus

   Never or rarely gets better after defecation (question 22=0)

5. Not fulfilling criteria for gallbladder and sphicter of Oddi disorders
6. Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

   Yes. (question 18 =1)

B2. Belching Disorders

B2a: Aerophagia

Diagnostic criteria*

Must include **all** of the following:

1. Troublesome repetitive belching at least several times a week

   Bothersome belching more than 1 day a week (question 42>4)

2. Air swallowing that is objectively observed or measured

   No question

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

   Yes. (question 43=1)

B2b. Unspecified Excessive Belching

Diagnostic criteria*

Must include **all** of the following:

1. Troublesome repetitive belching at least several times a week

   Bothersome belching more than 1 day a week (question 42 > 4)

2. No objective evidence that excessive air swallowing underlies the symptom

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

   Yes. (question 43=1)

B3a: Chronic Idiopathic Nausea

Diagnostic criteria*

Must include **all** of the following:

1. Bothersome nausea, occurring at least several times per week

   Nausea more than once a week (question 31>4)

2. Not usually associated with vomiting

   Vomiting less than one day a week (question 33<4)

3. Absence of abnormalities at upper endoscopy or metabolic disease that explains the nausea

   No question.

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 32=1)

B3b: Functional vomiting

Diagnostic criteria*

Must include **all** of the following:

1. On average one or more episodes of vomiting per week

   Vomiting occurs at least once a week (question 33>3)

2. Absence of criteria for an eating disorder, rumination, or major psychiatric disease according by DSM-IV

   Patient does not meet criteria for Rumination Disorder

   No questions for eating disorder or major psychiatric disease.

3. Absence of self-induced induced vomiting and chronic cannabinoid use and absence of abnormalities in the central nervous system or metabolic diseases to explain the recurrent vomiting

   Never or rarely make yourself vomit (question 35=0)

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 34=1)

B3c: Cyclic Vomiting Syndrome

Diagnostic criteria

Must include **all** of the following:

1. Stereotypical episodes of vomiting regarding onset (acute) and duration (less than one week)

   Vomiting occurs more often than 'never or rarely' (question 33>0)

2. Three or more discrete episodes in the prior year

   At least 3 episodes during the year. Yes. (question 37=1)

3. Absence of nausea and vomiting between episodes

   Occurred in separate episodes and then stopped at least sometimes (question 36>0)

B4: Rumination Syndrome in Adults

Diagnostic criteria*

Must include **all** of the following:

1. Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or remastication and swallowing

   Bring up food at least 1 day/week (question 38>3)

   Hold food in mouth before spitting or swallowing often (question 40>1)

2. Regurgitation is not preceded by retching

   Was bringing up food preceded by retching? No. (question 41=0)

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 39=1)

C. Functional Bowel Disorders

C1. Irritable Bowel Syndrome

Diagnostic Criterion*

Recurrent abdominal pain or discomfort** at least 3 days/month in last 3 months associated with *two or more* of criteria #1-#3 below.

Pain or discomfort at least 2 to 3 days/month (question 44 > 2)

For women, does pain occur only during menstrual bleeding?

(question 46=0 or 2)

1. Improvement with defecation

   Pain or discomfort gets better after defecation at least sometimes

   (question 49>0)

2. Onset associated with a change in frequency of stool

   Onset of pain or discomfort associated with more stools at least sometimes (question 50>0), OR

3. Onset associated with a change in form (appearance) of stool

   Onset of pain or discomfort associated with looser stools, at least sometimes (question 52>0), OR

   Onset of pain or discomfort associated with harder stools, at least sometimes (question 53>0)

*Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 48=1)

*** Discomfort" means an uncomfortable sensation not described as pain.*

In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation is recommended for subject eligibility.

D. Functional abdominal pain syndrome

Diagnostic criteria*

Must include **all** of the following:

1. Continuous or nearly continuous abdominal pain

   Pain or discomfort occurs every day (question 44=6)

   Subject experiences only pain, not discomfort (question 45=1)

2. No or only occasional relationship of pain with physiological events (e.g., eating, defecation or menses)

   Pain is affected by eating sometimes or less often (question 54<2)

   Pain stops or lessens with defecation sometimes or less often (question 49<2)

   Pain onset is associated with more frequent stools sometimes or less often (question 47<2)

   Pain onset is associated with fewer stools sometimes or less often (question 51<2)

   Pain onset is associated with looser stools (question 52<2)

Pain onset is associated with harder stools (question 53<2)

Pain or burning is associated with a change in stool consistency never, rarely, or sometimes (question 50<2)

Pain or burning is associated with a change in stool frequency never, rarely, or sometimes (question 48<2)

For women pain is not limited to menstrual bleeding, or question is not applicable (question 46=0 or 2)

3. Some loss of daily functioning

   Pain limits activity at least some of the time (question 47>0)

4. The pain is not feigned (e.g., malingering)

   No question

5. Insufficient symptoms to meet criteria for another functional gastrointestinal disorder that would explain the pain

   Epigastric pain syndrome criteria not met, &

   IBS criteria not met, &

   Anorectal pain criteria not met

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 48=1)

E. Functional Gallbladder and Sphincter of Oddi Disorders (for exclusion)

Diagnostic criteria

Must include episodes of pain located in the epigastrium and/or right upper quadrant

Steady pain which may occur less than once per month (question 24>0)

AND all of the following:

1. Episodes lasting 30 minutes or longer

   At least often (question 25>1)

2. Recurrent symptoms occurring at different intervals (not daily)

   At least often (question 27>1)

3. The pain builds up to a steady level

   At least often (question 26>1)

4. The pain is moderate to severe enough to interrupt the patient's daily activities or lead to an emergency department visit

   At least often (question 28>1)

5. The pain is not relieved by bowel movements

   Never or rarely. (question 49=0)

6. The pain is not relieved by postural change

   Never or rarely. (question 23=0)

7. The pain is not relieved by antacids

   Never or rarely. (question 21=0)

8. Exclusion of other structural disease that would explain the symptoms.

   No question.

E1. Functional Gallbladder Disorder

Diagnostic criteria

Must include **all** of the following:

1. Criteria for functional gallbladder and sphincter of Oddi disorders

   Yes.

2. Gallbladder is present

   Gallbladder has not been removed

   No. (question 29=0)

3. Normal liver enzymes, conjugated bilirubin and amylase/lipase

   No question. Laboratory studies needed.

E2. Functional Biliary Sphincter of Oddi Disorder

Diagnostic criteria

Must include **both** of the following:

1. Criteria for functional gallbladder and sphincter of Oddi disorders

   Yes.

   Gallbladder has been removed (question 29=1)

   Pain has recurred at least sometimes since gallbladder was removed (question 30>0)

2. Normal anylase/lipase

   No question. Laboratory studies needed.

E3. Functional Pancreatic Sphincter of Oddi Disorder

Diagnostic criteria

Must include **all** of the following:

1. Criteria for functional gallbladder and sphincter of Oddi disorder

   Yes.

2. Elevated amylase/lipase

   No question.

F2: FUNCTIONAL ANORECTAL PAIN

F2a: CHRONIC PROCTALGIA

Diagnostic criteria*

Must include **all** of the following:

1. Chronic or recurrent rectal pain or aching

   Pain or aching occurs more than once a month (question 57>2)

2. Episodes last 20 minutes or longer

   Pain or aching lasts more than 20 min (question 58=2)

3. Exclusion of other causes of rectal pain such as ischemia, inflammatory bowel disease, cryptitis, intramuscular abscess, anal fissure, hemorrhoids, prostatitis, and coccygodynia.

   No question.

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Yes. (question 60=1)

F2b: PROCTALGIA FUGAX

Diagnostic Criteria

Must include **all** of the following:

1. Recurrent episodes of pain localized to the anus or lower rectum

   Pain or aching in anorectal area occurs at least 1 day/month (question 57>1)

2. Episodes last from seconds to minutes

   Pain or aching lasts seconds to minutes, up to 20 minutes (question 58=1)

3. There is no anorectal pain between episodes.

   Pain in anus or rectum occurs and then completely disappears during the same day (question 59=1)

For research purposes criteria must be fulfilled for 3 months; however, clinical diagnosis and evaluation may be made prior to 3 months

2.4. Guidelines for repeat determinations of eligibility

While certain inclusion and exclusion criteria are more objective and are unlikely to change, others are more subjective and may change over time. Thus, participants who are deemed ineligible at the time of initial screening may be rescreened at a later time as follows:

- Age <18 years – the participant may be rescreened after his or her 18th birthday
- Unwilling to participate – the participant may be rescreened after 3 months at the discretion of the investigator
- Unable to complete gastric emptying scintigraphy – the participant may be rescreened when clinically indicated
- Creatinine test may be repeated twice to allow for registration

2.5. Co-enrollment in other GpCRC studies

- When a Gastroparesis Registry 2 (GpR 2) participant enrolls in another GpCRC study such as the APRON Trial or GLUMIT-DG study, the visit schedule and requirements of these shorter studies take precedence over the requirements for the GpR 2. GpR 2 requirements are suspended for the duration of the participant's time in these other GpCRC studies. The GpR 2 Closeout Form (CO) should be completed to suspend the GpR 2visits while the patient is enrolled in other GpCRC studies as they become available. The GpR 2 Standard Operating Procedures I, section 6.37 provides instructions, but if you cannot find the answer to your question, call the Scientific Data Research Center.

- Data requirements are not suspended while a patient participates in a GpCRC ancillary study

2.6. Enrollment and eligibility checking

Enrollment steps

- Complete collection of all required screening data and key all screening data forms within 16 weeks of registration date
- Run electronic check on eligibility (i.e., run the Enrollment Task and resolve any missing items or ineligibility conditions)
- Run the Enrollment Task; if the patient is eligible, this task will officially enroll the patient in the GpR 2 and materials needed in follow-up will be generated (i.e., labels, visit time windows)

Overriding eligibility criteria

- Requests overriding eligibility criteria must be made in writing to the SDRC (direct the request to Aynur Ünalp-Arida); the request must specify the eligibility criteria for which override is requested and the request must be justified; the request must come from the principal investigator of the clinical center
- The SDRC may require agreement to the override from other GpCRC investigators
- Override requests require time to review and the review process will not be shortened

Enrollment date

- The date the clinical center runs the Enrollment Task and enrolls the patient
- The "time zero" for reckoning the time windows specified on the patient's Registry visit time window guide is the date of enrollment

3. Certification

3.1. Certification overview

What is certification?

- It is an internal (i.e., related to the study) procedure designed to identify the staff responsible for specific data items or data collection procedures or decisions about eligibility
- It is a managerial and quality assurance tool for the study

Who and what does it apply to?

- It applies to:
  - Gastroparesis Registry 2 staff
  - Each clinical center
- Certification for the Gastroparesis Registry 2 is required before any patient visits or data collection may occur; patients may not begin any screening examinations, sign any consent statements, or complete any study forms until the clinical center has been certified for the study
- More than one staff member may be certified for a function and it is recommended that more than one staff member be certified for a function

Why do we require it?

- Primary purpose is to help assure consistent conduct of the study over time, within and across clinical centers. The conduct of procedures should be similar across patients and in serial testing of the same patient over the duration of follow-up.
- Study procedures may vary from the usual practice of a participating clinical center, but it is important that methods be carried out in the same manner within and across clinical centers.
- It identifies the staff and sites that carry out study procedures and identifies to staff that they and their site are a part of the GpR 2 study.
- It provides a mechanism for tracking who collected key data items or made key decisions.
- The certification process may help a clinical center prepare for study activities by presenting the training, facility, and equipment needs in an organized fashion and requiring acquisition or completion of these items before study specific activities may begin.

Is separate certification in each GpCRC study required?

- Certification requirements for each GpCRC study are issued through notification of each clinical center by a numbered Policy and Procedure Memorandum (PPM).

3.2. Clinical center certification

General comments

- Each clinical center participating in the Gastroparesis Registry 2 must be certified for that participation
- Completion of the Clinical Center Certification (CC) form will be required
- IRB approval for the Gastroparesis Registry 2 protocol and consents will be required

Purpose of clinical center certification

- Provide information regarding how the clinical center will conduct different aspects of the protocol and who will staff the study
- Guide a clinical center through the steps of getting ready for the Gastroparesis Registry 2 – provide a checklist of what needs to be in place before patient activities begin

Requirements for certification of a site

- Complete the Clinical Center Certification (CC) form
- Certify at least one person for each function that requires certification (a person may be certified for more than one function)
- Obtain IRB approval of the most current Gastroparesis Registry 2 protocol and consent documents
- Obtain NIDDK Repository approval of the most current Gastroparesis Registry 2 consent documents for each IRB-approved center
- Receive written notice of approval (email) from the Scientific Data Research Center that the site is certified

3.3. Personnel certification

Staff functions requiring certification

- Clinical Coordinator
- Study Physician
- Data Entry Technician

Requirements

- Everyone
  - Complete the Personnel Certification (PC) form; this form identifies the functions applied for and provides an assurance of data confidentiality and integrity
  - Read the Gastroparesis Registry 2 protocol and SOP I: Clinical Center Operations
  - Complete the Knowledge Assessment (KA) form; this is a written general knowledge assessment about the GpR 2 study (open book)
- Additional requirements for Study Physician
  - Study Physician must be an MD preferably a gastroenterologist
- Additional requirements for Data Entry Technician
  - Complete the Data Entry Certification/Decertification Request (DC) form
  - Complete the data system tutorial

Process

- Send required materials to the SDRC
- The SDRC will send written notice of approval for certification or pending certification
- Each staff member will be issued a Personnel Identification Number (PIN)

Staff PINs

- Each staff member certified for at least one function will be issued a PIN which will consist of 3 digits – the first digit will identify the clinical center and the next two digits will be a sequential number assigned by the Scientific Data Research Center
- The PIN is used when completing forms
- The Data Entry Technician uses his/her PIN when signing on to the GpR 2 data system
- Staff can be certified for more than one function but will have only one PIN

4. Human subjects

4.1. Background

Consent to participation in the Gastroparesis Registry 2 (GpR 2) must be completed before screening for the study may begin. The patient must consent to procedures offered to and performed on him/her for screening, as well as to the follow-up visits which the patient will face in the future.

The consent process is a dynamic process involving explanations, time to think, questions, clarifications, and advice that a patient may seek from relatives, friends or anybody else considered relevant. We wish to inform the prospective participant as much as possible and as accurately as possible about what will be offered to him/her, how it will be done, what are the reasonable risks and benefits, what are the alternatives, and what is expected of the patient. We wish to answer patients' questions in a consistent and complete way.

The Gastroparesis Registry 2 consent process has three major stages:

- The patient is asked to consent to screening and enrollment into the Gastroparesis Registry 2
- The patient is asked to consent to the collection, storage, and use of blood samples for genetic research
- The patient is asked to sign the HIPAA authorization to disclose protected health information
- Once the consent forms have been signed, proceed with the completion of the Registration (RG) form. At the end of the screening process, the patient is asked to re-affirm their consent on the Enrollment (EN) form

4.2. Institutional Review Board process

Two template consent statements have been prepared for the Gastroparesis Registry 2:

- Consent for screening and enrollment in the GpR 2 study
- Consent for the collection, storage, and use of blood samples for current and future genetic research

Clinical centers are expected to use these materials in their submissions to their Institutional Review Boards (IRBs) for approval to participate in the Gastroparesis Registry 2. Each clinic must send copies of the consent statements to be used in their clinic, stamped with their IRB's seal, to the Scientific Data Research Center prior to initiating patient activities in the Gastroparesis Registry 2. Scientific Data Research Center staff will review and compare the approved local consents to the template consents. Specific local additions to and editing of the templates may be required at individual institutions, but deletion of material and major rewording of text may need to be explained and justified. Once a consent form has been approved by an institution's IRB, it cannot be changed without the IRB's approval.

The study protocol, and consent documents (and data collection forms if necessary) will be submitted to each clinical center's IRB and to the Scientific Data Research Center's IRB. Additionally, each clinical center will submit to their IRB any recruitment materials to be used at their site. A clinical center may not initiate any patient contact about the GpR 2 study until the site has IRB approval for the GpR 2 and the Scientific Data Research Center has certified the site for initiation of patient activities. All study personnel will have completed training in the Protection of Human Subjects per NIH guidelines.

HIPAA authorization forms will be prepared by each clinical center according to local clinical center institutional requirements and guidelines.

4.3. Consent administration

Gastroparesis Registry 2 consents

It is assumed that patients referred to a clinical center for screening may have heard about the Gastroparesis Registry 2, but their level of knowledge and expectations may well differ. We wish to standardize the consent administration across clinical centers as much as possible. Administration of the Registry 2 consents involves two tasks:

(1) A Gastroparesis Registry 2 staff member must sit down with the patient and review the contents of the statement; explain the risks, benefits, and responsibilities of participation; review the alternatives to participation; and answer questions.

(2) A Gastroparesis Registry 2 certified study physician (i.e., a Gastroparesis Registry 2 Certified gastroenterologist) must sign the consent statement, taking overall responsibility for the patient's informed and voluntary consent.

Staff at each clinical center should be designated to carry out these tasks. The rationale for requiring that the consent statement be signed by a study physician is to help assure that the physician signing the consent is one who has a broad role in the study.

Generally, the consent statements should be offered to the patient to read through at least a day before signature is requested. The consent will then be reviewed with the patient by the staff member designated to obtain consent; the consenter may opt to read the statement to the patient, pausing to explain issues as needed. This activity should take place in a quiet, private, and relaxed setting in the clinical center.

The patient should sign the consent statement in the presence of the GpR 2 staff member after all questions have been answered and when the patient has asserted orally that he/she is ready to sign the consent. After the patient has signed and dated the consent, the patient should meet with a GpR 2 study physician for the physician to sign the consent statement; ordinarily this meeting should take place on the same day that the patient signed the consent statement. The physician should ask the patient to confirm his/her voluntary consent and query the patient about any questions or concerns the patient may have about participation. Both signatures on the consent form must be in a non- erasable ink pen. If the physician cannot meet with the patient on the same day that the patient signs the consent statement, the physician may sign on another day. It is good practice to make an entry in patient's chart that the consent form was discussed and consent was obtained.

Consent for genetic research

The consent for collection and banking of blood for genetic research should be administered in the same way that the GpR 2 consent is administered, except that it should not be signed until the patient has been determined to be eligible for the GpR 2 study.

4.4. Time considerations for obtaining consent

- The **Gastroparesis Registry 2 Consent and HIPAA authorization** must be obtained at the start of the initial screening visit; documents from the referring physician (if any) should have been reviewed prior to the visit and the patient judged eligible for screening prior to the visit. Signature of this consent is required prior to sending the patient for any Gastroparesis Registry 2 research tests. A check for signature of this consent statement occurs on the Registration (RG) form.

- The **GpR 2 Consent for Collection, Storage, and Use of Blood Samples for Current and Future Genetic Research** must be obtained after eligibility for the GpR 2 study has been established, during screening. Signature of this consent is required prior to drawing blood for genetic research for the Gastroparesis Registry 2; a check for signature of this consent statement occurs on the Genetic Consent and Blood Collection Documentation (CG) form. Signature of this consent statement is not required for Gastroparesis Registry 2 eligibility (i.e., the patient may choose not to participate in the genetic research component of the Gastroparesis Registry 2).

- A patient may be given the consent statements to review prior to the initiation of screening visit to meet patient needs with respect to review time. Whenever a consent is first given to a patient for review, it should be made clear to the patient that the consent should not be signed until requested by a Gastroparesis Registry 2 staff member. The consents may be mailed to the patient prior to screening visit. Whatever timing is used by a clinic, the patient should be allowed enough time to reflect about the proposed Gastroparesis Registry 2 procedures, pose questions, and consult with other individuals that he/she considers relevant to their participation in the Gastroparesis Registry 2. Patients may request and should be given time to "think it over" at home and come back at a later time.

4.5. Consent handling

- Signed consent statements are important legal documents. These signed statements should be kept in the patient's GpR 2 clinical center file together with his/her other GpR 2 forms and documents. These forms are not part of the individual's institutional medical record, but part of his/her study record in the GpR 2. Consent statements will be examined during site visits.

- Consents should be annotated with the patient's study identifiers (ID number and code).

- The Gastroparesis Registry 2 consent statement is an "all or none" form. The patient either accepts it in its entirety and signs it, or does not. The patient must consent to the evaluation procedures, the follow-up evaluations, and the banking of his/her serum and plasma. If the patient refuses any part, the patient may not enroll in the Gastroparesis Registry.

- The Gastroparesis Registry 2 Consent for Genetic Research has been made a separate consent statement so that the patient can opt out of genetic research and still participate in the Gastroparesis Registry 2.

4.6. Informing participants of changes to consent document after enrollment

As new data become available during the conduct of the Gastroparesis Registry 2, the consent documents may need to be changed to reflect the current assessment of risks and benefits to participants in the study.

Procedures for dissemination of revisions of consent documents from the SDRC

- Changes deemed necessary will be made to the template consent documents
- Revisions of the template consent documents will be distributed to sites via a numbered Policy and Procedure Memorandum (PPM) with instructions to submit the revised consent to their IRB

Procedures for reviewing changes to consent documents with participants

- Clinical center personnel will develop and maintain a chronology of IRB approved changes to the consent documents used at their site
- At each follow-up visit, staff will use the chronology of consent changes to review with the participant any changes to the consent since the last visit. This review does not require obtaining the participant's signature on a new consent document, unless the local IRB requires obtaining a signature.
- Review changes to the consent documents with participants at follow-up visits
- This review process is not intended to be a reaffirmation of consent. The clinical center, if required by their local IRB, may develop procedures for reaffirmation of consent.

4.7. HIPAA considerations

Gastroparesis Registry 2 study staff have access to patient health information and to participant identifiers, such as name, address, and telephone number. Study records are to be kept in a secure place. Only people working on the GpR 2 study should have access to these records. However, these records could be reviewed to make sure that the study is being done as it should. People who may see medical records supporting study records are:

- Officials of your institution
- Your institution's research ethics committee
- Monitors from the GpCRC Scientific Data Research Center at the Johns Hopkins University, or other individuals selected by the GpCRC Steering Committee to monitor the study
- Members of the Data and Safety Monitoring Board (DSMB) to monitor overall progress of the study
- Government officials from the Office of Human Research Protections or the National Institutes of Health

Each clinical center should take steps to protect participant privacy. The assigned patient ID number and code should be used to identify patients on all forms and in the data files. Personal information such as name, address, and telephone number should be kept only at the clinical center where a participant completes visits.

People outside the clinical center who will receive Gastroparesis Registry 2 study data include:

- The GpCRC Scientific Data Research Center at the Johns Hopkins University in Baltimore, Maryland (or its successor) to maintain the central study database
- The GpCRC Data and Safety Monitoring Board to review the Gastroparesis Registry 2 data for performance and safety
- The NIDDK Genetics Repository at Rutgers, the State University of New Jersey in New Brunswick, New Jersey (or its successor) will receive participants' blood to obtain DNA; the blood samples for a particular participant will be identified by the participant's study ID number and code, not by name
- The NIDDK Biosample Repository at Fisher Bioservices in Germantown, Maryland (or its successor) will receive participants' serum and plasma; the samples for a particular participant will be identified by the participant's study ID number and code, not by name
- The GpCRC investigators, as well as outside researchers, to analyze and report Gastroparesis Registry 2 study data. Participant identity will not be disclosed in any reports or publications resulting from the study. While the Gastroparesis Registry 2 is ongoing, the use of the Gastroparesis Registry 2 study data must be approved by the GpCRC Steering Committee and by the research ethics committee at your institution.

4.7. HIPAA considerations

Participant agreement to join the Gastroparesis Registry 2 indicates that the participant also agrees to the use of study data as described above. If a participant does not agree to the described uses of study data, the participant may not enroll in the Gastroparesis Registry 2. The only exception is refusal to provide blood for genetic research; participants may refuse to provide blood for genetic research and still enroll in the Gastroparesis Registry 2.

5. Study visits

5.1. Overview of visit schedule

Screening visits(must be completed within 16 weeks of registration date)

- s: Consent, baseline medical history, physical exam, fasting blood draw for serum and plasma banking; blood draw for DNA banking and any laboratory measures (hematology (complete blood count): white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count; comprehensive metabolic panel: sodium, potassium, chloride, carbon dioxide, calcium, BUN, creatinine, glucose, and liver panel including: total protein, albumin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase; lipid panel: total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides; antinuclear antibody (ANA), high sensitivity C-reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR), thyroid stimulating hormone (TSH), vitamin B12 and 25-hydroxy vitamin D levels) if not available from archival records; upper endoscopy and gastric emptying of solids and liquids scintigraphy as needed; questionnaires on quality of life (Beck Depression Inventory (BD), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life [PAGI-QOL] (UG), Patient Health Questionnaire [PHQ-15] (PQ), State Trait Anxiety Inventory [STAI](SE), SF-36 Health Survey(QF); diet (Block 2005 questionnaire) (FQ); physical activity (Block Energy Expenditure Survey)(PD) and gastroparesis symptoms (Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity [PAGI-SYM](GD), Rome III Diagnostic Questionnaire (FD), Brief Pain Inventory (PI), Abdominal Pain Questionnaire (AP), Nausea Profile and Vomiting Questionnaire (NV), Neuropathy Total Symptoms Score-6) (NS). Results of procedures will be recorded on the following data collection forms: Electrogastrogram with Nutrient Meal Test (ST) form documents the electrogastrogram results at baseline and after ingestion of the SmartBar and SmartPill wireless motility capsule; the WM- Wireless Motility Capsule Report Form documents the results received from the wireless motility capsule receiver; the Electrogastrogram with Water Load Satiety Test (WL) form documents the electrogastrogram results and after ingestion of a volume of water and the Autonomic Function Testing (AN) form documents the participant's heart rate and blood pressure responses to assess sympathetic adrenergic function. The last form to be completed at screening should be the GpR 2 Enrollment form (EN) which reaffirms the patient's consent to participate in the Gastroparesis Registry 2.

Enrollment

- en: Enrollment is an event, not a necessarily a separate visit; enrollment occurs when the clinical center staff runs the enrollment task on the Gastroparesis Registry 2 data system and the participant is found to be eligible.

Follow-up

- f024: Follow-up medical history (FH), physical examination (PE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients) (form LR), collection of findings from any interim upper endoscopy or gastric emptying scintigraphy if needed (EG or GT); and the following questionnaires will be completed: Beck Depression Inventory (BD), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), State Trait Anxiety Inventory (SE): Complete the Adverse Event Report (AE) and Endoscopy Documentation (if needed).

- f048: (2 separate days of testing)

  Day 1: The week 48 follow-up visits require 2 separate days of testing and participants will come fasting for each day of testing. Medications that delay gastric emptying such as narcotic analgesics and medications that enhance gastric emptying such as prokinetics will be stopped for 3 days prior to the visits. A follow-up medical history (medication changes/additions, symptom exacerbations or interventions, surgeries, hospital admissions, new diagnoses of co-morbidities, complications interventions such as infections, documentation of any additional GI tests performed as part of standard of care), and physical examination (PE), including weight, height, and waist/hip circumference, blood pressure, heart rate, respiratory rate and body temperature will be performed. For diabetic patients, a fasting blood glucose level must be checked within the hour prior to the gastric emptying test to ensure it is less than 270 mg/dL. Patients will also complete the PAGI-SYM questionnaire (GD) immediately prior to the gastric emptying test.
  Participants will have a repeat 4 hour gastric emptying scintigraphy test of solids only performed, using the standard Egg Beaters® with toast and jam meal. Medications taken during the past week will be recorded. Results should be documented on the GT-Gastric Emptying Test Documentation - Follow-up form. A fasting blood collection will done for laboratory measures if needed (HbAlc required for diabetic patients) (LR), and for serum and plasma banking (BP). The following questionnaires will be completed:
  Beck Depression Inventory (BD), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), State Trait Anxiety Inventory (SE), SF-36 Health Survey (QF), Block 2005 questionnaire (FQ); Block Energy Expenditure Survey (PD), Rome III Diagnostic Questionnaire (FD), Brief Pain Inventory (PI), Abdominal Pain Questionnaire (AP), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms

Score-6 (NS). Complete the Endoscopy Documentation (EG) and Adverse Event Report (AE) forms.

Day 2: Autonomic function testing (AFT) followed by an EGG with water load satiety testing. On the morning of the AFT, EGG and water load satiety testing, the patient will arrive fasting. Patients may take their usual medications with a small amount of water (up to 4 oz) up to two hours prior to the study, but should refrain from coffee, tea, or juice. For the autonomic function test, participant will sit straight up with feet flat on the floor and arms resting comfortably at their sides. Blood pressures will be taken 6 times during the test and there are six phases of the test (3 baselines, 2 breathing exercises, 1 stand challenge). After arriving to the clinic, the patient's blood glucose level must be checked to ensure it is less than 270 mg/dL. If the patient's blood glucose level is greater than 270 mg/dL the EGG and water load satiety test must be rescheduled for another day.

Baseline symptoms prior to EGG recording will be obtained using visual analog scales for stomach fullness, hunger, nausea, bloating, and abdominal discomfort. The subject will mark each symptom line with a vertical line to indicate how they currently feel in terms of that symptom. Once the EGG and respiratory signals are stable, the baseline EGG recording period can begin. Patients will undergo a 15 minute baseline EGG in a reclining chair with the subject positioned at a 30-45 degree tilt.

Patients will begin the Water Load Satiety Test (WL). For this, participants will sit upright. During the test, participants will drink cool water for a 5 minute period until they feel "completely full." The total volume of water consumed will be recorded.

A continuous 30 minute EGG recording is then obtained. The patient's symptoms are recorded using VAS at 10, 20, and 30 minutes after ingestion of the water (at the end of the 0-10 minute, 11-20 minute, and the 21-30 minute post-satiety periods). The test is completed after the 30 minute recording period and the electrodes are removed.

- f072: Follow-up medical history (FH), physical examination (PE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients) (form LR), adverse event form (AE), collection of findings from any interim upper endoscopy or gastric emptying scintigraphy if needed (EG or GT); and the following questionnaires will be completed:
  Beck Depression Inventory (BD), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS), Patient Assessment of

Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), State Trait Anxiety Inventory (SE).

- f096: Follow-up medical history (FH), physical examination (PE), adverse event (AE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients), fasting blood draw for serum and plasma banking(BP), collection of findings from any interim upper endoscopy and gastric emptying scintigraphy as needed (results should be documented on the EG or GT form). The following questionnaires will be completed: Beck Depression Inventory (BD), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life [PAGI-QOL](UG), Patient Health Questionnaire (PQ), State Trait Anxiety Inventory (SE), SF-36 Health Survey (QF), Block 2005 questionnaire (FQ); Block Energy Expenditure Survey (PD), Rome III Diagnostic Questionnaire (FD), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity [PAGI-SYM] (GD), Brief Pain Inventory (PI), Abdominal Pain Questionnaire (AP), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS).

- f120: Follow-up medical history (FH), physical examination (PE), adverse event (AE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients) (form LR), collection of findings from any interim upper endoscopy or gastric emptying scintigraphy if needed (EG or GT); and the following questionnaires will be completed:
  Beck Depression Inventory (BD), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), State Trait Anxiety Inventory (SE).

- f144: Follow-up medical history (FH), physical examination (PE), adverse event (AE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients), fasting blood draw for serum and plasma banking(BP), collection of findings from any interim upper endoscopy and gastric emptying scintigraphy as needed (results should be documented on the EG or GT form). The following questionnaires will be completed: Beck Depression Inventory (BD), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), State Trait Anxiety Inventory (SE), SF-36 Health Survey (QF), Block 2005 questionnaire (FQ); Block Energy Expenditure Survey (PD), Rome III Diagnostic Questionnaire (FD), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), Brief Pain Inventory (PI), Abdominal Pain Questionnaire (AP), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS).

- f168: Follow-up medical history (FH), physical examination (PE), adverse event (AE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients) (form LR), collection of findings from any interim upper endoscopy or gastric emptying scintigraphy if needed (EG or GT); and the following questionnaires will be completed:
  Beck Depression Inventory (BD), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), State Trait Anxiety Inventory (SE).

- f192: Follow-up medical history (FH), physical examination (PE), adverse event (AE), blood draw for laboratory measures if needed (HbAlc required for diabetic patients) (LR), fasting blood draw for serum and plasma banking (BP), collection of findings from any interim upper endoscopy and gastric emptying scintigraphy as needed (results should be documented on the EG or GT form). The following questionnaires will be completed: Beck Depression Inventory (BD), Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (UG), Patient Health Questionnaire (PQ), State Trait Anxiety Inventory (SE), SF-36 Health Survey (QF), Block 2005 questionnaire (FQ); Block Energy Expenditure Survey (PD), Rome III Diagnostic Questionnaire (FD), Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity (GD), Brief Pain Inventory (PI), Abdominal Pain Questionnaire (AP), Nausea Profile and Vomiting Questionnaire (NV), and Neuropathy Total Symptoms Score-6 (NS).

5.2. Visits, data forms, and procedures

Phase/ Visit	Form abbr	Procedure
Screening		
	RG	Registration (document consent, sociodemographics, assign IDs)
	BH	Baseline Medical History
	PL	Patient Location (patient contact information)
	EG	Upper Endoscopy Documentation
	GE	Gastric Emptying Scintigraphy Documentation
	LR	Laboratory Results (The following laboratory test results are **required** to be recorded during screening: hematology, hepatic panel, clinical chemistry, HbA1c, antinuclear antibody [ANA], scleroderma antibody [Scl-70], serum eletrophoresis [SPEP], C-reactive protein [CRP]
	CG	Genetic Consent and Blood Collection Documentation
	BP	Blood Processing for Plasma and Serum
	GP	NIDDK Genetics Phlebotomy Form
	PE	Physical Examination
	GD	Patient Assessment of Upper Gastrointestional Disorders Symptom Severity Index (PAGI-SYM)
	AN	Autonomic Function Testing
	AP	Abdominal Pain Questionnaire
	BD	Beck Depression Inventory
	FD	Rome III Diagnostic Questionnaire
	FQ	Food Questionnaire Documentation (completion of Block 2005 Food Questionnaire)
	NS	Neuropathy Total Symptoms Score-6 (NTSS-6)
	NV	Nausea Profile and Vomiting Questionnaire
	PD	Physical Activity Documentation (to be used with Block Energy Expenditure Survey)
	PI	Brief Pain Inventory
	PQ	Patient Health Questionnaire (PHQ-15)
	QF	SF-36 Health Survey
	SE	State-Trait Anxiety Inventory (STAI)
	ST	Electrogastrogram and Nutrient Meal Test (*GD form required again)
	UG	Patient Assessment of Upper Gastrointestional Disorders - Quality of Life (PAGI-QOL)

Phase/ Visit	Form abbr	Procedure
	WL	Electrogastrogram and Water Load Test
	WM	Wireless Motility Capsule Report Form
	EN	Registry Enrollment
Follow-up phase		
24 week follow-up visit		
f024	AE	Adverse Event Report
	FH	Follow-up medical history
	PE	Physical Examination
	AE	Adverse Event Report
	EG	Endoscopy Documentation (if upper endoscopy is reported on form FH)
	GT	Gastric Emptying Scintigraphy Documentation (if gastric emptying test is reported on form FH)
	LR	Laboratory test results will be recorded if available during follow-up (hematology, hepatic, clinical chemistry, if needed; HbAlc required for diabetic patients)
	PL	Patient Location (update as needed)
	BD	Beck Depression Inventory
	GD	PAGI-SYM questionnaire
	NS	Neuropathy Total Symptoms Score-6 (NTSS-6)
	NV	Nausea Profile and Vomiting Questionnaire
	PQ	Patient Health Questionnaire (PHQ-15)
	SE	State-Trait Anxiety Inventory (STAI)
	UG	PAGI-QOL questionnaire
48 week follow-up visits		*The patient should be in a fasting state for both days of this follow-up visit.*
f048	AE	Adverse Event Report
	FH	Follow-up medical history
	PE	Physical Examination
	AE	Adverse Event Report
	EG	Endoscopy Documentation
	LR	Laboratory test results will be recorded if available during follow-up (hematology, hepatic, clinical chemistry, if needed; HbAlc required for diabetic patients)
	PL	Patient Location (update as needed)
	BP	Blood processing for plasma and serum
	FQ	Food Questionnaire Documentation (completion of Block 2005 Food Questionnaire)

5.2. Visits, data forms, and procedures

Phase/ Visit	Form abbr	Procedure
	GT	Gastric Emptying Scintigraphy Documentation -Follow-up
	AP	Abdominal Pain Questionnaire
	GD	PAGI-SYM questionnaire (done just prior to scintigraphy)
	BD	Beck Depression Inventory
	FD	Rome III Diagnostic Questionnaire
	NS	Neuropathy Total Symptoms Score-6 (NTSS-6)
	NV	Nausea Profile and Vomiting Questionnaire
	PD	Physical Activity Documentation (to be used with Block Energy Expenditure Survey)
	PI	Brief Pain Inventory
	PQ	Patient Health Questionnaire (PHQ-15)
	QF	SF-36 Health Survey
	SE	State-Trait Anxiety Inventory (STAI)
	UG	PAGI-QOL questionnaire
	AN	Autonomic Function Testing*
	WL	Electrogastrogram and Water Load Test*
*AN and WL tests to be performed on a different day from scintigraphy		
72 week follow-up visit		
f072		Same as 24 week follow-up visit
96 week follow-up visit		*The patient should be in a fasting state for this follow-up visit.*
f096	AE	Adverse Event Report
	FH	Follow-up medical history
	PE	Physical Examination
	EG	Endoscopy Documentation
	LR	Laboratory test results will be recorded if available during follow-up (hematology, hepatic, clinical chemistry, if needed; HbAlc required for diabetic patients)
	PL	Patient Location (update as needed)
	BP	Blood processing for plasma and serum
	FQ	Food Questionnaire Documentation (completion of Block 2005 Food Questionnaire)
	GT	Gastric Emptying Scintigraphy Documentation (*if GES is reported on form FH)
	AP	Abdominal Pain Questionnaire
	GD	PAGI-SYM questionnaire
	BD	Beck Depression Inventory
	FD	Rome III Diagnostic Questionnaire

5.2. Visits, data forms, and procedures

Phase/ Visit	Form abbr	Procedure
	NS	Neuropathy Total Symptoms Score-6 (NTSS-6)
	NV	Nausea Profile and Vomiting Questionnaire
	PD	Physical Activity Documentation (to be used with Block Energy Expenditure Survey)
	PI	Brief Pain Inventory
	PQ	Patient Health Questionnaire (PHQ-15)
	QF	SF-36 Health Survey
	SE	State-Trait Anxiety Inventory (STAI)
	UG	PAGI-QOL questionnaire
120 week follow-up visit		
f120		Same as 24 week follow-up visit
144 week follow-up visit		*The patient should be in a fasting state for this follow-up visit.*
f144		Same as 96 week follow-up visit
168 week follow-up visit		
f168		Same as 24 week follow-up visit
192 week follow-up visit		*The patient should be in a fasting state for this follow-up visit.*
f192		Same as 96 week follow-up visit
As needed		
CO		Registry 2 closeout

5.3. Guide for screening visit at baseline

Procedures

- Obtain signed consent for the Gastroparesis Registry 2 (consent form(s) and HIPAA authorization form)
- Obtain patient location information
- Obtain permission to abstract data from patient's medical records
- Initiate data collection for screening and baseline values
  - Physical exam and anthropometric measurements (height, weight, waist circumference, hip circumference, temperature, blood pressure, resting radial pulse, respiratory rate)
  - Interview for baseline medical history (responses may be modified or expanded upon chart review)
  - Laboratory testing: Hematology(complete blood count): white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count; HbA1c , comprehensive metabolic panel: sodium, potassium, chloride, carbon dioxide, calcium, BUN, creatinine, glucose, total protein albumin, and liver panel including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase; Lipid panel: total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides; ANA= antinuclear antibody, hs-CRP= high sensitivity C- reactive protein, ESR= erythrocyte sedimentation rate, TSH= thyroid stimulating hormone, vitamin B12 and 25-hydroxy vitamin D levels
    - Specimen banking (serum, plasma, and DNA)
    - Upper endoscopy results documentation
    - Gastric emptying scintigraphy results documentation
    - Questionnaires regarding quality of life, diet and gastroparesis symptoms

Data collection forms

- Forms completed for all patients

RG	Registration (document consent, sociodemographics, assign IDs)
PL	Patient Location (patient contact information)
BH	Baseline Medical History
LR	Laboratory Results (The following laboratory test results are required to be recorded during screening: hematology, hepatic panel, clinical chemistry, HbA1c, antinuclear antibody [ANA], scleroderma antibody [Scl-70], serum eletrophoresis [SPEP], C-reactive protein [CRP]
CG	Genetic Consent and Blood Collection Documentation
BP	Blood Processing for Plasma and Serum
GP	NIDDK Genetics Phlebotomy Form (as needed)
PE	Physical Examination
GD	Patient Assessment of Upper Gastrointestional Disorders Symptom Severity Index (PAGI-SYM)

AN Autonomic Function Testing
AP Abdominal Pain Questionnaire
BD Beck Depression Inventory
FD Rome III Diagnostic Questionnaire
FQ Food Questionnaire Documentation (completion of Block 2005 Food Questionnaire)
NS Neuropathy Total Symptoms Score-6 (NTSS-6)
NV Nausea Profile and Vomiting Questionnaire
PD Physical Activity Documentation (to be used with Block Energy Expenditure Survey)
PI Brief Pain Inventory
PQ Patient Health Questionnaire (PHQ-15)
QF SF-36 Health Survey
SE State-Trait Anxiety Inventory (STAI)
ST Electrogastrogram and Nutrient Meal Test (*GD form required again)
UG Patient Assessment of Upper Gastrointestional Disorders - Quality of Life (PAGI-QOL)
WL Electrogastrogram and Water Load Test WM
Wireless Motility Capsule Report Form EN
Registry Enrollment

Forms for clinical center use only

- PL - Patient Location
- Medical records release (use local form)
- GP - NIDDK Genetics Phlebotomy Form

Before the patient leaves the clinical center

- Register patient on clinic data system
- Apply labels to forms as needed if they are taking any of the forms with them
  Review the responses on questionnaires to ensure answers are clear, skips were followed, etc.
- Set up Gastroparesis Registry chart for patient and file the completed forms

Suggested Patient Flow for GpR 2:
Scenario for Patient Visits and Tests for Enrollment
Study Visit 1: Identify Patient for Registry 2 {approximately 1 hour}
Review study and consent form with patient (10 minutes)
Patient signs consent forms
Assign ID number (if new patient) and Register patient into GpR 2 (RG form)
Review patient chart for standard of care baseline laboratory data (have patient get blood drawn if needed)

5.3. Guide for screening visit at baseline

Laboratory test results required:

- ANA (results from tests in the last year are acceptable),
- CBC, ESR, CRP, CMP, TSH, Vitamin B12, Vitamin D (25hydroxyVit D), HgbA1c, lipid panel (total cholesterol, LDL, HDL, triglycerides) (test must have been done within 16 weeks prior to registration)
- Review patient chart for standard of care upper endoscopy (complete EG form) performed within last 2 years (schedule EGD or UGI as needed)
- Review patient chart for standard of care gastric emptying of solids and liquids test with accompanying PAGI-SYM completed at a GpCRC center in last 6 months (schedule as needed)

Standard of care gastric emptying of solids and liquids scintigraphy visit: 4-6 hours
Review patient chart for gastric emptying of solids and liquids test with accompanying PAGI-SYM completed at a GpCRC center in last 6 months. Schedule new one for clinical care, if needed. (Some centers may be doing this as standard of care; so it may have been done prior to registration for GpR 2.)
Patient must be off prokinetic, constipation and narcotic medications for 3 days prior to test.
If the patient normally takes insulin, they will be asked to take only half of their normal long-acting insulin.
Record fasting glucose for diabetic patients; the blood glucose level must be checked within the hour prior to the test to ensure it is less than 270 mg/dL to continue with the test. Patients should fill out the PAGI-SYM at time of scintigraphy test.
Standard of care upper endoscopy (as needed)

Fill out data collection forms: Baseline History (BH), Physical Examination (PE), Gastric Emptying Scintigraphy Documentation- Screening (GE)

Have patient complete the following questionnaires: PAGI-SYM (if not done as part of scintigraphy)(GD), Beck Depression Inventory-II (BD), PAGI-QOL (UG), SF-36 (QF), Brief Pain Inventory (PI): 60 minutes

Schedule study visit 2. Instruct patient to return fasting for visit 2 and to:
1) Discontinue use of proton pump inhibitors for **7 days** prior to visit 2
2) Discontinue use of histamine 2 antagonists, prokinetics, narcotics, anticholinergics, constipation medications and cannabinoids for **3 days** prior to the visit.

5.3. Guide for screening visit at baseline

Study screening visit 2: Wireless Motility Capsule (WMC) and EGG {approximately 2-4 hours}:
Patient fasting
Prior to testing, a urine pregnancy test will be done for female participants.
If the patient normally takes insulin, they will be asked to take only half of their normal long-acting insulin. Record fasting glucose for diabetic patients; the blood glucose level must be checked to ensure it is less than 270 mg/dL to continue with the test.

Inclusion criteria:
1) Patient stopped proton pump inhibitors for 7 days prior to visit 2
2) Patient stopped histamine 2 antagonists, prokinetics, narcotics, anticholinergics, constipation medications (over the counter laxatives, isotonic PEG electrolyte preparations (e.g. MiraLax), and prescription laxatives (e.g. lubiprostone) and cannabinoids for 3 days prior to the visit.

Exclusion criteria:
Pregnancy, bezoars (retained liquid or poorly organized solids are permitted), dysphagia, prior gut lumen surgery, known strictures, prior inflammatory bowel disease, prior diverticulitis, chronic frequent NSAID use, and cardiac medical devices (gastric stimulators, insulin pumps, continuous glucose monitors are permitted).

The PI will review the Baseline Medical History and complete a brief Physical Examination. All participants will complete the PAGI-SYM questionnaire (GD form) assessing symptoms over the past 2 weeks (use visit code s2 for this visit in item 5 of GD form) and the Rome III (FD form). Baseline symptoms will be assessed using a Visual Analog Score (VAS) and will be completed on the ST form. A fasting EGG will be performed for 15 minutes before SmartBar® ingestion. The WMC (SmartPill Corp.) will be activated and calibrated.

After the baseline EGG recording and symptom questionnaire is completed, the patient will begin the standard solid meal test by sitting up in the chair and ingesting one SmartBar® in a 10 minute period. Subjects may ingest up to 50 ml of water during ingestion of the SmartBar®. It is expected that 100% of the bar will be ingested. The percentage of the SmartBar® that is consumed will be documented. After the SmartBar® is consumed; the SmartPill® capsule will be ingested with another 50 ml of water and another VAS symptoms score sheet will be completed.

The subject will then recline in a comfortable position in the recliner (30-45 degree position) that they were in for the fasting baseline condition. The electrodes should be checked to verify that they are well adhered to the skin before starting the EGG recording for the 90 minute postprandial period. The respiratory belt should be checked to verify it is snug. Symptoms will be assessed using VAS at the at 15, 30, 45, 60, and 90 minute time periods after ingestion of the SmartPill®. The patient may get out of the chair to stretch for 2 minutes at 30 and 60 minutes if necessary. At the 90 minute point, the test is completed and the electrodes are removed. (Further details of the EGG recording and questionnaires will be in SOP I.)

5.3. Guide for screening visit at baseline

Study participants will be permitted to leave the study center after completion of the 90 minute EGG recording after SmartPill® ingestion.

Study participants will leave with instructions to:
1) Remain fasting for 6 hours after SmartPill® ingestion; thereafter resume a normal diet; maintain a diary recording times of meal ingestion, bowel movements, and sleep; wear the receiver at all times and within 3 feet while sleeping or showering for the next for 4-7 days. An event marker on the receiver will be depressed for diary entries.
2) Complete any remaining questionnaires for GpR 2: Block 2005 Food Frequency Questionnaire (FQ), Block Energy Expenditure Survey (PD), Nausea and Vomiting questionnaire (NV), Neuropathy Total Symptoms Score-6 (NS), Abdominal Pain Questionnaire (AP), State Trait Anxiety (SE), Patient Health Questionnaire (PQ)
3) Continue to abstain from proton pump inhibitors, prokinetics, and 'over the counter' laxatives, isotonic PEG electrolyte preparations (e.g. MiraLax), and prescription laxatives (e.g. lubiprostone) after ingesting the SmartPill® until they return for the follow-up visit
4) Return fasting for a follow-up visit 4-7 days after SmartPill® ingestion to return the receiver, questionnaires, and diaries.
Schedule study visit 3.

Study Visit 3 (4-7 days after visit 2- Patient fasting): {approximately 2.5 hours)
Collect SmartPill® receiver and download: 15 minutes
Autonomic function testing: 20 minutes
EGG with water load satiety test: 90 minutes
Blood drawing for DNA and serum/plasma banking: 20 minutes (if not already done)
Autonomic function testing using ANSAR ANX system: 20 minutes
Instruct patient to sit straight up with feet flat on the floor and arms resting comfortably at their sides. Patient should remain as still as possible and simply breathe freely at a comfortable pace unless instructed to do otherwise.

- No talking during the test. Use **F10** key to record any events (cough, sneeze, talking, etc.)
- Blood pressure will be taken 6 times during the test.
- 6 Phases of the test (3 baselines, 2 breathing exercises, 1 stand challenge)
- Thirty seconds before the end of each phase, the time on the clock will switch to red. This is a reminder for you and the patient that the next challenge is about to begin.
- Have patient practice deep breathing and Valsalva challenges before the test begins.

Initial Baseline – 5 minutes of relaxed, normal, regular breathing. First blood pressure will be taken when the clock reads 2:00.

Deep Breathing – 1 minute of slow, easy, relaxed, deep breaths: 5 seconds in, 5 seconds out. NOTE: If patient is light-headed or dizzy, discontinue and use **F10** to record event.

5.3. Guide for screening visit at baseline

Baseline – 1 minute of relaxed, normal breathing.

Valsalva – Like you are trying to blow up a balloon that is difficult to blow up. Take a quick, deep breath in, hold the breath, and then bear down. Focus on bearing down in the chest and stomach and keep arms as relaxed as possible. Tell the patient that he/she will be performing 5 Valsalva maneuvers. See chart below for assistance.

Begin Time	Hold Time	Release Time
1:35	**:15**	**1:20**
1:00	**8 – 10 seconds**	**:50**
:45	**8 – 10 seconds**	**:35**
:30	**8 – 10 seconds**	**:20**
:15	**8 – 10 seconds**	**:05**

EGG with water load satiety test: 90 minutes

Record fasting blood glucose level for diabetic patients; level must be below 270 mg/dL to proceed with testing. If the patient's blood glucose level is greater than 270 mg/dL the EGG and water load satiety test must be rescheduled for another day.

Baseline symptoms prior to EGG recording will be obtained using visual analog scales for stomach fullness, hunger, nausea, bloating, and abdominal discomfort. Once the EGG and respiratory signals are stable, the baseline (pre-prandial) EGG recording period can begin. Patients will undergo a 15 minute baseline EGG in a reclining chair with the subject positioned at a 30-45 degree tilt.

Patients will begin the Water Load Satiety Test. For this, subjects will sit up. During the test, subjects will drink bottled spring water for a 5 minute period until they feel "completely full." The patient's symptoms are recorded at 10, 20, and 30 minutes after ingestion of the bottled spring water and the total volume consumed will be recorded on page 3 of the WL form.

Instructions to patients for Satiety Test are as follows: "You will be given a cup of bottled spring water to drink for 5 minutes until you feel completely full. You will have up to 5 minutes to drink the cup of bottled spring water. You may use all of this time, if needed. After you finish, we will ask about your feeling of fullness on a five-point scale, that is 0, 1, 2, 3, 4, 5 where 0 is not full at all and 5 is completely full. You will stop drinking when you become completely full from the bottled spring water. This is not a test to see how much you can drink, but simply to have you drink until you feel completely full."

A continuous 30 minute EGG recording is then obtained. At the end of the 0-10 minute period, you will have the subject complete a symptoms score sheet. At the end of the 11-20 minute postprandial period, you will have the subject complete a symptoms score sheet. At the end of the 21-30 minute postprandial period, you will have the subject complete a symptoms score sheet. The

test is over after the 30 min recording period, the electrodes are removed and the subject may be discharged.

After the patient leaves the clinical center

- Ship whole blood specimen for DNA extraction to NIDDK Genetics Repository by overnight Fed Ex delivery service
- Serum and plasma tubes are centrifuged and separated into aliqots of .5mL each into corresponding pre-labeled cryovials and stored at -70° C at clinical center
- Frozen serum and plasma samples are batch shipped to NIDDK Biosample Repository every month
- Key completed data forms
- Verify all information has been gathered and all forms completed and keyed
- Key the Enrollment form (EN)
- Run Enrollment task in web-based data management system
- Enroll patient in the data system
- Schedule follow-up visit in 24 weeks using the participant's visit windows as a guide

5.4. Visit windows: enrollment and follow-up

- **Enrollment** must occur within 16 weeks of initiating screening (completion of the Registration (RG) form)
- **f024**: window opens 12 weeks +1 day from date of enrollment and runs through 36 weeks after enrollment, ideal date is 24 weeks (168 days) after enrollment date
- **f048**: window runs from (36 weeks+1 day) through 60 weeks, must be at least 12 weeks after f024; ideal date is 48 weeks (336 days) after enrollment date
- **f072**: window runs from (60 weeks+1 day) through 84 weeks, must be at least 12 weeks after f048; ideal date is 72 weeks (504 days) after enrollment date
- **f096**: window runs from (84 weeks+1 day) through 108 weeks, must be at least 12 weeks after f072; ideal date is 96 weeks (672 days) after enrollment date
- **f120**: window runs from (108 weeks+1 day) through 132 weeks, must be at least 12 weeks after f096; ideal date is 120 weeks (840 days) after enrollment date
- **f144**: window runs from (132 weeks+1 day) through 156 weeks, must be at least 12 weeks after f128; ideal date is 144 weeks (1008 days) after enrollment date
- **f168**: window runs from (156 weeks+1 day) through 180 weeks, must be at least 12 weeks after f144; ideal date is 168 weeks (1176 days) after enrollment date
- **f192**: window runs from (180 weeks+1 day) through 204 weeks, must be at least 12 weeks after f168; ideal date is 192 weeks (1344 days) after enrollment date

5.5. Interim (unscheduled) visits or telephone contacts

- Unscheduled visits or telephone contacts may occur as needed. No time windows or minimum time separations are imposed for such visits or contacts.

- Data collection forms are not required at interim visits. However, if lab results are available or procedures such as endoscopy or scintigraphy are performed, then the corresponding data forms (LR, EG, GT) should be completed using visit code 'n'.

- If gastroparesis symptom exacerbation occurs for a Gastroparesis Registry 2 patient between scheduled GpR 2 visits, complete the Interim Event Report (IE) form; the visit code for the form will be 'n'. If more than one event is reported on the same calendar day (i.e., same date in item 4 for all events), use visit code 'n' for first event, 'n' for the second event, etc.

6. Study procedures

6.1. Screening Contact Log (SL Form)

What

- Screening Contact Log

Purpose

- To record information on patients who are contacted as prospective participants for enrollment in the Gastroparesis Registry 2

When

- As prospective participants are contacted regarding enrollment

Procedure

- Document your contact with each prospective participant on a single line of the Screening Contact Log (SL) form
- Each line should be numbered sequentially and the patient identifier may be a name or chart number (this information is not keyed to the data system)
- Complete items a-k for every prospective participant contacted
- Number the Screening Contact Log (SL) forms in sequential order
- Weekly or once you have filled a Screening Contact Log form (10 patients contacted) please key the entire form to the web-based data management system.
- Key any partial forms during the last week of each month to ensure that your clinical center's recruitment efforts may be summarized accurately in the monthly performance reports
- Retain the SL forms in your clinical center's GpR 2 files along with other study forms

6.2. Assignment of study identifiers

What

- The GpCRC uses 2 identifiers for patients
  - ID number (4 digits)
  - ID code (3 alphabetic characters)
- These identifiers help assure confidentiality of patient identity

Materials

- ID number and code labels received from the Scientific Data Research Center
- Registration (RG) form

When

- Screening visit s

By whom

- Clinical Coordinator

Procedures

- Complete the GpR 2 Registration (RG) form; if the participant remains eligible at the close of the form, assign the ID number and code by peeling a label off the label sheet and affixing it to the specified item on form RG
- The patient will be known by these IDs for the duration of the GpCRC, including participation in any other GpCRC studies
- Key the Registration (RG) form into GpR 2 data system; this must be the first form keyed and no other forms may pre-date the date of the RG form

Important note:

- **Once an ID number and its associated ID code are assigned, these IDs must be used by the patient for the duration of the GpCRC and cannot be changed**
- **Do NOT reassign or reuse IDs assigned to patients found to be ineligible or who refuse enrollment**

6.3. Gastric emptying scintigraphy procedure

Gastric emptying of solids and liquids scintigraphy required for enrollment

The gastric emptying test required for enrollment into GpR 2 is a combined simultaneous gastric emptying of solids and liquids using the Egg Beaters® meal protocol. Liquid egg white will be labeled with Tc-99m and water labeled with Indium-111. The liquid emptying is measured in the presence of the solid meal. An allergy to eggs is a contraindication to this test.

Patients are instructed to stop medications that could affect gastrointestinal motility for the 3 days prior to the gastric emptying scintigraphy. This includes prokinetic agents, narcotic analgesics, and anticholinergic agents. Participants should come for the test in the morning after fasting overnight with nothing to eat after midnight, (an 8 hour fast). (It is all right for the patient to have taken medications with some water on arising) The participant should fill out the PAGI-SYM questionnaire assessing symptoms over the past 2 weeks. Diabetic patients must have a fasting blood glucose level checked within the hour prior to consumption of the meal.

Gastric emptying scintigraphy is performed using a standard low-fat, Egg Beaters® (egg white) meal to measure solid emptying. The Egg Beaters® are radiolabeled with 0.5 -1 microcurie technetium-99m sulfur colloid and served with two pieces of white bread and strawberry jam. The meal has a caloric value of 255 kcal (nutritional composition: 72% carbohydrate, 24% protein, 2% fat, and 2% fiber). The participant is instructed to ingest the meal within 10 minutes. Each participant then drinks 120 mL of water containing 125 microcurie (4.6 MBq) of Indium 111-DTPA (diethylene triamine pentacetic acid) for the measurement of liquid gastric emptying and small bowel and/or colon transit.

For quality control, the staff technologist records how long it takes the participant to consume the meal and how much they consume. The patient should ingest the whole meal. If the patient cannot eat the entire meal, at least 50% of each component should be consumed for the test. If the patient vomits part of the meal at any time during the test, this should be indicated on the report. Clinically the study is non-diagnostic for gastroparesis if normal and only a small portion is eaten. If gastric emptying is delayed for a small meal ingested it can, however, indicate delayed gastric emptying.

Combined technetium-99m and Indium-111 imaging begins immediately after consumption of the liquid and is repeated at 30 min, 1 hour, 2 hours, 3 hours, and 4 hours to record gastric emptying of liquids and solids. If small bowel transit is to be obtained, then In-111 imaging is also performed at 5 and 6 hours after meal ingestion. Between all image sets, the participants are permitted normal quiet activity (e.g., reading, watching television and/or videos) in the standing or sitting position.

6.3. Gastric emptying scintigraphy procedure

Note: If gastric emptying of liquids is performed on a separate day than gastric emptying of solids, the patient consumes an unlabeled Egg Beaters® meal (Egg Beaters®, bread, jam) with the radiolabeled water.

Analysis of the gastric emptying data is performed. Images are recalled from a computer disc and analyzed to determine gastric counts. Regions of interest (ROIs) are manually drawn around the total stomach at each time interval. A geometric mean of the anterior and posterior values is used to correct for depth changes (geometric mean counts = square root [anterior counts posterior counts]) and counts are corrected for radioisotope decay.

Normal values for gastric emptying scintigraphy and small bowel transit have been established in earlier studies using healthy volunteers. Gastric retention of Tc-99m > 60% at 2 hours and/or > 10% at 4 hours was considered evidence of delayed gastric emptying of solids. Rapid gastric emptying of solids was defined as < 35% retention of Tc-99m at 1 hour. Delayed gastric emptying of liquids in the presence of solids is greater than 50% retention of In-111 at 1 hour emptying, a value representing the mean plus 2 standard deviations of values derived from 20 normal subjects from prior studies using a similar solid and liquid meal.

Gastric emptying of solids scintigraphy required for follow-up visit f048

The gastric emptying of solids only scintigraphy will be performed at the 48 week follow-up visit. The meal will consist of a low fat Egg Beaters meal radiolabelled with 0.5 -1 mCi 99Tc; which is scrambled and cooked. This is served with 2 pieces of toast, jam, and water. The meal has a caloric value of 255 kcal (nutritional composition: 72% carbohydrate, 24% protein, 2% fat, and 2% fiber). The meal is adopted from the multi-center study using a low fat meal by Tougas et al.

Items needed for Egg Beaters Gastric Emptying Scintigraphy

Egg Beaters (egg substitute): 99% real eggs, cholesterol free, fat free, low calorie
(120 g Egg Beater, 60 kcal, approx two large eggs)
2 slices of bread (120 kcal),
Strawberry jam (30 g, 74 kcal)
Water (120 ml).
Technetium-99m 0.5 -1 mCi

To prepare the meal, the Egg Beaters is poured into a bowl, sprinkled with 0.5 - 1 mCi 99Tc sulfur-colloid marker on top, mixed, and cooked in a microwave. Alternative is to use a skillet (nonstick frying pan). The Egg Beater mixture is stirred once or twice during cooking and is cooked until it has the consistency of an omelet (3-5 min). The bread is toasted. Jelly is spread on the bread, and a sandwich is made of the jellied bread and cooked egg mixture. The subject completes the

sandwich meal within 10 minutes. The staff technologist records how long it takes the subject to consume the meal and how much they consume.

Immediately after meal ingestion, the subject will be placed in front of a gamma camera with images taken in the 140 keV 99Tc peak with a 20% window (140 keV ± 10%). 1 minute of anterior and 1 minute of posterior measurements will be taken. Subsequent images are taken at least 1, 2, and 4 hours after meal ingestion. It would be helpful to obtain these images at 30 minutes, 1 hour, 2 hours, 3 hours, and 4 hours after meal ingestion. This may help improve the test. The times of the images should be recorded.

In the time between images, subjects can be sitting, standing, or walking but should remain in close proximity to the nuclear medicine section.

Analysis is performed using the geometric mean of the anterior and posterior images for each time point which are then corrected for decay. Results expressed as percent remaining in the stomach.

The gastric emptying tests will be performed at the local GpCRC centers and the images saved to a CD/DVD. The centers will need to de-identify the patient information using available software and send the images **every 3 months in DICOM format** with a completed TS form via two-day delivery service with ability to track the shipment to:

John Dodge/Laura Miriel
GpCRC SDRC
415 N. Washington Street
Second Floor
Baltimore, MD 21231
Telephone (443) 287-3170.

References:

1. Tougas GH, Eaker EY, Abell T, et al. Assessment of gastric emptying using a low fat meal: establishment of international control values. Am J Gastroenterol 2000;95(6):1456-62.
2. Vijayamkumar V, Briscoe EG, Boysen TL, Jimenez YM. Assessment of the practical role of a low-fat-meal solid gastric emptying study. J Nucl Med Technol 2006;34:82-85.

6.4. Gastric Emptying Test Documentation - Screening only (GE form)

Purpose

- To record results from the combined solid and liquid gastric emptying scintigraphy to determine eligibility and patient category

When

- Screening visit s (the gastric emptying scintigraphy must have been performed at a GpR 2 clinical center within 6 months prior to registration). **The gastric emptying scintigraphy must be performed at a GpCRC clinical center using the standard test meal and protocol.**

Procedure

- Information not included in the report (i.e., blood glucose) should be gathered directly from the patient before or immediately after the test if possible.

- For quality control, the staff technologist records how long it takes the participant to consume the meal and how much they consume. The patient should ingest the whole meal. If the patient cannot eat the entire meal, at least 50% of each component should be consumed for the test. If the patient vomits part of the meal at any time during the test, this should be indicated on the report in item 17, 22, or 27. Complete section C items 13-17 only if the gastric emptying scintigraphy of solids and liquids was done as a combined test. Complete sections D and E items 18-27 if the gastric emptying test of solids and liquids were performed on different days. The Study Physician should complete the remainder of this form (items 28-32) using the report(s) generated by the gastric emptying scintigraphy. Study Physician completes the form using the gastric emptying scintigraphy report

  - Per GpR 2 protocol, the gastric emptying tests will be performed at the GpCRC centers and the images saved to a CD or DVD. The centers will need to de-identify the patient information using available software and send the images every 3 months in DICOM format to the SDRC with the completed TS form via two-day delivery service with ability to track the shipment to: John Dodge/Laura Miriel
    GpCRC SDRC
    415 N. Washington Street
    Second Floor
    Baltimore, MD 21231
    Telephone (443) 287-3170.

6.5. Gastric Emptying Test Documentation - Follow-up (GT form)

Purpose

- To record results from the solid phase only gastric emptying scintigraphy performed during follow-up

When

- Follow-up visit f048. If a participant has an additional gastric emptying scintigraphy during study participation, results should be recorded on the GT form. **The gastric emptying scintigraphy must be performed at a GpCRC clinical center using the standard test meal and protocol.**

Procedure

- For quality control, the staff technologist records how long it takes the participant to consume the meal and how much they consume. The patient should ingest the whole meal. If the patient cannot eat the entire meal, at least 50% of each component should be consumed for the test. If the patient vomits part of the meal at any time during the test, this should be indicated on the data form in item 17. If a STOP is reached for any item then STOP filling out and do not enter the form.

- Study Physician completes the form using the gastric emptying scintigraphy report

- Any necessary information not contained in the report should be gathered from the participant immediately after the test

- Per GpR 2 protocol, the gastric emptying tests will be performed at the GpCRC centers and the images saved to a CD or DVD. The centers will need to de-identify the patient information using available software and send the images every 3 months in DICOM format with the completed TS form via two-day delivery service with ability to track the shipment to:

  John Dodge/Laura Miriel
  GpCRC SDRC
  415 N. Washington Street
  Second Floor
  Baltimore, MD 21231
  Telephone (443) 287-3170

6.6. Upper Endoscopy Documentation (EG form)

Purpose

- To document the results of the upper gastrointestinal endoscopy to determine patient eligibility

When

- Screening visit s (the upper gastrointestinal endoscopy must have been performed within 24 months prior to registration)

- The form should be completed at visits f048, f096, f144 and f192. If patient has had an endoscopic procedure since the last study visit, results should be recorded on this form. If no results are available, complete items 1-8 and Section G. If more than one endoscopy has been performed in the same visit window, use visit code "n" for the 2nd endoscopy, "n1" for the 3rd endoscopy, etc.,

Procedure

- Study Physician or Clinical Coordinator completes the form using the available reports (surgical and histology) of the upper gastrointestinal endoscopy procedure

- A copy of the available report(s) should be attached to the form

6.7. Baseline Medical History (BH form)

Purpose

- To collect baseline history information about the participant to screen for potential enrollment into the Gastroparesis Registry 2.

When: Screening visit s.

Who:

- Study Physician and Clinical Coordinator query the participant
- Study Physician and Clinical Coordinator sign the form

What

- The form queries:
  - Symptoms of gastroparesis
  - Medical history (answer items based on information from all sources available to you)
  - Medication used currently and in the past 6 months and corresponding response

When

- Screening visit

How

- Mix of interview data and data obtained by chart review
- Other questions on the BH form can be answered by interview with the patient – i.e., use all sources to get the most accurate information that you can

6.8. Physical Examination (PE form)

Who

- All GpR 2 participants

When

- Screening visit s and follow-up visits f024, f048, f072, f096, f120, f144, f168, and f192

What

- Anthropometry
  - Height
  - Weight
  - Waist circumference
  - Hip circumference
- Vital signs
  - Temperature
  - Blood pressure
  - Resting radial pulse
  - Respiratory rate
- System review
  - Chest and lungs
  - Heart
  - Abdomen
  - Abdomen abnormality
  - Liver and spleen
  - Nervous system

How

- Ideally, use a stadiometer for height measurement
- Ideally, use the Gulick II tape measure for waist and hip measurement; this device may be obtained from www.fitnessmart.com (608-735-4718, model 67019, listed at $36); it is manufactured by Country Technology Inc: 608-735-4718
- See the sections that follow which detail the protocol for measurement of height, weight, waist circumference, and hip circumference

6.9. Height and weight measurements

Height measurements

- Height may be recorded in inches or centimeters
- Ideally, a wall-mounted stadiometer with a horizontal measuring block (or fixed angle) is used; other height measuring devices are acceptable
- Follow the manufacturer's recommendation regarding method and frequency of calibration of the stadiometer
- The participant stands erect on the platform with his/her back parallel to the vertical mounted measure scale (but not touching the wall), looking straight ahead with his/her head in the Frankfort horizontal plane (the horizontal plane defined by the lower margin of the bony orbit (the bony socket containing the eye) and the most forward point in the supratragal notch (the notch just above the anterior cartilaginous projections of the external ear)
- The horizontal measuring block is brought down snugly, but not tightly, on the top of the head
- Record the height to the nearest tenth of the unit of measurement (1 decimal place)

Weight measurements

- Follow the manufacturer's recommendation regarding method and frequency of calibration of the scale
- Weight may be recorded in pounds or kilograms
- Ideally, weight is measured in the morning after voiding and before breakfast; if this is not possible, try to measure the participant's weight at the same time of day and under the same conditions as the baseline measurements are obtained
- Participant should be wearing light clothing (e.g, short sleeve shirt or blouse or surgical gown), shorts, socks and without shoes; pockets should be empty
- Participant should stand still in the middle of the scale platform with head erect and eyes looking straight ahead
- Record the weight to the nearest tenth of the unit of measurement (1 decimal place)
- Participants who have limb amputations or who are wearing casts should have weight measured, but note this on the form on the margin (the notes may be keyed at data entry in the General Comments area of the keying)

6.10. Waist circumference measurement

- Waist circumference may be recorded in inches or centimeters
- Two measurements are recorded
- Ideally, a Gulick II Tape Measure will be used; this tape measure is designed to eliminate the guesswork by applying a known amount of tension (4 ounces) to the measuring tape; when used properly, tape tension is always 4 ounces; the self-retracting tape is kept at the desired length until the retract button is pushed
- If an ordinary tape measure (without the special 4 ounce tension indicator device) is used, the measurement will be affected by how tightly the tape is pulled
- Participant should be wearing light clothing (e.g., short sleeve shirt or blouse or surgical gown), shorts, socks and without shoes; pockets should be empty
- Ideally, waist circumference is measured in the morning after voiding and before breakfast; if this is not possible, try to measure the participant's waist at the same time of day and under the same conditions as the baseline measurements are obtained
- Participant should stand with feet together
- Pull an appropriate amount of tape out of the housing
- Ask the participant to bare his/her waist
- Wrap the tape once around the waist: the measure should be taken around the abdomen horizontally at the midpoint between the highest point of the iliac crest and lowest part of the costal margin in the mid-axillary line
- Mark the midpoint on both sides of the participant using a washable marker
- Participant may be asked to assist in passing the tape around the abdomen by holding the end of the tape in position
- When the tape is positioned in the horizontal plane at the correct height, the participant should be asked to keep his/her arms at the sides and breathe naturally; ask the participant to breathe in and out and hold at the end of a normal exhalation
- Align the tape's zero line along side of the tape graduations; pull on the end of the tensioning mechanism until you see just one colored bead
- Record the measurement to the nearest tenth (one decimal place)
- Remove the tape, retract the tape, and repeat the procedure
- If the tape cannot be made horizontal across the waist markings, default to the right hip and note this in the margin of the form

6.11. Hip circumference measurement

- Hip circumference may be recorded in inches or centimeters
- Two measurements are recorded
- Ideally, a Gulick II Tape Measure will be used; this tape measure is designed to eliminate the guesswork by applying a known amount of tension (4 ounces) to the measuring tape; when used properly, tape tension is always 4 ounces; the self-retracting tape is kept at the desired length until the retract button is pushed
- If an ordinary tape measure (without the special 4 ounce tension indicator device) is used, the measurement will be affected by how tightly the tape is pulled
- Participant should be wearing light clothing (e.g., short sleeve shirt or blouse or surgical gown), shorts, socks and without shoes; pockets should be empty
- Ideally, hip circumference is measured in the morning after voiding and before breakfast; if this is not possible, try to measure the participant's hips at the same time of day and under the same conditions as the baseline measurements are obtained
- Participant should stand with feet together
- Pull an appropriate amount of tape out of the housing
- Ask the participant to adjust his/her clothing to allow measuring the hips over the participant's underwear
- Wrap the tape once around the hips over the underwear: the measure should be taken at fullest part of the hips (maximum extension of the buttocks)
- Participant may be asked to assist in passing the tape around the hips by holding the end of the tape in position
- When the tape is positioned correctly, the participant should be asked to keep his/her arms at the sides and breathe naturally; ask the participant to breathe in and out and hold at the end of a normal exhalation
- Align the tape's zero line along side of the tape graduations; pull on the end of the tensioning mechanism until you see just one colored bead
- Record the measurement to the nearest tenth (one decimal place)
- Remove the tape and repeat the procedure

6.12. Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM) (GD form)

What

- Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM)

Purpose

- To obtain the participant's views of the severity of his/her gastroparesis symptoms

When

- Screening visit s and s2: This form should be completed at the time of the gastric emptying scintigraphy whenever possible using the visit code **s**. This form will be completed a second time as part of the EGG and Nutrient Meal Test, using **s2** for the visit code in item 5.
- All follow-up visits (i.e., visits f024, f048, f072, f096, f120, f144, f168, and f192)

Procedure

- Clinical Coordinator should complete Part A of each form and apply MACO labels to pages 2-3 before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center

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6.13. Recommendations for recording high quality EGGs

A. Room Preparation and Subject Comfort

1. Make a sign to hang on the door of the room where the EGG recording is performed in order to reduce unexpected noise and interruptions. (e.g., "Test in Progress, Please Knock")

2. All noise or distractions should be avoided (no cellular phones, tablets, TV, etc.)

3. The room should be a comfortable temperature; if the subject is cold, provide a cotton blanket for warmth.

4. The subject should rest comfortably in a reclining position, about 30-45 degrees, in a reclining chair or electronic bed.

5. A technician or nurse should be present at all times during the EGG recording to record subject activity or movements and the time of these actions.

6. Subjects should change into a hospital gown. Tight fitting blouses, shirts, and bras may create artifact by rubbing along electrodes or leads.

7. The subjects' pants or skirts must be very loose around the abdomen, pulled down to the level of the hips.

B. Skin Preparation, Placement of Electrodes, and Respiration Belt

1. Locate sites for placement of electrodes (see SOP section 6.13.1 or 3CPM user manual for details on how to locate where the electrodes should be placed).

2. Use a razor to remove all hair from each of the electrode sites.

3. The skin must be slightly reddened with a rough pad (e.g. 4 x 4 gauze or BuffPuff) and cleaned with an alcohol swab to remove skin oils, lotions, etc. These actions will decrease skin resistance and improve electrical transmission for the EGG signal.

4. Make certain that the EGG electrodes are fresh and are properly positioned and securely placed on the abdomen. 3CPM recommends you purchase only 3M brand elctrodes.

5. Make certain the respiration belt is on tight; you must ask the subject if the belt is on too tight! A high quality respiratory signal recording is crucial for detection of movement. The respiration signal will help identify breathing or movement artifact in the EGG signal.

6. Be certain you see a good respiration recording on the respiration channel before starting the baseline test period.

7. After placing the electrodes precisely in the location described in the manual, allow 5 minutes to elapse before starting the EGG recording. This time allows stabilization of the electrical current from the stomach through the skin to the electrodes.

C. Subject Movement During the EGG Recording

1. Place the 3CPM Human Interface Device (HID) at a location where it will not be bumped or moved during the procedure:
    - **a.** Do not bump the HID or the electrode wires connected to the subject as this may cause an artifact in the EGG signal.
    - **b.** If electrode wires or the 3CPM human interface device are bumped or moved, mark the time and note if movement took place on the EGG test

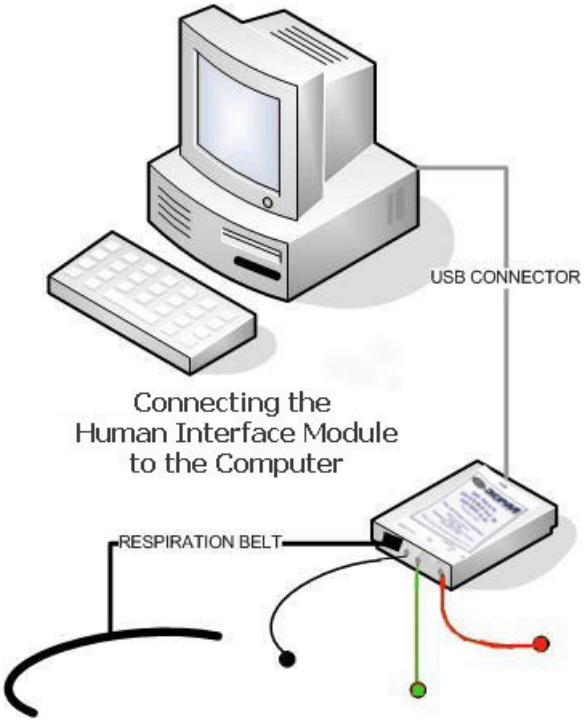
2. Before starting the EGG recording, review the specific protocol for that study (e.g. Smart Bar, section 6.15 or water load, section 6.18):
    - **a.** During the **equipment test** that occurs for 2-5mins prior to the baseline EGG recording, please confirm that a clear EGG and respiration signal are present. Ask these questions:
        1. Does the respiration signal appear regular and clearly seen?
        2. Should the respiration belt be tighter?
        3. Does the EGG signal have regular waves? Is the signal flat?
        4. Are the EGG electrodes loose?
    - **b.** **Baseline & Post Stimulation Periods** should follow time guidelines for each protocol. For example:
        - **i.** Baseline & Post Stimulation periods should start at the minute defined by protocol. (e.g., baseline should start at minute 0, not minute 4.)
        - **ii.** All periods should end at the minute defined by the protocol. (e.g., the last post stimulation period should not end at minute 35 if the protocol states that the last stimulation period should end at minute 30.)
        - **iii.** During the last post stimulation period, if the allotted time for that post stimulation period is surpassed, please select ALL recorded minutes for the "length period." When the "good minutes," or minutes chosen for analyses are selected, only select the minutes within the parameters of the protocol.

3. Mark the time that any body movements occur (e.g. subject crosses legs, arches back, coughs, sneezes, moves arms, excess talking, etc.) during the EGG recording. Mark the time the movements occur on the EGG signal/tracing on the computer while the test is in progress.

4. When the subject sits up or moves in any way to complete the Visual Analogue Scale (VAS), mark the time that movement occurs. Movement almost always occurs during the VAS and movement may create movement artifact.

6.13.1. Equipment set up and patient prep instructions

Equipment set-up:



Technique for skin preparation and electrode placement

1. Prepare to position the EGG electrodes as shown in the 3CPM User Manual:

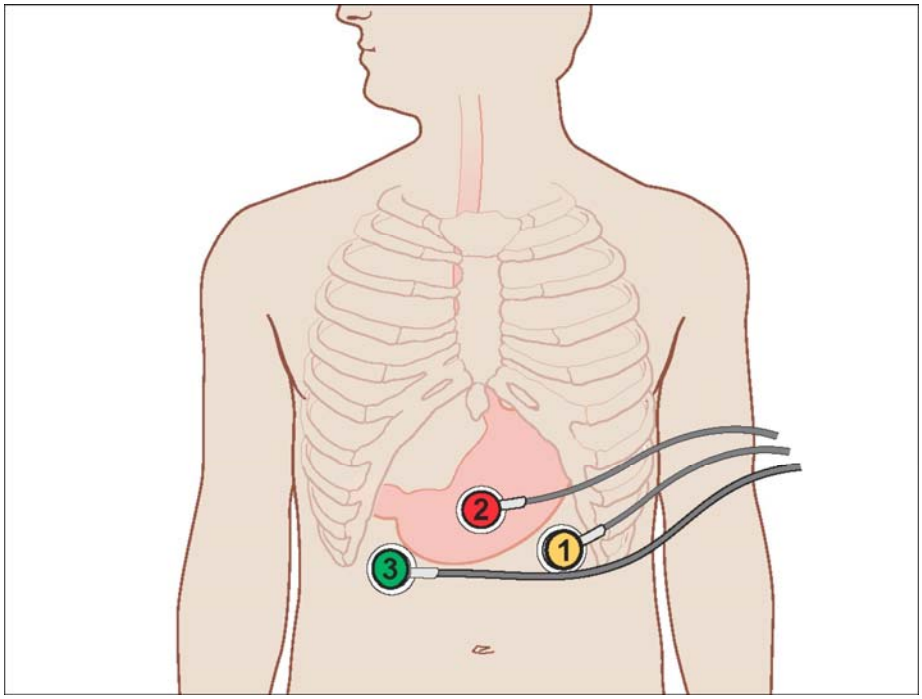
   – The RED EGG lead wire and electrode (+) is placed on the left mid-clavicular line (left side) approximately two inches below the left costochondral margin (lower ribs).

   – The BLACK EGG lead wire and electrode (-) is placed approximately midway between the xiphoid process and the umbilicus, along the line from the xyphoid process to the umbilicus

   – The GREEN EGG lead wire and electrode (ground) is placed is placed two inches below the right costochondral margin (lower ribs) along the right midclavicular line.

2. Preparing the skin
   - Shave off abdominal hair that is present in these locations for electrodes 1, 2, and 3.
   - Gently abrade the skin in the areas of the electrode positions using a course cloth, 4x4 gauze, or "Buff-Puff'.

3. Positioning the electrodes on the skin
   a) Connect the color-coded EGG lead wires to the Human Interface Module, by matching the lead wire color to the corresponding color-coded plug-in as designated on the Module label.
   b) Attach the pre-jelled electrodes to the snap-on ends of the EGG lead wires.
   c) Remove the plastic covers from the adhesive side of the electrode, and place on the skin according to the instructions in #1 above.



4. Positioning and connecting the belt for recording respiration rate
   The subject should be in the recording reclining chair at a 45 degree angle which is comfortable for the subject. Attach the belt across the upper chest with the belt clip placed under the armpits and the entire belt pulled snugly to obtain the clearest respiration signal. Check the EGG leads to verify that they are well adhered to the skin before starting the EGG recording.

6.13.1. Equipment set up and patient prep instructions

Equipment test

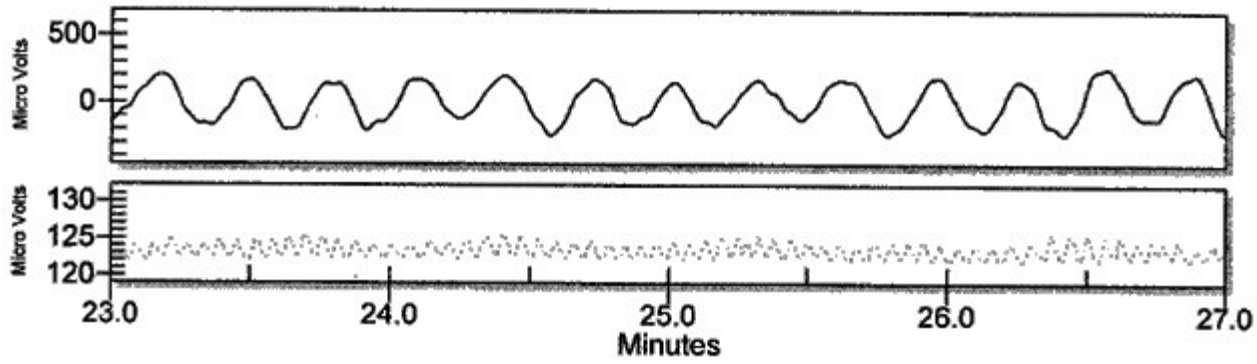
This section of the study makes sure that the signals (EGG and Respiration) are stable. Both signals must be stable for 2 minutes. The initial screen shows the Respiratory sensor and Gastric electrodes in large red dots. When these turn green, the system is ready to start the baseline recording. The EGG signal, shown in red is in the top graph. The Respiration signal, shown in black is in the bottom graph.

To start the equipment test, select the ***Start Equipment Test*** button. When both the Respiratory sensor and the Gastric electrodes turn green, the ***Begin Baseline*** button gets enabled. Then to start the Baseline, select this button.

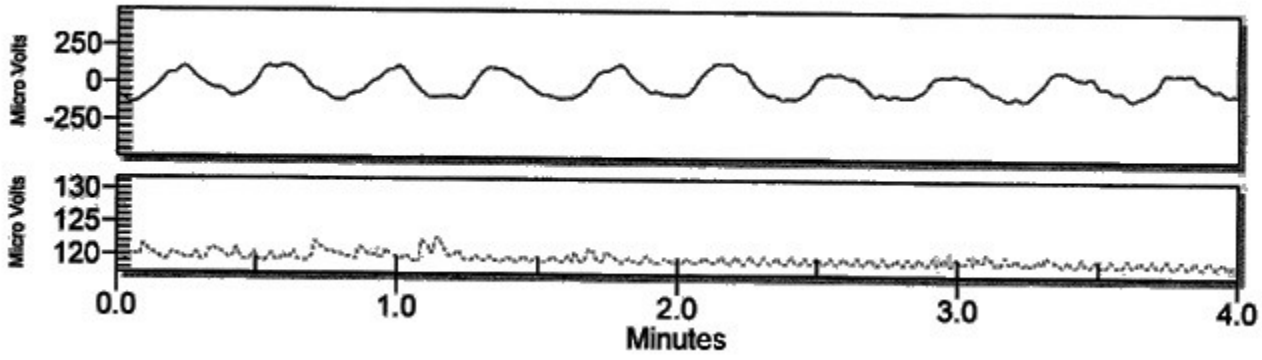
6.13.2. EGG Analysis-Rules for selection of good EGG minutes

In general, use all possible artifact free minutes of EGG signal. At least 4 artifact free minutes of EGG signal are required for computer analysis.

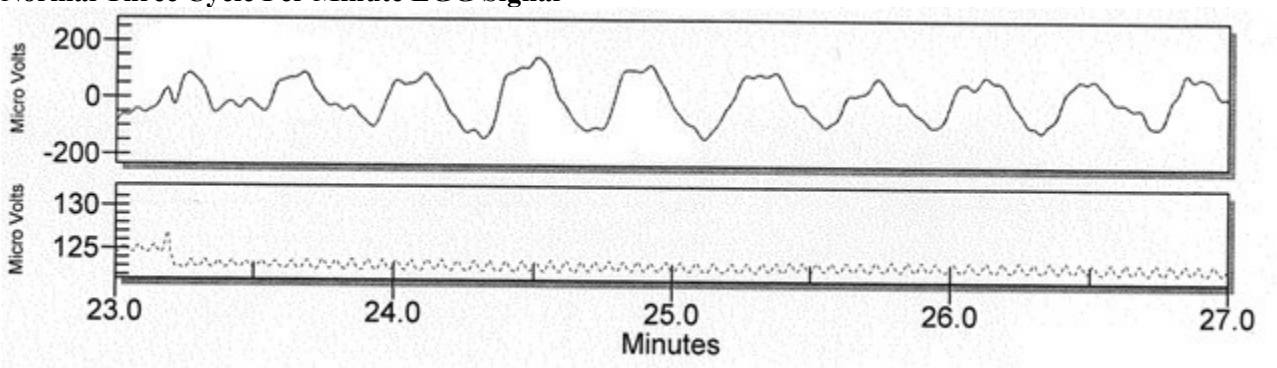
Normal Three Cycle Per Minute EGG Signal



Normal Three Cycle Per Minute EGG Signal



Normal Three Cycle Per Minute EGG Signal

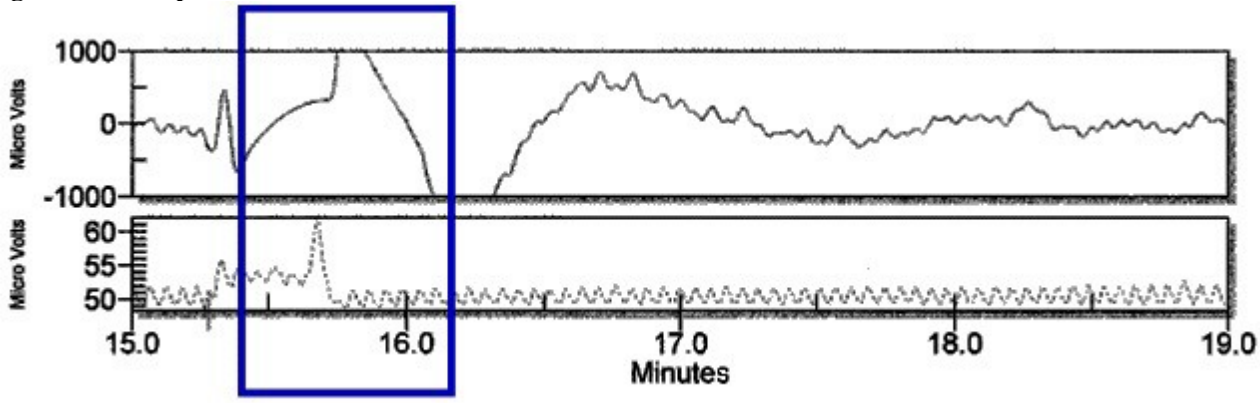


Note: The figures above show a normal, three cycles per minute EGG signal. A regular respiration pattern is also visible within the respiration channel.

Rules to Identify Artifact in the EGG Recording

Rule 1. If the EGG signal is off scale (that is, the peak or trough cannot be determined) and there is a matching disruption in the breathing pattern, then do not select these minutes for computer analysis (See Figure 1).

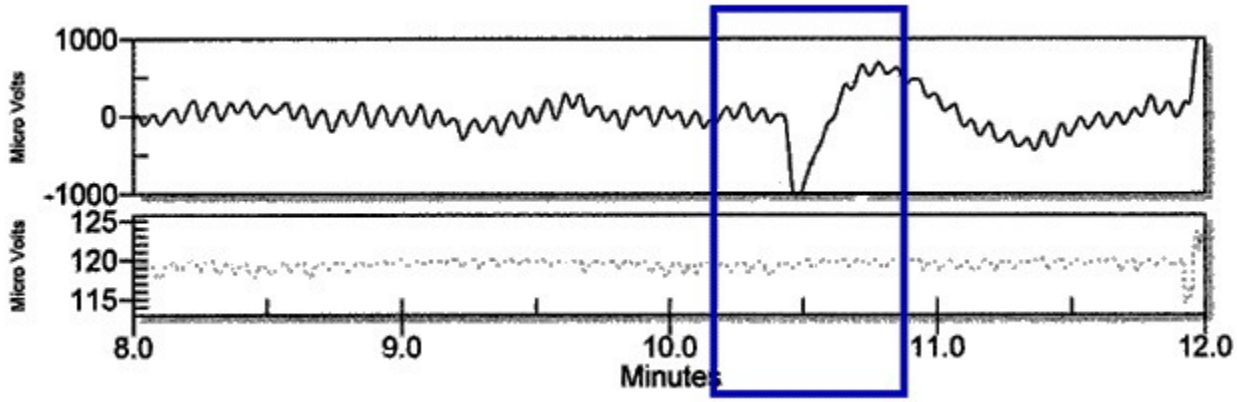
Figure 1. Example of Rule 1



Note: In Figure 1, the area within the box shows an EGG signal that is off scale (the peak of the wave is outside of the EGG channel). At the same time, a deflection is seen in the respiration signal indicating respiratory or body movement occurred. Thus, the EGG signal contains a movement artifact and this minute of the EGG signal should *not* be selected for computer analysis.

Rule 2. If the EGG signal is off scale and there is *NO* disruption in breathing pattern, then select these minutes for computer analysis (See Figure 2).

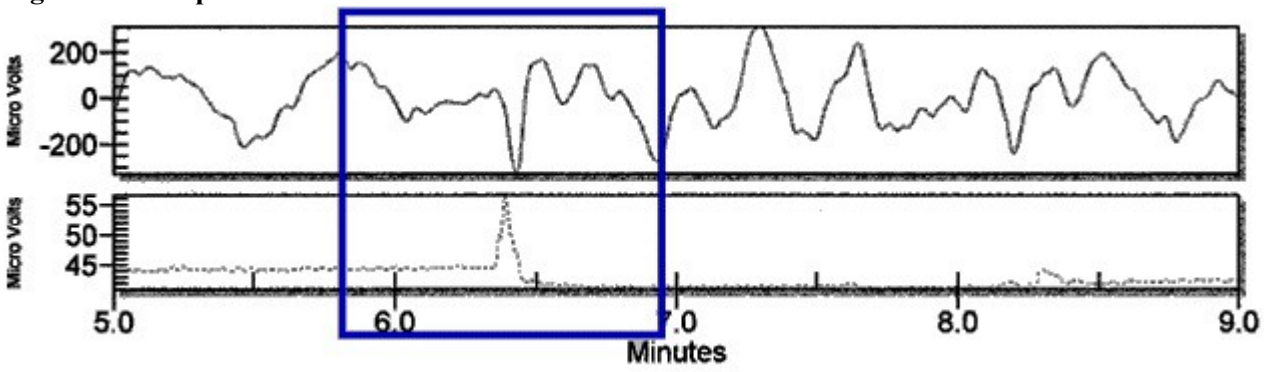
Figure 2. Example of Rule 2



Note: In Figure 2, the area within the box shows an EGG signal that is off scale (the trough of the wave is outside of the EGG channel). At the same time the EGG signal is off scale, the respiration signal is regular with no disruption. Thus, no respiratory or body movement artifact is detected and the EGG signal in minute 10 may be included for computer analysis.

Rule 3. If the EGG signal is "just touching" the top or bottom line of the channel and there is a matching disruption in the breathing pattern, then do not select these minutes for computer analysis (See Figure 3).

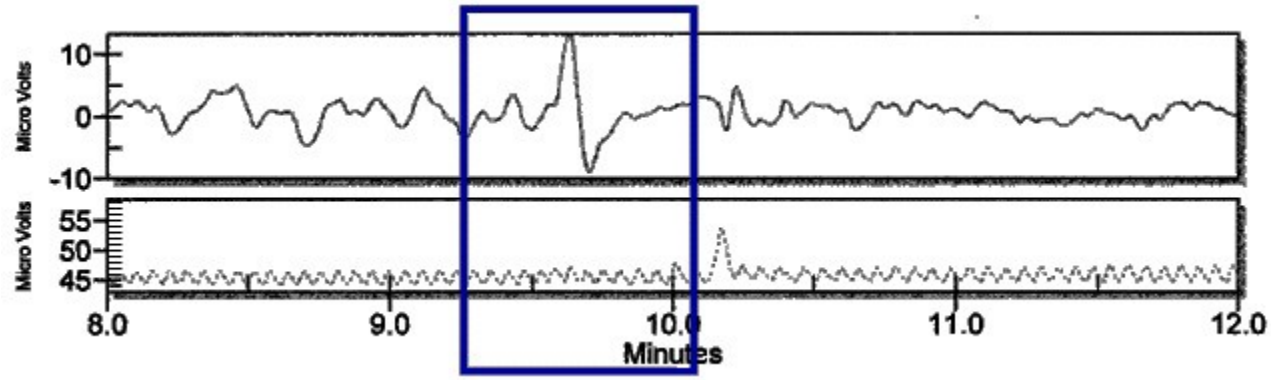
Figure 3. Example of Rule 3



Note: In Figure 3, the area within the box shows an EGG signal that is "just touching" the bottom of the EGG channel. At the same time, a clear deflection in the respiration signal occurs. Therefore, the EGG signal includes a respiratory or body movement artifact and this minute of EGG recording is *not* selected for computer analysis.

Rule 4. If the EGG signal is "just touching" the top or bottom line of the channel and there is *NO* disruption in the breathing pattern, then keep these minutes for computer analysis (See Figure 4).

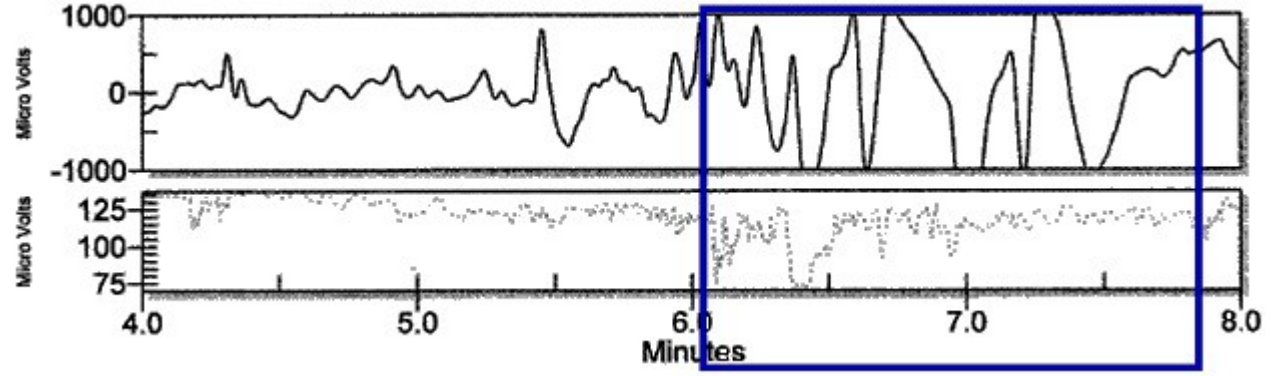
Figure 4. Example of Rule 4



Note: In Figure 4, the area within the box shows an EGG signal that is "just touching" the top of the EGG channel. This event occurs when the respiration signal is regular and undisturbed. Therefore, this minute of EGG signal may be selected for computer analysis.

Rule 5. If the EGG signal is "just touching" the top or bottom line of the channel and/or is off scale multiple times (i.e, off scale two or more times) during a one to two minute period, then do not select these minutes for computer analysis. In these cases, breathing pattern may or may not be disrupted (See Figures 5-8).

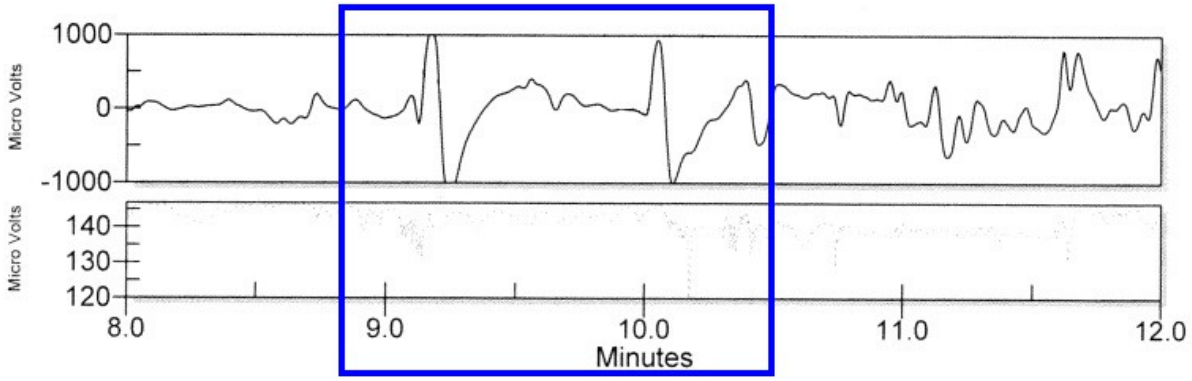
Figure 5. Example of Rule 5: EGG signal touches and goes off scale multiple times within a one to two minute period



Note: In Figure 5, the area within the box shows EGG signals that are off scale and "just touching"

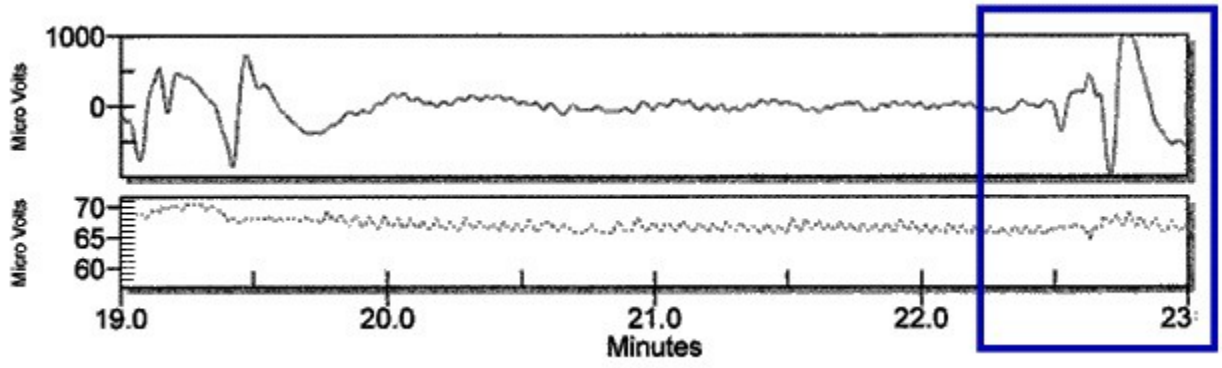
the top and bottom of the EGG channel numerous times within a one to two minute period. These minutes of EGG signal are *not* selected for computer analysis.

Figure 6. Example of Rule 5: EGG signal touches and goes off scale three times within a one to two minute
period



Note: In Figure 6, the area within the box shows EGG signals that are off scale and "just touching" the top and bottom of the EGG channel three times within a one to two minute period. These minutes of EGG signal are *not* selected for computer analysis.

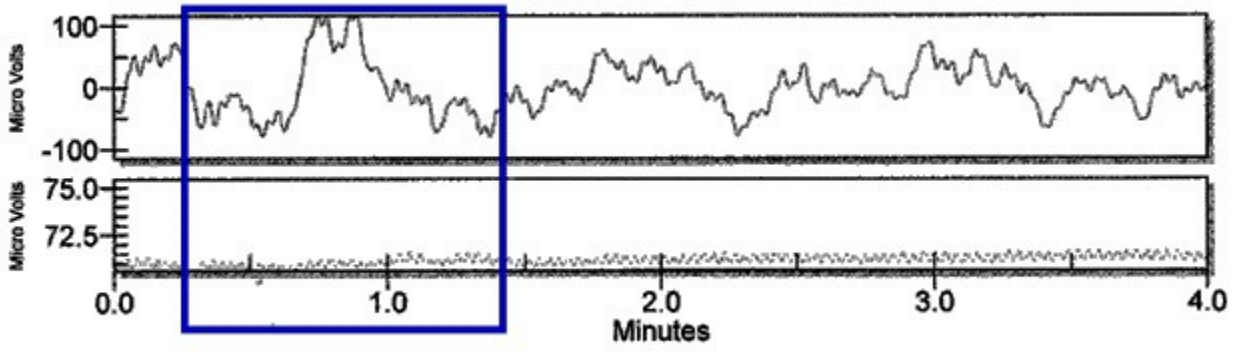
Figure 7. Example of Rule 5: EGG signal touches and goes off scale two times within a one minute period



Note: In Figure 7, the area within the box shows EGG signals that are off scale and "just touching" the top and bottom of the EGG channel two times within a one minute period. These minutes of EGG signal are *not* selected for computer analysis.

6.13.2. EGG Analysis-Rules for selection of good EGG minutes

Figure 8. Example of Rule 5: EGG signal shows a few small touches within a one minute period



Note: In Figure 8, the area within the box shows EGG signals that are "just touching" the top of the EGG channel multiple times within a one to two minute period. These minutes of EGG signal are *not* selected for computer analysis.

6.13.3. EGG Definition of Terms

1. **EGG Channel:** The EGG channel is the upper channel on the computer screen. The EGG signal is recorded within this channel.

2. **Respiration Channel:** The respiration channel is the channel located below the EGG channel on the computer screen. The respiration signal is recorded in this channel.

3. **Within the EGG Channel:** The peak or trough of the EGG signal is visible within the EGG channel.

4. **Off Scale:** Off scale means the peak or trough of the EGG signal or respiration signal cannot be determined because the peak or trough is beyond the bottom or top line of the EGG channel.

5. **Normal EGG Signal:** The normal EGG signal has three waves (or cycles) per minute that are clearly seen within the boundaries of the EGG channel.

6. **Normal Respiration:** The normal respiration signal has regular waves, reflecting the respiration rate, that are clearly seen within the boundaries of the respiration channel.

7. **Respiration Artifact in the EGG signal:** This artifact disrupts the EGG signal and is created by a visible disruption in the respiration pattern caused by deep breath, cough, or talking (observed by the technician).

8. **Movement Artifact in the EGG signal:** This artifact disrupts the EGG signal and is created by a body movement that usually disrupts the respiration signal. Thus, movement of arms, legs, body, or any physical activity by the subjected (observed by the technician) may cause movement artifact in the EGG signal.

6.13.4. 3CPM Technical Issues

The following listed items and action objectives are generated to clarify current and potential future potential issues.

1) Addition of non-authorized software or hardware to the 3CPM EGG device
    a. In order to retain the integrity of the 3CPM system, no hardware or software should be added or used without testing and approval by 3CPM.
        i. Even the most innocuous appearing software or hardware can corrupt the computer's operating system or the 3CPM software (even USB drives).
    b. Prior to using ANY software or hardware not specifically provided with the system, approval must be given.
    c. 3CPM will evaluate devices or software deemed critical by GpCRC to determine compatibility.
        i. In particular, USB keys used should be the same at all sites.

The SDRC will provide example of USB key and 3CPM will test and approve and distribute to all centers.

2) Need for computer hardware changes in the future
    a. It is anticipated that hardware may become non-functional in the future due to the age of the system or need to update the operating system (OS) to Windows 7 or 8.
        i. 3CPM will replace the computer and/or replaceable failing components
            1. Cost will be calculated as the cost of the hardware + GpCRC preferential shop rate + shipping.
            2. Arrangements should be made directly thru the SDRC
            3. Assurance of uniformity of signal generation and recording
    a. Electrode pads
        i. There have been recent changes in electrode pad construction by different manufacturers.
        ii. 3CPM has tested several different manufacturers' products and currently recommends using only 3M brand ECG electrodes for recordings.
        iii. The uniform use of the same disposable electrode pads is also important to insure uniformity of signal/data collected for analysis, and avoid the potential question of variability in signal that could be raise by using different pads.

6.14. Rome III Diagnostic Questionnaire (FD form)

Purpose

- To classify patients by the Rome III symptom-based diagnostic criteria into functional gastrointestinal disorders.

When

- Screening visit s
- Annual follow-up visits (i.e., f048, f096, f144 and f192)

Procedure

- Clinical coordinator should complete Part A of each form and apply MACO labels to subsequent pages 2-17 before giving the form to patient to complete
- The patient should meet with the Clinical Coordinator, be trained in completion of the form, and then should complete pages 2-17.
- Self administered, without help from spouse or family
- Clinical coordinator should check returned forms for completeness before the participant leaves the clinical center. Page 1 should be reattached to pages 2-17 and then the clinical coordinator should complete section B

6.15. Electrogastrogram with Nutrient Meal and SmartPill® (ST form)

At the initial screening visit, the participant will be advised to

1) Stop proton pump inhibitors for 7 days prior to the next study screening visit
2) Stop histamine 2 antagonists, prokinetics, narcotics, anticholinergics, constipation medications (over the counter laxatives, isotonic PEG electrolyte preparations (e.g. MiraLax), and prescription laxatives (e.g. lubiprostone) and cannabinoids for 3 days prior to the visit.

The participant will return for an additional screening visit in a fasting state, that is, nothing to eat or drink except for 4 oz of water after midnight the night before the test. Participants may take their usual medications with a small amount of water (up to 4 oz) up to two hours prior to the study, but should refrain from coffee, tea, or juice. If the patient normally takes insulin, they will be asked to take only half of their normal long-acting insulin. Record fasting glucose for diabetic patients; the blood glucose level must be checked to ensure it is less than 270 mg/dL to continue with the test. Prior to testing, a urine pregnancy test will be done for female participants.

Test Exclusion criteria:

Pregnancy, bezoars (retained liquid or poorly organized solids are permitted), dysphagia, prior gut lumen surgery, known strictures, prior inflammatory bowel disease, prior diverticulitis, chronic frequent NSAID use, and cardiac medical devices (gastric stimulators, insulin pumps, continuous glucose monitors are permitted).

Test protocol

The Study Physician will review the Baseline Medical History and complete a brief Physical Examination. The participant should be given the opportunity to use the bathroom. All participants will complete the PAGI-SYM questionnaire (GD form) assessing symptoms over the past 2 weeks (use visit code s2 for this visit in item 5 of GD form) and the Rome III (FD form).

Electrogastrography is the recording of the electrical activity of the smooth muscle, nerves, and interstitial cells, in the stomach using electrodes similar to those used to record the electrocardiogram (ECG). EGG electrodes are placed on the abdominal skin. Skin preparation for these electrodes will consist of cleaning the skin and then applying pre-gelled electrodes. If needed, the abdominal surface where electrodes will be positioned is shaved. The recording is performed in a quiet room with the subject reclining at a 45 degree angle.

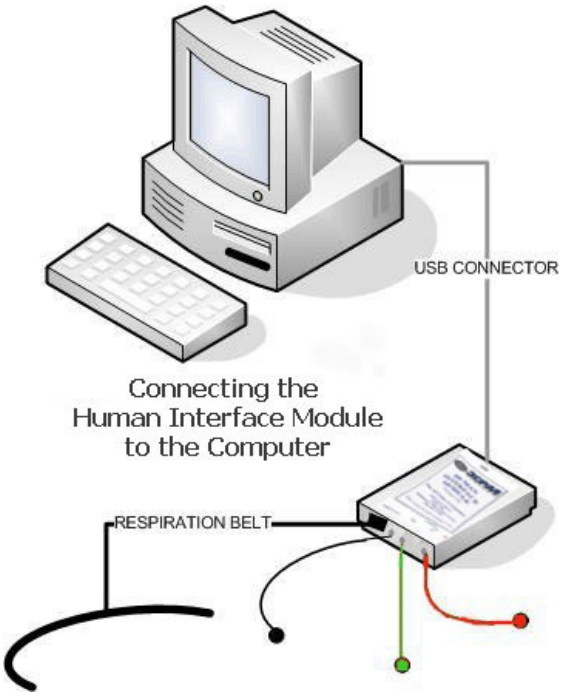
The following practical points will help to ensure a quality EGG recording:

- Record the EGG in a quiet room with subdued light
- Avoid all loud noises or distracting voices
- Position the patient in a comfortable chair or recliner (offer a blanket)
- Instruct the subject to keep arms and legs still, and to avoid any quick body movements.
- Talking should be avoided during the recording. Should an event such as coughing, movement, nausea, talking, etc happen during the baseline or post-stimulation periods of the EGG recording; you can mark the event by placing the mouse cursor over the desired minutes on the EGG tracing (the cursor will change to a pointer finger) and click the left mouse button. A screen will appear that gives you options for marking the event (cough, movement, etc) and a description box if you would like to record something other than the selections available. Once you select or enter the event, choose the "OK" button to complete the recording of the event. You may record an event as many times as one occurs. The object should be to have as many 4 minute segments without any events, so use the event recording only in cases of severe changes in the EGG tracing.

Equipment set-up:

Technique for skin preparation and electrode placement

1. Prepare to position the EGG electrodes as shown in the 3CPM User Manual:



– The RED EGG lead wire and electrode (+) is placed on the left mid-clavicular line (left side) approximately two inches below the left costochondral margin (lower ribs).

– The BLACK EGG lead wire and electrode (-) is placed approximately midway between the xiphoid process and the umbilicus, along the line from the xyphoid process to the umbilicus

– The GREEN EGG lead wire and electrode (ground) is placed is placed two inches below the right costochondral margin (lower ribs) along the right midclavicular line.

2. Preparing the skin
   – Shave off abdominal hair that is present in these locations for electrodes 1, 2, and 3.
   – Gently abrade the skin in the areas of the electrode positions using a course cloth, 4x4 gauze, or "Buff-Puff'.

3. Positioning the electrodes on the skin
   a) Connect the color-coded EGG lead wires to the Human Interface Module, by matching the lead wire color to the corresponding color-coded plug-in as designated on the Module label.
   b) Attach the pre-jelled electrodes to the snap-on ends of the EGG lead wires.
   c) Remove the plastic covers from the adhesive side of the electrode, and place on the skin according to the instructions in #1 above.

4. Positioning and connecting the belt for recording respiration rate
   The subject should be in the recording reclining chair at a 45 degree angle which is comfortable for the subject. Attach the belt across the upper chest with the belt clip placed under the armpits and the entire belt pulled snugly to obtain the clearest respiration signal. Check the EGG leads to verify that they are well adhered to the skin before starting the EGG recording

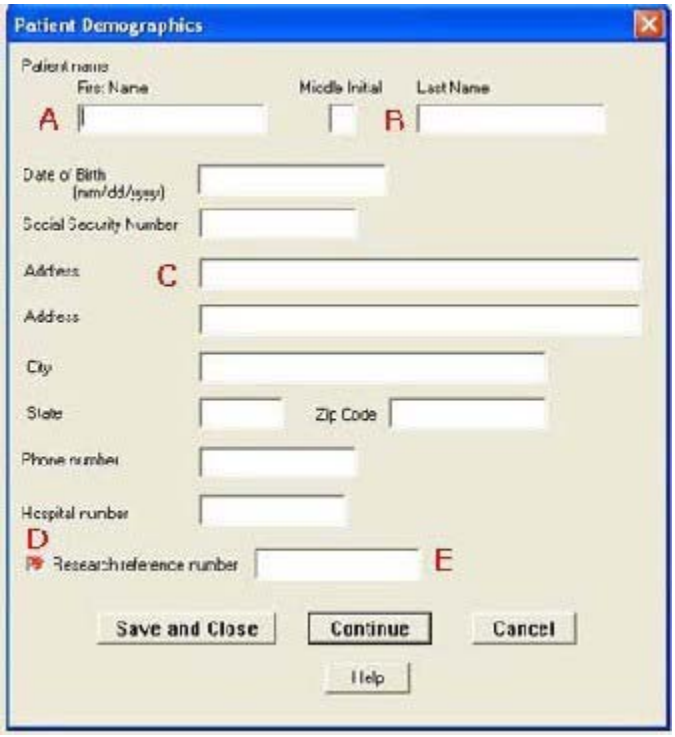
   – Baseline symptoms prior to EGG recording will be obtained using visual analog scales (VAS) for stomach fullness, hunger, nausea, bloating, and abdominal discomfort.

   – The subject will mark each symptom line with a vertical line to indicate how they currently feel in terms of that symptom on the ST form.

   You may elect to start a study for a new patient in one of two ways:
   • Select the icon for a new file, from the toolbar just under the top menu.
   • Select File from the top menu, then select ***New Study***, and then select ***New Patient***.

De-identifying patient data:

- For EGG recordings in the GpR2 study, **do not enter** patient addresses, phone numbers, or social security numbers into the Patient Demographics screen. This will prevent protected health information (PHI) from being displayed, printed, or transferred to Dr. Kenneth Koch at Wake Forest University or the SDRC for central reading. It is the responsibility of the clinical center staff to ensure that system protections are utilized to meet HIPAA requirements followed at your institution and implemented by the Gastroparesis Clinical Research Consortium Steering Committee.
- **Do not** follow the guidelines outlined in the 3CPM User Manual for entering patient demographic for GpR 2 study research purposes. Instead, enter the participant's information as shown in the figure below:



A. Enter the GpCRC 4-digit ID number in the **First Name** field (i.e., 9000)
B. Enter the 3-letter patient ID code in the **Last Name** field, followed by the form code (ST or WL) and visit code (s or f48) (i.e., zzzsts;zzzwls, or zzzwlf48)
C. Enter the study name in the **Address** field (i.e., GpR2 etc.).
D. Always check the **Research Reference Number** box.
E. Re-enter the GpCRC 4-digit ID and the 3-letter patient code separated by a hyphen, followed by the study, form code and visit code (i.e., 9000-zzzGpR2sts for the screening visit).

Once the demographics have been entered, click on ***Continue*** to continue with the study.
Cancel stops the study without saving any information.
Save and Close saves the patient demographics and ends the study. The patient won't be available if you try to select a patient study as there is no study yet. However, if at a later date, you start a study again with this patient, the program allows you to use the previously entered patient demographics.

When ***Continue*** is selected, you may then enter pre-study information.

Equipment test

This section of the study makes sure that the signals (EGG and Respiration) are stable. Both signals must be stable for 2 minutes. The initial screen shows the Respiratory sensor and Gastric electrodes in large red dots. When these turn green, the system is ready to start the baseline recording. The EGG signal, shown in red is in the top graph. The Respiration signal, shown in black is in the bottom graph.

To start the equipment test, select the ***Start Equipment Test*** button. When both the Respiratory sensor and the Gastric electrodes turn green, the ***Begin Baseline*** button gets enabled. Then to start the Baseline, select this button.

Recording of EGG and respiratory signals

- Allow 2-3 minutes before initiating the study in order to establish a stable skin-to-electrode interface. Obtain the first set of baseline symptoms using the symptoms score sheet (visual analog scale) page 2 of the EGG and Satiety Test (ST) form.

- Once the EGG and respiratory signals are stable, the baseline (pre-prandial) EGG recording period can begin. A fasting baseline EGG will be performed for 15 minutes before SmartBar® ingestion. The WMC (SmartPill Corp.) will be activated and calibrated.

- Select the ***Start Baseline*** button to start the baseline part of the study. The baseline period should last at least 15 minutes. Once the 15 minutes (baseline) have been reached, select the ***Stop Baseline*** button. You will have the options to select ***Pause Study, Skip Stimulation, and Stimulation Medium***. You will **always** select the ***Stimulation Medium*** button and leave this box open during the nutrient meal test.

The patient will begin the standard solid meal test by sitting up in the chair and ingesting one SmartBar® in a 10 minute period. Subjects may drink up to 50 ml of water during ingestion of the

SmartBar® . It is expected that 100% of the bar will be ingested. The percentage of the SmartBar®

be ingested with another 50 ml of water and another VAS symptoms score sheet will be completed. When the subject has completed the ingestion of the SmartBar® and SmartPill® with water, you will enter the amount consumed in this box.

- The subject returns to the same 30-45 degree position that they were in for the fasting baseline condition.
- The electrodes should be checked to verify that they are well adhered to the skin before starting the EGG recording for the 90 minute post-prandial period (after the meal is completed). The respiratory belt should be checked to verify it is snug.
- Symptoms will be assessed using VAS at the at 15, 30, 45, 60, and 90 minute time periods after ingestion of the SmartPill® . The patient may get out of the chair to stretch for 2 minutes at 30 and 60 minutes if necessary.

Starting the EGG study recording (post satiety testing)

Once you have entered the amount of the SmartBar® that was consumed (in the ***Stimulation Medium box***) you will have two options: the ***Start Study*** and the ***Cancel*** button. You will always select the button "Start Study. You will then select the ***Begin Study*** button; this will start the 90 minute post satiety EGG recording.

- A continuous 90 minute EGG recording is then obtained.
- At the end of the 0-15 minute period, you will have the subject complete a symptoms score sheet (ST form page 6). **Do not select the Finish button** in order for the subject to complete the symptoms score sheet; the EGG should continue to run during this period. At the end of the 16-30 minute postprandial period, you will have the subject complete a symptoms score sheet (ST form page 7). At the end of the 31-45 minute postprandial period, you will have the subject complete a symptoms score sheet (ST form page 8). At the end of the 46-60 minute postprandial period, you will have the subject complete a symptoms score sheet (ST form page 9). At the end of the 61-90 minute postprandial period, you will have the subject complete a symptoms score sheet (ST form page 10). Select the ***Finished*** button. A check box will appear and you will check the ***"Finish the Study***" box and then select the "***OK***" button. Once the study is complete, **save it immediately**. To save the study, click on the icon for saving a file. You can also select **File** from the top menu and then select **Save Patient**. When the study is complete, the raw EGG and respiration signals are displayed for the baseline period. Any events that have been marked are also displayed.
- The electrodes will be removed at this time. This concludes the study.

Selecting minutes for your report:

Once the study is finished you will select good minutes for the Baseline part of the study first. To do this enter the full 15 minute baseline in the box "***Select the Length***" by making the Start Period 0.0 and the End Period 15.0. Once these numbers are entered then check the ***Set Period Length*** check box . You will then enter into the second set of boxes the artifact free ***Start minute*** and ***End Minutes***. (Example: 4.0 start minute and 14.0 end minute) Once the minutes are entered, you will check the ***Set Good Minutes*** check box.

Now you can go to the post baseline period, which is after the patient ingested the stimulation medium (SmartBar). You can do this by using one of the 4 following methods.

1. Select the go to next period icon, at the top of the screen.
2. Select ***Go to*** from the top menu and then select ***Next period***.
3. Select ***Analyze*** from the top menu and then select ***Post stimulation period 1***. While in this menu item (if you have completed analyzing the baseline period), you will notice that there is a check mark next to the ***Baseline period*** menu item. This indicates that the baseline period has been analyzed.
4. Open the pull-down list at the top of the screen and select ***Post stimulation period 1***. Select the length of the initial period for analysis (minutes 0-15), by setting the ***Start minute*** and ***End minute***.

NOTICE: The first post stimulation period includes all the minutes of the study (0.0 Start Minute and 90.0 End minute). You will change this and select the length of the first 0 to 15 minute period by making the Start Period 0.0 and the End Period 15.0 then check the ***Set Period Length*** check box. The remaining minutes (after the last minute in the period) will create the second post stimulation period (minutes 16-30). **Do not select more than 15 minutes for any period length.**

Select the artifact free good minutes within the period just created by setting the ***Start minute*** and ***End Minutes***. Choose whole minutes only. Choose **at least 4** consecutive good minutes, up to 15 minutes. Enter the artifact free minutes into the select Start and End boxes and then check the ***Set Good Minutes*** check box.

This same procedure (***Post Stimulation Period 2***) is used for selecting the period length for the remaining minutes 16.0-30.0 and for selecting good minutes.

This same procedure (***Post Stimulation Period 3***) is used for selecting the period length for the remaining minutes 31.0-45.0 and for selecting good minutes.

This same procedure (***Post Stimulation Period 4***) is used for selecting the period length for the remaining minutes 46.0-60.0 and for selecting good minutes.

This same procedure (***Post Stimulation Period 5***) is used for selecting the period length for the remaining minutes 61.0-90.0 and for selecting good minutes.

Use the EGG report to complete pages 11-13 of the ST form.

Best practices when performing the EGG:

- When selecting minutes: choose whole minutes only; choose **at least 4** consecutive good minutes, up to 15 minutes. Do not select more than 15 minutes for any period.
- Attach a copy of the EGG report to the ST form. Save the raw digital EGG data to a USB flash drive.
- EGG and satiety tests should immediately be saved in at least two locations (1) EGG machine's hard drive and (2) the back-up USB drive provided.
- Web support from 3CPM: http://www.3cpmcompany.com/Product_Support1.htm is now used by 3CPM to track support requests from the individual centers. Each person performing EGG's should create an account on the web support page.

Exporting the EGG files:

The 3CPM Export Manual and an updated EGGSAS Research User manual are posted to the GpCRC website. From the home page www.gpcrc.us, click on Documents, then click on *Electrogastrography* and the last bullet is the Export manual.

The export program does not create a location to hold the exported files. Instead it points by default to the 3CPM folder itself. You must create a folder to export to each time you do an export. Please create a master folder called "GpR2 Exported Data", then create individual subfolders each time you export a group of patient EGG files. This will organize and archive exported GpR2 patient data to a specific folder in a way that the data may be tracked and documented. For quality assurance purposes, each clinical center should forward their first two GpR2 EGG with satiety test recordings to Wake Forest University for review by Dr. Kenneth Koch. These EGG recordings should be de-identified (see prior EGG PPM 26: Certification for electrogastrography (EGG) and satiety testing in NORIG), do not enter any patient demographics when prompted. Enter the 4-digit patient ID number under **First Name** and the 3-letter patient code in the **Last Name** field. Follow the directions outlined in section 2.2 of the 3CPM EGGSAS Export program manual to select the studies you wish to export to the "GpR2 Exported Data" folder.

The EGG file (.egg) and the database file (.mdb) should be exported to the USB flash drive provided to your center by the SDRC. The USB drive should be mailed to the address below. Please email John Dodge (jdodge3@ufl.edu) and Laura Miriel (laura.miriel@jhu.edu) from the Scientific Data Research Center and let them know the USB drive has been sent. The SDRC will return the USB flash drive to you once the EGG files are copied.

Ship by two-day delivery service with ability to track the shipment to:
John Dodge/Laura Miriel
GpCRC SDRC
415 N. Washington Street
Second Floor
Baltimore, MD 21231
Telephone (443) 287-3170

6.15. SmartPill and electrogastrogram

Study participants will be permitted to leave the study center after completion of the 90 minute EGG recording after SmartPill® ingestion. Study participants will leave with instructions from the last page of the ST form which instruct them to:

1. Remain fasting for 6 hours after SmartPill® ingestion; thereafter resume a normal diet; maintain a diary recording times of meal ingestion, bowel movements, and sleep; wear the receiver at all times and within 3 feet while sleeping or showering for the next for 4-7 days. An event marker on the receiver will be depressed for diary entries.
2. Complete any remaining questionnaires for GpR 2: Block 2005 Food Frequency Questionnaire, Block Energy Expenditure Survey, Nausea and Vomiting questionnaire, Neuropathy Total Symptoms Score-6 (NS), Abdominal Pain Questionnaire, State Trait Anxiety, Patient Health Questionnaire (PQ)
3. Continue to abstain from proton pump inhibitors, prokinetics, and 'over the counter' laxatives, isotonic PEG electrolyte preparations (e.g. MiraLax), and prescription laxatives (e.g. lubiprostone) after ingesting the SmartPill® until they return for the follow-up visit
4. Return fasting for a follow-up visit 4-7 days after SmartPill® ingestion to return the receiver, questionnaires, and diaries.

6.16. Wireless Motility Capsule Report (SmartPill) (WM form)

Purpose

- To document results of the wireless motility capsule (WMC) test in patients with gastroparesis.

When

- Second screening visit s. This form should be completed at the time of the participant returns with the SmartPill® receiver and the data is retrieved.

Procedure

- The Clinic Coordinator should complete section A. The Study Physician and/or Clinical Coordinator should use the SmartPill® test report and the patient diary to complete sections B and C. The Study Physician and Clinical Coordinator should complete Section D.

.

- Attach a copy of the SmartPill® test report to the WM form.

- Save the raw SmartPill® data to a USB flash drive

6.17. Autonomic function testing (AN form)

Purpose

- To record results reported by the ANX 3.0 System in order to detect dysfunction of the autonomic nervous system.

When

- Second screening visit s and f048.

Procedure

Patient Preparation Instructions
The ANSAR test is non-invasive and does not include exercise or needles. It should not cause any discomfort.

For the physician:
Patients whose pacemakers will pace continuously throughout the 15 minutes of the ANSAR test are the only patients contra-indicated for the test.

While the ANSAR test is very safe, patients will perform at least one short Valsalva maneuver (up to five, total, short Valsalva maneuvers, if they can). Therefore, if physicians wish to order the ANSAR test for their high-risk patients without the Valsalva challenge, technicians should instruct the patients to sit quietly and breath normally throughout the Valsalva challenge and log the reason.

While the ANSAR test is very safe, patients at risk for fainting or Vagal episodes are at risk of demonstrating symptoms during the test. Technicians should be alerted.

Patient preparation PRIOR TO ARRIVING AT OFFICE:

- Patient should maintain their normal routine.
- DO NOT DISCONTINUE OR CHANGE ANY MEDICATION OR THERAPY, unless expressly ordered by their physician.
- Wear a two piece outfit with loose fitting collar.
- Refrain from wearing skin lotions, body powers, or body oils.
- Do not have a significant meal within a half an hour of the ANSAR test.
- Do not engage in a significant exercise period within one hour of the ANSAR test.
- Do not wear jewelry or other objects with metal that is worn across the front of the chest.

6.17. Autonomic function testing

Patient preparation AFTER ARRIVING AT OFFICE:

- Patients will sit in a straight back chair and stand for five minutes at the end of the ANSAR test.
- Patients should bring devices needed to help them stand, or notify the office that they cannot stand so the office may prepare to place the patient flat on a bed or exam table and have the patient sit with proper seated posture during the stand challenge.
- Patients are not permitted to read, chew gum, suck candy or the like during the ANSAR test.
- Patients will have three EKG electrodes place on their chest and don a BP cuff.
- Patients should notify the office if they have stents or mastectomies which may alter placement of the BP cuff.
- Patients should notify the office if they have an implanted cardiac device which may alter the placement of the EKG electrodes.
- Patients should use toilet facilities before sitting for the ANSAR test.

How to administer a test:

For more information on administering the autonomic function test, please refer to the document ‘‘How to administer a test’’ on the GpCRC website by clicking on Studies > Gastroparesis Registry 2 Study > Autonomic Function Testing.

A. Equipment Setup

- Plug the main power cord into the wall. (Make sure the light on the surge protector and the printer is on).
- Turn on the physiologic monitor by switching the power button to the ON position.
- Turn on the laptop unit by pressing the On/Off button on the keyboard.

B. Patient Setup

- Have the patient sit on a chair that does not tilt, swivel, or have wheels.
- Place the Blood Pressure cuff on the patient’s upper left arm according to the drawing on the cuff (“this side to patient”). You should be able to place two fingers underneath the cuff comfortably.

- Place the electrodes on the patient's chest just below the clavicle; white on right, **black** on left, red on the patient's left lower rib cage. Each electrode should be placed on a smooth, clean, dry surface. Shave if necessary.

C. Entering Patient Data

- Click **Acquire New Data.** Click **Continue.** Then click **Begin.**

- For a new patient, enter the patient ID and letter code information (9999-yzx) in the Patient Demographics box. Use the **TAB** key to move to another field.

- To test a returning patient, click the Return Patient tab and click on the ID of the patient you wish to retrieve.

- To select medications, click on the drop down menu and click on the medication. Repeat to add more medications. Generic and Brand names are both listed in the menu. IF the medication is not on the list, type the medication in the '"Other Medications & Symptoms" section. NOTE: These medications will not be factored into the 'Medication State Graph.' Then click **Next**.

- Use the **Back** button to revise information, otherwise click **OK.** Review instructions with the patient. See section D.

D. Patient Testing

- Instruct participant to sit straight up with feet flat on the floor and arms resting comfortably at their sides. The participant should remain as still as possible and simply breathe freely at a comfortable pace unless instructed to do otherwise. The participant should not talk during the test. Use the F10 key to record any events (cough, sneeze, talking, etc). There are 6 Phases of the test (3 baselines, 2 breathing exercises, 1 stand challenge). Thirty seconds before the end of each phase, the time on the clock will switch to red. This is a reminder for you and the participant that the next challenge is about to begin. Have participant practice deep breathing and Valsalva challenges before the test begins.

1) Initial Baseline - 5 minutes of relaxed, normal, regular breathing. First blood pressure will be taken when the clock reads 2:00.
2) Deep Breathing - 1 minute of slow, easy, relaxed, deep breaths: 5 seconds in, 5 seconds out. NOTE: If patient is light-headed or dizzy, discontinue and use F10 to record event.
3) Baseline - 1 minute of relaxed, normal breathing.
4) Valsalva - Like you are trying to blow up a balloon that is difficult to blow up. Take a quick, deep breath in, hold the breath, and then bear down. Focus on bearing down in the chest and stomach and keep arms as relaxed as possible. Tell the patient that he/she will be

performing 5 Valsalva maneuvers. See chart below for assistance.

Begin Time	Hold Time	Release Time
1:35	:15	1:20
1:00	8 – 10 seconds	:50
:45	8 – 10 seconds	:35
:30	8 – 10 seconds	:20
:15	8 – 10 seconds	:05

5) Baseline - 2 minutes of relaxed, normal breathing. Do NOT remind patient that stand phase is about to begin. Make certain that lead/blood pressure wires are not under patients feet.
6) Stand - At the sound of the tone, instruct patient to stand. Stand next to patient in the event they need help standing or become dizzy upon standing. Patient should remain still and breathe normally.

- At the end of the test, a directory of IDs (filenames) will appear along with the ID/file name for the participant just tested. Click **Save**.

- Save the raw data to a USB flash drive.

E. Printing Reports

- At the next screen, click **Report_Gen** (see flashing red button).
- When prompted, click **Printer.**
- The default reports are pre-selected; you will see a dot in the circle next to the name of the report. To print the Multi-Parameter Interpretation Guide, click in the circle next to the report named "Multi-Parameter Interpretation Guide"
- Click Print.
- At the next screen, click **Send** (see flashing red button).
- Click **Quit**, then **Yes**.
- **Attach a printed copy of the report to the AN form and file in the patients GpR 2 study file.**
- NOTE: You can also print reports from the **Review Reports** Menu. Click on the patient's ID and then click **Print Report.** Follow instructions for **Printing Reports** above.

F. Printing a list of patients that were tested.

- Click on **Review Reports** from the Main Menu screen.

- Click **View History Log**. You will see a list of the patients that were tested. You have the ability to sort by date by clicking the arrow buttons at the top of the screen.
- Click **Print**.
- Click **Done**.
- Click **Exit** to return to the Main Menu.

G. Viewing an Interpretation

- Click on Review Reports from the Main Menu screen.
- Click on the patient's name and the click **View Interpretations**.
- Use the Next button to scroll through the pages of the Interpretation Report.

H. Saving a report to the Hard Drive

- You have the ability to save patient reports to the hard drive and view them without using ANX 3.0 software. At the end of the test, you will automatically save the patient report as an ANS file. After you click Save, the next screen appears, click **Report_Gen.**

- When prompted, click **Hard Disk or Floppy. Click** Save**.** Then click **Hard Disk.** The patient report will be saved in the C:\ drive, under the **Patient_Reports_html** folder. You can view these image files on any computer.

I. Equipment Shutdown

- Click **Shut Down** from the Main Menu screen.
- Flip the power switch on the back of the physiologic monitor to the OFF position. If necessary, turn off the surge protected power strip.

Additional AFT information is located on the Autonomic Function Testing webpage:
https://jhuccs1.us/gpcrc/closed/studies/GpR2/aftgpr2.htm

6.18. EGG and water load satiety test (WL form)

Pre-test procedures for water load satiety testing

The patient should fast after midnight the night before the test (nothing to eat or drink except for 4 oz (120 mL) of water the night before). The patient is generally scheduled for a morning appointment at about 8 am for the electrogastrogram (EGG) and water load satiety test. If the patient normally takes insulin, they will be asked to take only half of their normal long-acting insulin.

The EGG will be performed using 3CPM equipment. For each EGG study, the clinical center needs to have:

- A bottle of spring water refrigerated at 4 degrees C for each patient
- A cup that has a 50 mL measured mark
- 3 EGG leads
- A dedicated quiet area for the EGG recording
- A reclining chair
- A blanket
- Metric ruler
- 3CPM EGG equipment

Test protocol

On the morning of the EGG and water load satiety test, the patient will arrive fasting, that is, nothing to eat or drink except for 4 oz of water after midnight the night before the test. Patients may take their usual medications with a small amount of water (up to 4 oz) up to two hours prior to the study, but should refrain from coffee, tea, or juice. After arriving to the clinic, the patient's blood glucose level must be checked to ensure it is less than 270 mg/dL. If the patient's blood glucose level is greater than 270 mg/dL the EGG and water load satiety test must be rescheduled for another day.

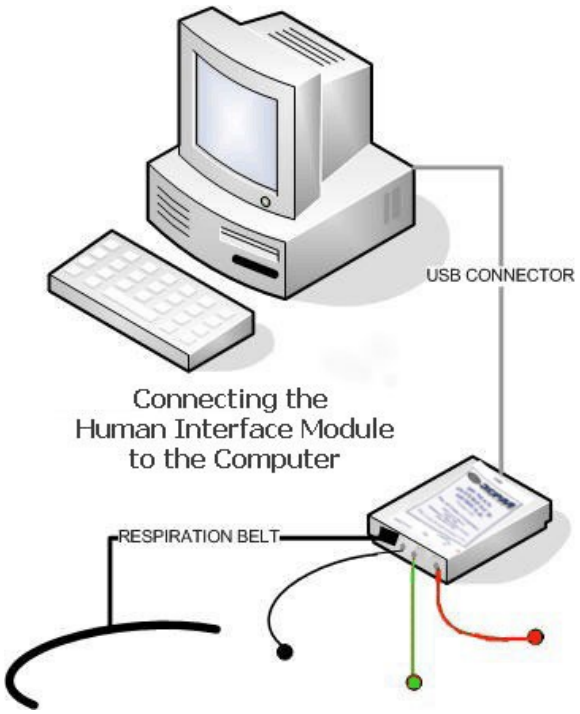
The patient should be given the opportunity to use the bathroom. Take the bottled water out of the refrigerator just prior to starting the EGG baseline recording.

Electrogastrography is the recording of the electrical activity of the smooth muscle, nerves, and interstitial cells, in the stomach using electrodes similar to those used to record the electrocardiogram (ECG). EGG electrodes are placed on the abdominal skin. Skin preparation for these electrodes will consist of cleaning the skin and then applying pre-gelled electrodes. If needed, the abdominal surface where electrodes will be positioned is shaved. The recording is performed in a quiet room with the subject reclining at a 45 degree angle.

The following practical points will help to ensure a quality EGG recording:

- Record the EGG in a quiet room with subdued light
- Avoid all loud noises or distracting voices
- Position the patient in a comfortable chair or recliner (offer a blanket)
- Instruct the subject to keep arms and legs still, and to avoid any quick body movements.
- Talking should be avoided during the recording. Should an event such as coughing, movement, nausea, talking, etc happen during the baseline or post-stimulation periods of the EGG recording; you can mark the event by placing the mouse cursor over the desired minutes on the EGG tracing (the cursor will change to a pointer finger) and click the left mouse button. A screen will appear that gives you options for marking the event (cough, movement, etc) and a description box if you would like to record something other than the selections available. Once you select or enter the event, choose the "OK" button to complete the recording of the event. You may record an event as many times as one occurs. The object should be to have as many 4 minute segments without any events, so use the event recording only in cases of severe changes in the EGG tracing.

Equipment set-up:



6.18. EGG and water load satiety test

Technique for skin preparation and electrode placement

1. Prepare to position the EGG electrodes as shown in the 3CPM User Manual:

   – The RED EGG lead wire and electrode (+) is placed on the left mid-clavicular line (left side) approximately two inches below the left costochondral margin (lower ribs).

   – The BLACK EGG lead wire and electrode (-) is placed approximately midway between the xiphoid process and the umbilicus, along the line from the xyphoid process to the umbilicus

   – The GREEN EGG lead wire and electrode (ground) is placed is placed two inches below the right costochondral margin (lower ribs) along the right midclavicular line.

2. Preparing the skin
   – Shave off abdominal hair that is present in these locations for electrodes 1, 2, and 3.
   – Gently abrade the skin in the areas of the electrode positions using a course cloth, 4x4 gauze, or "Buff-Puff'.

   Positioning the electrodes on the skin
   a) Connect the color-coded EGG lead wires to the Human Interface Module, by matching the lead wire color to the corresponding color-coded plug-in as designated on the Module label.
   b) Attach the pre-jelled electrodes to the snap-on ends of the EGG lead wires.
   c) Remove the plastic covers from the adhesive side of the electrode, and place on the skin according to the instructions in #1 above.

4. Positioning and connecting the belt for recording respiration rate
   The subject should be in the recording reclining chair at a 45 degree angle which is comfortable for the subject. Attach the belt across the upper chest with the belt clip placed under the armpits and the entire belt pulled snugly to obtain the clearest respiration signal. Check the EGG leads to verify that they are well adhered to the skin before starting the EGG recording.

   – Baseline symptoms prior to EGG recording will be obtained using visual analog scales for stomach fullness, hunger, nausea, bloating, and abdominal discomfort on the WL- EGG and Water Load Satiety Test form.

   – The participant will mark each symptom line with a vertical line to indicate how they currently feel in terms of that symptom.

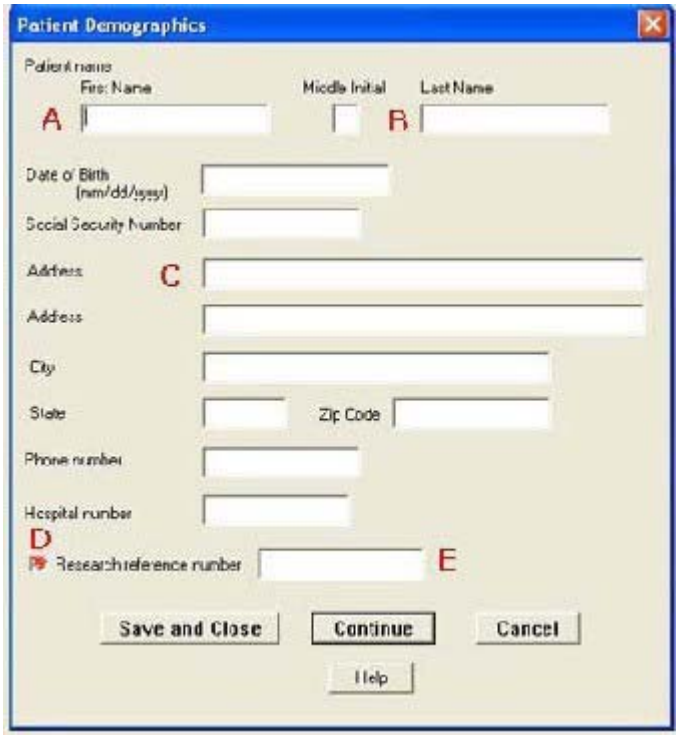
You may elect to start a study for a new patient in one of two ways:

- Select the icon for a new file, from the toolbar just under the top menu.
- Select File from the top menu, then select ***New Study***, and then select ***New Patient***.

De-identifying patient data:

– For EGG recordings in the GpR 2 study, do not enter patient addresses, phone numbers, or social security numbers into the Patient Demographics screen. This will prevent protected health information (PHI) from being displayed, printed, or transferred to Dr. Kenneth Koch at Wake Forest University or the SDRC for central reading. It is the responsibility of the clinical center staff to ensure that system protections are utilized to meet HIPAA requirements followed at your institution and implemented by the Gastroparesis Clinical Research Consortium Steering Committee.

– **Do not follow** the guidelines outlined in the 3CPM User Manual for entering patient demographics for GpR 2 research study purposes. Instead, enter the participant's information as shown in the figure below:



A. Enter the GpCRC 4-digit ID number in the **First Name** field (i.e., 9000)
B. Enter the 3-letter patient ID code in the **Last Name** field, followed by the form code (ST or WL) and visit code (s or f48) (i.e., zzzsts;zzzwls, or zzzwlf48)
C. Enter the study name in the **Address** field (i.e., GpR2 etc.).
D. Always check the **Research Reference Number** box.
E. Re-enter the GpCRC 4-digit ID and the 3-letter patient code separated by a hyphen , followed by the study, form code and visit code (i.e., 9000-zzzGpR2wls for the screening visit or 9000-zzzGpR2wlf48 for the f048 visit).

Once the demographics have been entered, click on ***Continue*** to continue with the study.
Cancel stops the study without saving any information.
Save and Close saves the patient demographics and ends the study. The patient won't be available if you try to select a patient study as there is no study yet. However, if at a later date, you start a study again with this patient, the program allows you to use the previously entered patient demographics.

When ***Continue*** is selected, you may then enter pre-study information.

Equipment test

This section of the study makes sure that the signals (EGG and Respiration) are stable. Both signals must be stable for 2 minutes. The initial screen shows the Respiratory sensor and Gastric electrodes in large red dots. When these turn green, the system is ready to start the baseline recording. The EGG signal, shown in red is in the top graph. The Respiration signal, shown in black is in the bottom graph.

To start the equipment test, select the ***Start Equipment Test*** button. When both the Respiratory sensor and the Gastric electrodes turn green, the ***Begin Baseline*** button gets enabled. Then to start the Baseline, select this button.

Recording of EGG and respiratory signals

- If you have not yet removed the bottled spring water from the refrigerator, remove it now, prior to the 15 minute baseline recording period.

- Allow 2-3 minutes before initiating the study in order to establish a stable skin-to-electrode interface. Obtain the first set of baseline symptoms using the symptoms score sheet (visual analog scale) page 2 of the EGG and Water Load Satiety Test (WL) form.

- Once the EGG and respiratory signals are stable, the baseline (pre-prandial) EGG recording period can begin.

- Patients will undergo a 15 minute baseline EGG in a reclining chair with the subject positioned at a 30-45 degree tilt, which is comfortable for the subject.

  – Select the ***Start Baseline*** button to start the baseline part of the study. The baseline period should last at least 15 minutes. Once the 15 minutes (baseline) have been reached, select the ***Stop Baseline*** button. You will have the options to select ***Pause Study, Skip Stimulation, and Stimulation Medium***. You will **always** select the ***Stimulation Medium*** button and leave this box open during the satiety test. When the subject has completed the satiety test, you will enter the amount of water consumed in this box.

Satiety test

Patients will begin the Water Load Satiety Test. For this, subjects will sit up. During the test, subjects will drink bottled spring water for a 5 minute period until they feel "**completely full**." The time the satiety test is started and completed and the total volume consumed will be recorded on page 3 of the WL form. The patient's symptoms are recorded at 10, 20, and 30 minutes after ingestion of the bottled spring water on pages 4, 5, and 6 respectively.

Instructions to patients for Satiety Test are as follows:

"You will be given a cup of bottled spring water to drink for 5 minutes until you feel completely full. You will have up to 5 minutes to drink the cup of bottled spring water. You may use all of this time, if needed. After you finish, we will ask about your feeling of fullness on a five-point scale, that is 0, 1, 2, 3, 4, 5 where 0 is not full at all and 5 is completely full. You will stop drinking when you become completely full from the bottled spring water. This is not a test to see how much you can drink, but simply to have you drink until you feel completely full."

- The total volume of bottled spring water consumed (WL form page 3) will be entered into the "stimulation medium" box at this time.

- The subject returns to the same 30-45 degree position that they were in for the fasting baseline condition.

- The electrodes should be checked to verify that they are well adhered to the skin before starting the EGG recording for the 30 minute post water load satiety period (after the drink is completed). The respiratory belt should be checked to verify it is snug.

Starting the EGG study recording (post water load satiety testing)

Once you have entered the amount of bottled spring water that was consumed (in the ***Stimulation Medium box***) you will have two options: the ***Start Study*** and the ***Cancel*** button. You will always select the button "Start Study. You will then select the ***Begin Study*** button; this will start the 30 minute post satiety EGG recording.

- A continuous 30 minute EGG recording is then obtained.

- At the end of the 0-10 minute period, you will have the subject complete a symptoms score sheet (WL form page 4). **Do not select the Finish button** in order for the subject to complete the symptoms score sheet; the EGG should continue to run during this period. At the end of the 11-20 minute postprandial period, you will have the subject complete a symptoms score sheet (WL form page 5). At the end of the 21-30 minute postprandial period, you will have the subject complete a symptoms score sheet (WL form page 6). Select the ***Finished*** button. A check box will appear and you will check the ***"Finish the Study***" box and then select the "***OK***" button. Once the study is complete, **save it immediately**. To save the study, click on the icon for saving a file. You can also select **File** from the top menu and then select **Save Patient**. When the study is complete, the raw EGG and respiration signals are displayed for the baseline period. Any events that have been marked are also displayed.

- The electrodes will be removed at this time. This concludes the study.

Selecting minutes for your report:

Once the study is finished you will select good minutes for the Baseline part of the study first. To do this enter the full 15 minute baseline in the box "***Select the Length***" by making the Start Period 0.0 and the End Period 15.0. Once these numbers are entered then check the ***Set Period Length*** check box . You will then enter into the second set of boxes the artifact free ***Start minute*** and ***End Minutes***. (Example: 4.0 start minute and 14.0 end minute) **Choose only whole numbers. Do not select more than 15 minutes for the baseline period.** Once the minutes are entered, you will check the ***Set Good Minutes*** check box.

Now you can go to the post baseline period, which is after the patient ingested the stimulation medium (bottled spring water). You can do this by using one of the 4 following methods.

1. Select the go to next period icon, at the top of the screen.
2. Select ***Go to*** from the top menu and then select ***Next period***.
3. Select ***Analyze*** from the top menu and then select ***Post stimulation period 1***. While in this menu item (if you have completed analyzing the baseline period), you will notice that there is a check mark next to the ***Baseline period*** menu item. This indicates that the baseline period has been analyzed.
4. Open the pull-down list at the top of the screen and select ***Post stimulation period 1***. Select the length of the initial period for analysis (minutes 0-10), by setting the ***Start minute*** and ***End minute***.

NOTICE: The first post stimulation period includes all the minutes of the study (0.0 Start Minute and 30.0 End minute). You will change this and select the length of the first 0 to 10 minute period by making the Start Period 0.0 and the End Period 10.0 then check the ***Set Period Length*** check box. The remaining minutes (after the last minute in the period) will create the second post stimulation

period (minutes 11-20) and third post-stimulation period (minutes 21-30). **Do not select more than 10 minutes for any period length.**

Select the artifact free good minutes within the period just created by setting the ***Start minute*** and ***End Minutes***. Choose whole minutes only. Choose **at least 4** consecutive good minutes, up to 10 minutes. Enter the artifact free minutes into the select Start and End boxes and then check the ***Set Good Minutes*** check box.

This same procedure (***Post Stimulation Period 3***) is used for selecting the period length for the remaining 21-30 minute period for selecting good minutes. Use the EGG report to complete pages 7-8 of the WL form.

Electrogastrogram and Satiety Test (WL form)

The Electrogastrogram and Water Load Satiety Test (WL) form is used to document symptoms and results of the water load satiety test and electrogastrogram in GpR 2 study participants.

- Complete the WL form during screening and at follow-up visit f048.
- Have the patient respond to symptom evaluations by marking a vertical line in each of the visual analog scales on pages 2, 4, 5, and 6. The scales are 100 mm in length and should be measured from left to right with a metric (SI) ruler. Enter the value closest to the patient's vertical line in millimeters (0-100 mm) in items 10, 15, 16, and 17.
- Using the EGG report, complete section **F. EGG data** following the rounding rules
- The Study Physician and Clinical Coordinator should complete section **G. Administrative information**

Best practices when performing the EGG:

- When selecting minutes: choose whole minutes only; choose **at least 4** consecutive good minutes, up to 10 minutes. Do not select more than 10 minutes for any post-satiety period.
- Attach a copy of the EGG report to the WL form. Save the raw digital EGG data to a USB flash drive (provided by the SDRC).
- EGG and satiety tests should immediately be saved in at least two locations (1) EGG machine's hard drive and (2) the back-up USB drive provided.
- Web support from 3CPM: http://www.3cpmcompany.com/Product_Support1.htm is now used by 3CPM to track support requests from the individual centers. Each person performing EGG's should create an account on the web support page.

Exporting the EGG files:

The 3CPM Export Manual and an updated EGGSAS Research User manual are posted to the GpCRC website. From the home page www.gpcrc.us, click on Documents, then click on *Electrogastrography* and the last bullet is the Export manual.

The export program does not create a location to hold the exported files. Instead it points by default to the 3CPM folder itself. You must create a folder to export to each time you do an export. Please create a master folder called "GpR2 Exported Data", then create individual subfolders

each time you export a group of patient EGG files. This will organize and archive exported GpR 2 participant data to a specific folder in a way that the data may be tracked and documented.

For quality assurance purposes, each clinical center must forward their first two GpR 2 EGG with satiety test recordings to Wake Forest University for review by Dr. Kenneth Koch. These EGG recordings should be de-identified (see prior instructions), do not enter any patient demographics when prompted. Follow the directions outlined in section 2.2 of the 3CPM EGGSAS Export program manual to select the studies you wish to export to the "GpR 2 Exported Data" folder.

The EGG file (.egg) and the database file (.mdb) should be exported to the USB flash drive provided to your center by the SDRC. The USB drive should be mailed to the address below. Please email John Dodge (jdodge3@ufl.edu) and Laura Miriel (laura.miriel@jhu.edu) from the Scientific Data Research Center and let them know the USB drive has been sent. The SDRC will return the USB flash drive to you once the EGG files are copied.

Ship by two-day delivery service with ability to track the shipment to:
John Dodge/Laura Miriel
GpCRC SDRC
415 N. Washington Street
Second Floor
Baltimore, MD 21231
Telephone (443) 287-3170

6.19. Food frequency questionnaire (Block and FQ form)

What

- Block 2005 Food Frequency Questionnaire
- Food Questionnaire Documentation (FQ) form
- Portion size illustration (part of the Block 2005 Food Frequency Questionnaire booklet)

Purpose

- To determine patient's usual eating habits over the past year or so, including all meals or snacks, at home or in a restaurant or carry-out.
- To assess food frequency and quantity over the preceding year

When

- Screening visit s
- Annual follow-up visits (ie, visits f048, f096, f144, and f192)

Procedure

- Use #2 pencil and fill in the bubble areas completely
- Before giving the booklet to the participant to complete, the Clinical Coordinator must:
  - Affix the Food Questionnaire ID label in the area where the participant is instructed to complete his/her name
  - Mark the participant's four digit ID # in the bubble area of the front page of the booklet
  - Mark the date in the bubble area of the front page of the booklet – THIS IS VERY IMPORTANT TO DO CORRECTLY – when the analysis is returned by the Block staff, date is the item which will distinguish screening from follow-up questionnaires
  - Mark the participant's gender in the bubble area of the front page of the booklet
  - Mark the participant's age at last birthday in the bubble area of the front page of the booklet
- Provide the participant with:
  - #2 pencil
  - Booklet
  - Portion size illustration
- Instruct the participant on completion of the booklet
  - Participant enters his/her best estimate of height and weight
  - Participant enters his/her best estimate of food eaten in the past year, frequency of eating a food, and portion size
  - Participant is not to skip any foods and to mark "NEVER" if he/she did not eat a certain food
- Remain available to answer questions as participant completes the booklet

6.19. Food questionnaire (Block Brief and FQ form)

- Review the completed booklet for completeness and consistency and color in any bubble areas that are partially or lightly completed or go over in #2 pencil any response marked in ink
- Complete the Food Questionnaire Documentation (FQ) form
- Put the completed booklet in a box (or other collection site) at the clinical center to hold for batch mailing to the SDRC

Mailing completed questionnaires to the SDRC

- Batch mail monthly using a mailing service that tracks packages
- Use the Transmittal Log for Food Questionnaires (TB) as a shipping list for the batch shipment
- Address the batch to:

Food Questionnaire Coordinator
GpCRC Scientific Data Research
Center 615 North Wolfe Street,
Room 5010
Baltimore, MD 21205
410-955-8175

Comments

- The Block 2005 Food Frequency questionnaires are obtained from the SDRC; contact Pat Belt (pbelt@jhsph.edu) or Laura Miriel (lmiriel@jshph.edu) to obtain additional copies
- The diet analysis provided by the Block group will be sent to the SDRC

6.20. Block Energy Expenditure Survey (PD and Block form)

What

- Block Energy Expenditure Survey
- Physical Activity Documentation (PD) form

Purpose

- To determine participant's usual physical activity over the past year or so

When

- Screening visit s
- Annual follow-up visits (ie, visits f048, f096, f144, and f192)

Procedure

- Use #2 pencil and fill in the bubble areas completely
- Before giving the survey to the participant to complete, the Clinical Coordinator must:
  - Affix the Energy Expenditure Survey MACO ID label in the area where the participant is instructed to complete his/her name
  - Mark the participant's four digit ID # in the bubble area of the front page of the survey
  - Mark the date in the bubble area of the front page of the survey – THIS IS VERY IMPORTANT TO DO CORRECTLY – when the analysis is returned by the Block staff, date is the item which will distinguish screening from follow-up surveys
  - Mark the participant's gender in the bubble area of the front page of the survey
  - Mark the participant's age at last birthday in the bubble area of the front page of the survey
- Provide the participant with:
  - #2 pencil
  - Survey
- Instruct the participant on completion of the survey
  - Participant enters his/her best estimate of frequency and type of activity
- Remain available to answer questions as participant completes the survey
- Review the completed survey for completeness and consistency and color in any bubble areas that are partially or lightly completed or go over in #2 pencil any response marked in ink
- Complete the Physical Activity Documentation (PD) form
- Put the completed survey in a folder (or other collection site) at the clinical center to hold for batch mailing to the SDRC

6.20. Block Energy Expenditure Survey (PD and Block form)]

Mailing completed surveys to the SDRC

- Batch mail monthly using a mailing service that tracks packages
- Use the Transmittal Log for Energy Expenditure Surveys (EQ) as a shipping list for the batch shipment
- Address the batch to:

Block Energy Expenditure Survey Coordinator
GpCRC Scientific Data Research Center
615 North Wolfe Street, Room 5010
Baltimore, MD 21205
410-955-8175

Comments

- The Block Energy Expenditure Surveys are obtained from the SDRC; contact Pat Belt (pbelt@jhsph.edu) or Laura Miriel (lmiriel@jshph.edu) to obtain additional copies
- The activity provided by the Block group will be sent to the SDRC

6.21. Patient Assessment of Upper Gastrointestinal Disorders - Quality of Life (PAGI-QOL) (UG form)

What

- Patient Assessment of Upper Gastrointestinal Disorders - Quality of Life (PAGI-QOL) (UG) form

Purpose

- To evaluate correlations between self-reported quality of life and disease severity

When

- Screening visit s
- All follow-up visits (i.e., visits f024, f048, f072, f096, f120, f144, f168, and f192)

Procedure

- Clinical Coordinator should complete Part A and apply labels to subsequent pages as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned form for completeness before the participant leaves the clinical center

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6.22. Patient Health Questionnaire (PHQ-15) (PQ form)

What

- Patient Health Questionnaire (PHQ-15) is a 15 item somatic symptom severity scale

Purpose

- To obtain the participant's views of his/her health while in the GpR 2 study

When

- Screening visit s
- All follow-up visits (i.e., visits f024, f048, f072, f096, f120, f144, f168, and f192)

Procedure

- Clinical Coordinator should complete Part A of each form and apply labels to subsequent pages as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center

6.23. Brief Pain Inventory (PI form)

What
- Brief Pain Inventory

Purpose
- To assess the severity and impact on daily functions of the participant's pain.

When
- Screening visit s
- Follow-up visits f048, f096, f144, and f192)

Procedure
- Clinical Coordinator should complete Part A of each form and apply labels to subsequent pages as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center

6.24. State-Trait Anxiety Inventory (Self-Evaluation Questionnaire) (SE form)

What

- Self-Evaluation Questionnaire (STAI)

Purpose

- To collect data on the psychosocial aspects of GpR 2 study participants with gastroparesis

When

- Screening visit s
- Annual follow-up visits (i.e., visits f048, f096, f144, and f192)

Procedure

- Clinical Coordinator should complete Part A and apply labels to subsequent pages as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center, then complete section B
- Clinical coordinator must score the questionnaire using the key provided in the form

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6.25. Beck Depression Inventory (BD form)

What

- Beck Depression Inventory Questionnaire

Purpose

- To collect data on the psychosocial aspects of patients with gastroparesis

When

- Screening visit s
- Annual follow-up visits (i.e., visits f048, f096, f144, and f192)

Procedure

- Clinical Coordinator should complete Part A and apply labels to subsequent pages as needed before giving the questionnaire to the participant to complete
- Self administered
- Clinical Coordinator should check returned questionnaire for completeness before the participant leaves the clinical center, then complete sections B and C
- The score is the sum of 21 items. If the participant has made more than one choice for an item, use the highest scoring item. The maximum total score is 63.

  The box below provides guidelines on depression level for participants within certain scoring ranges.

Total Scores	Range
0-13	minimal
14-19	mild
20-28	moderate
29-63	severe

- Special attention should be paid to item 2 and to item 9. Participants admitting to suicide ideation (as measured by item 9) and/or hopelessness (as measured by item 2) with a rating of 2 or 3 should be flagged for further clinical care.

- Special attention should be paid to item 16 and item 18. Where there are seven answer options (0, 1a, 1b, 2a, 2b, 3a, 3b). If a participant indicates a different answer for either of these questions as compared to when they last completed the form, this should be noted for clinical care.

- Implement a plan of action per your clinical center's guidelines for caring for participants with:
  a total score between 29-63;
  a response of 2 or 3 on item 2 or item 9.

6.26. SF-36 Health Survey (QF form)

What

- SF-36 Health Survey (QF) form

Purpose

- To evaluate correlations between self-reported quality of life and disease severity

When

- Screening visit s
- Annual follow-up visits (i.e., visits f048, f096, f144, and f192)

Procedure

- Clinical Coordinator should complete Part A and apply labels to subsequent pages as needed before giving the form to the patient to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned form for completeness before the patient leaves the clinical center

6.27. GpCRC abdominal pain questionnaire (AP form)

What

- Abdominal pain questionnaire developed by the GpCRC

Purpose

- To assess the severity and nature of abdominal pain in gastroparesis patients.

When

- Screening visit s
- Follow-up visits f048, f096, f144, and f192)

Procedure

- Clinical Coordinator should complete Part A of each form and apply labels to subsequent pages 2-7 as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center

6.28. Nausea profile and vomiting questionnaire (NP form)

Purpose

- To obtain the patient's frequency and intensity of symptoms due to nausea and/or vomiting while in the GpR 2 study.

When

- Screening visit s
- All follow-up visits (i.e., visits f024, f048, f072, f096, f120, f144, f168, and f192)

Procedure

- Clinical Coordinator should complete Part A of each form and apply labels to subsequent pages 2-7 as needed before giving the form to the participant to complete
- Self administered, without help from spouse or family
- Clinical Coordinator should check returned forms for completeness before the participant leaves the clinical center

6.29. Neuropathy Total Symptoms Score (NS form)

Purpose

- To obtain the patient's frequency and intensity of symptoms due to diabetic peripheral neuropathy.

When

- Screening visit s
- Follow-up visits f024, f048, f072, f096, f120, f144, f168 and f192.

Procedure

- The Clinical Coordinator should complete sections A-B and attach a MACO labels to pages 2-5 before giving the questionnaire to the diabetic patient for completion. The Clinical Coordinator should review the completed form for missing responses and resolve any problems before the patient leaves the clinical center. Page 1 should be reattached to pages 2-5, and the Clinical Coordinator should complete section C.

6.30. Laboratory Results (LR form)

Who

- All Gastroparesis Registry 2 participants

What

- Form LR covers assessments collected during screening and follow-up:
  - Hematology: complete blood count (white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count);
  - Erythrocyte sedimentation rate (ESR);
  - Comprehensive metabolic panel (sodium, potassium, chloride, carbon dioxide, calcium, BUN, creatinine, glucose, and liver panel including total protein, albumin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase);
  - Thyroid stimulating hormone (TSH);
  - Vitamin B12;
  - 25-hydroxy vitamin D level;
  - Lipid profile (total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides);
  - HbA1c;
  - Anti-nuclear antibody (ANA);
  - High sensitivity C-reactive protein (hs-CRP)

When

- All laboratory test results are required at screening visit s
- When laboratory results are available during follow-up
- HbAlc is required at all follow-up visits for diabetic participants

Instructions for form LR

- The measures on form LR are intended to be obtained by chart review, both at screening and during follow-up; the time window for each type of assessment is specified on the form
- During screening, if the chart review tests are out of the time window or the test conditions can't be ascertained or differ from what is required, the chart review tests cannot be entered on the LR form and the tests should be repeated
- During follow-up, the time window for the assessment is "in the time window for the follow-up visit (check the participant's Visit time window guide)" – e.g., f048 has an acceptable calendar time period within which it may be done; if you can find a hematology assessment in the participant's chart that was done under the same conditions as required by the study and which provides the required values and was done within the time window for visit f048, you can enter this information on the LR form for visit f048

6.31. Plasma and serum collection for Biosample Repository (BP form)

Purpose

- Collection of whole blood from Gastroparesis Registry 2 participants
- Separation of plasma and serum at clinical center: ten 0.5 mL aliquots of plasma and ten.5 mL aliquots of serum are to be obtained in 2.0 mL cryogenic vials
- Store plasma and serum aliquots at -70°C prior to batch shipping to the NIDDK Biosample Repository

Forms / Materials

- BP - Blood Processing for Plasma and Serum
- Labels (MACO) for heparin (green top) tubes and serum separator SST tube (red-gray top)
- Labels for plasma and serum cryovials
- SS - Specimen Shipment log
- NIDDK Biosample Repository shipper

When

- Screening visit s
- Annual follow-up visits (i.e., f048, f096, f144, f192, and f240)
- Batch shipments: Monthly or semi-monthly, Mon -Wed

By whom

- Phlebotomist
- Clinical Coordinator

Equipment

Blood tubes/aliquot vials

- One 10 mL sodium heparin (green top) tube - *provided by clinical centers*
  - Model/product number: Becton Dickinson product number #367874
  - 100 tubes/pack @ $41.49

- One 10 mL plastic SST (red-gray top) tube with silica clot activator- *provided by clinical centers*
  - Model/product number: Becton Dickinson product number #367985
  - 100 tubes/pack @ $24.56

- Up to 20 2.0 mL cryogenic vials - *provided by clinical centers*
  - vials should be able to withstand -196 degrees C
  - vials should be self standing (flat bottom, not curved), externally threaded, 13.5 mm wide x 48.3 mm tall, with silicone washers

- Model/product number: Model #CV200-2
- Vendor contact information:

1) Cryogenic Storage Systems and Supplies
   243 Lawyers Road, NW
   Vienna, VA 22180
   703-319-8247
   877-738-8247
   703-938-9351 (fax)

2) Corning External Thread Cryogenic Vials
   Catalog # 430659
   50 per pack, 500pk/case: $204.17
   Telephone: 1-800-492-1110

3) Fisher
   1-800-766-7000
   Catalog #10-500-26

Labels

- Preprinted labels for whole blood collection tubes (10 mL heparin tube and 10 mL SST tube) and preprinted labels for Form BP – *labels are printed at the clinical center via web-based data management system; use MACO ML-5000 1" x 1 ½" labels, 50 labels/page*
- Preprinted polypropylene labels for 2.0 mL cryogenic vials – *provided by the SDRC*

Equipment

- Centrifuge
- -700°C freezer
- Swing out rotor
- 5 mL pipettes
- Barcode scanner (provided by the SDRC)

Blood collection and processing procedures

- Participant instructed to fast 8 hours prior to blood draw
- Collect whole blood into one pre-labeled 10 mL heparin (green top; Becton-Dickinson #367874) tube for plasma
- Collect whole blood into one pre-labeled 10 mL SST (red-gray top; Becton-Dickinson #367985) tube for serum
- Blood for plasma and serum to be centrifuged, aliquoted, and frozen within one hour
- If sample appears to have hemolyzed; do not aliquot. Re-draw blood.

6.31. Plasma and serum collection for Biosample Repository (BP form)

Plasma

- Collect blood into heparin (green top; Becton-Dickinson) tube. Ensure that heparin tubes have not expired. (*check that date shown above "Exp" in lower right corner of label is later than current month*)
- Completely fill vacutainer tube
- Mix gently by inversion 5 times
- Within 30 minutes, centrifuge at 1800 x g for 15 minutes at 4°C, preferably with a swing out rotor
- Immediately after centrifugation, insert a 5 mL pipette below surface of plasma
- Remove the clear plasma while avoiding blood cells
- Transfer plasma into aliquots of 0.5 mL each into 10 labeled 2.0 mL cryovials
- Freeze at -70°C immediately

Serum

- Collect blood into serum separator (red-gray top) tube. Ensure that SST tubes have not expired. (*check that date shown above "Exp" in lower right corner of label is later than current month*)
- After filling, invert SST tube gently at least 5 times
- Allow blood to clot for **at least 30 minutes** at room temperature
- Centrifuge at 1800 x g for 15 minutes at 4C, preferably with a swing out rotor
- Transfer 0.5 mL of serum into 10-14 labeled 2.0 mL cryovials
- Freeze at -70°C immediately

Note: Separated serum and plasma may be stored at -20°C for up to one day before transfer to -70°C while ensuring samples remain frozen during the transfer.

Blood Processing for Plasma and Serum (BP) form

- Affix aliquot "00" cryovial labels to the BP form
- Complete the Blood Processing for Plasma and Serum (BP) form
- Affix MACO labels for the heparin plasma and the SST serum to the BP form

Applying labels to cryovials

- Attach the label to the vial when the vial is at room temperature
- Leave the cap on the vial when labeling; the inside of the vial is sterile
- Apply the label to the vial so that the long edge of the label is parallel to the floor when the vial is held in an upright position. The label should not trail off the bottom of the vial or over the cap
- While holding the vial in an upright position, affix the colored portion of the label to the vial first
- Wrap the clear tail around the perimeter of the vial. The end of the clear tail should overlap the colored portion of the label
- Press firmly on the entire label. Verify that all edges of the label adhere to the vial
- When possible, allow newly labeled cryovials to set at room temperature for several hours prior to subjecting them to colder temperatures. (24-48 hours is optimal)
-

6.31. Plasma and serum collection for Biosample Repository (BP form)

Barcode Scanners

- Plug the scanner to the USB port on your computer
- Open your template Excel shipping manifest file (filename GpCRC_Site6xx_shipdate.xls) and replace the x with the last digit for your clinical center's site ID and replace ship date with the date of shipment
- Place the cursor in the first cell under Barcode number
- Hold the scanner approximately 4-8 inches from the cryovial barcode you wish to scan. (The scanner will emit a red light as it searches for the barcode and will emit a beep and a green dot when the barcode has been successfully read.)
- The scanner automatically enters the barcode into the proper field and immediately goes to the next cell
- Scan all the cryovials you are shipping to the NIDDK Biosample Repository into the Excel spreadsheet
- Place the cryovials back in the freezer or pack in shipper with dry ice to prevent thawing
- For each cryovial barcode scanned, enter the following in the corresponding column of your Excel file: Site ID-Participant ID numbers, the 3 letter participant code, the date the sample was collected (mm/dd/yy format) and the specimen type (S = serum; P = plasma). The volume should be a standard 0.5 and the unit of measure will always be milliliters Enter a 5 for the study number (GpR 2 = 5)
- Save the Excel spreadsheet with the correct ship date at the end of the file name (Click on File then click on Save As) and print 2 copies

Packaging Procedures

- Each STP 320 T shipper (provided by the Repository) can accommodate aliquots for 8 participants, depending on the number of aliquots obtained for each participant (maximum capacity of each shipper is 230 aliquots)
- Check that 1 absorbent pad is in the Saf T Pack Bio hazard plastic bag
- Insert frozen cryovial into small cardboard boxes with dividers. Place only one tube into each cardboard cell. Each cardboard box may hold 81 cryovials
- Insert each cardboard box with cryovials into its own plastic bag and seal
- Place each plastic bag with specimen box into its own STP-710 Tyvek envelope and seal.
- Place each Tyvek envelope into STP-111 inner brown cardboard box. No more than 3 Tyvek envelopes containing boxes with cryovials can be placed into the STP-111 inner brown cardboard box. If shipping only 1 or 2 specimen boxes, fill the rest of the space inside the cardboard inner box with bubble wrap to prevent movement
- Tape the inner cardboard box closed before placing into the styrofoam cooler
- Place cardboard box in upright position in bottom of styrofoam cooler
- Surround the STP-111 inner brown cardboard box with about 8 kg of 2" blocks or nuggets of Dry Ice
- Fill excessive room left in the insulated freezer box with bubble wrap to stabilize specimens in transit
- Place the polystyrene lid onto the freezer box

- Place the "Empty Packaging" cover and shipping form on the top of the cooler lid
- Place a completed Specimen Shipment Log (Form SS) stapled to the printed copy of the Excel spreadsheet of scanned cryovials on top of the cooler lid
- Close and seal outer cardboard box with tape

Labeling Shipper:

The shipper should be pre-labeled. Confirm the following:

1. A checkmark is in the block on the outer cardboard box next to "BIOLOGICAL SUBSTANCE, CATEGORY B". Do not cover this marking with labels.
2. A label with your name and return address appears in the "Shipper:" block.
3. The repository address label is to the side of the box in the "Consignee:" block.
4. The dry ice label below the repository address label is prefilled.
5. The "UN3373 BIOLOGICAL SUBSTANCE, CATEGORY B" label is affixed.
6. Use the provided preprinted Federal Express label to ship specimens to the NIDDK Biosample Repository.
7. Place pre-printed Federal Express label in the pouch on the outside of the shipper. Call Federal Express at 1-800-463-3339; give them the tracking number.

Do not write on exterior of box

Do not ship frozen packages on Thursday or Friday; the repository is closed on weekends

Shipping samples to the NIDDK Biosample Repository

- Complete the Specimen Shipment Log (Form SS), staple to the printed corresponding Excel spreadsheet of scanned cryovials and enclose a copy with each shipment of specimens.
- Keep a notebook of all original completed Specimen Shipment Logs (Form SS) stapled with the corresponding Excel spreadsheet of scanned cryovials so that you have a record of all shipments to the NIDDK Biosample Repository
- Specimens are to be batch-shipped monthly to the NIDDK Biosample Repository at Precision for Medicine every month on a **Monday, Tuesday or Wednesday**.
- For each shipment, email the Excel spreadsheet to the Biosample Repository at niddk.mailbox@precisionformedicine.com and eduard.chani@precisionformedicine.com with the Fed Ex tracking number in the subject line of the email.
  Important: This email will ensure that you receive a replacement shipper.

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6.32. Whole blood collection for Genetics Repository (CG and GP forms)

Purpose

- Collection of whole blood from Gastroparesis Registry 2 patients who consent for genetic research was SUSPENDED as of 7 December 2016.

Forms

- Gastroparesis Registry 2 consent for genetic research- do not consent patients after 7 Dec 16
- Genetic Consent Documentation (CG) form
- Blood Collection for DNA (BC) form

- For GpR2 participants currently in screening who have consented to blood collection for DNA banking; do not collect blood for DNA banking. Complete the CG - Genetic Consent and Blood Collection Documentation form, answering No in item 15, specify 'DNA collection suspended' then skip to item 20 and complete the form.
- Until further notice, do not consent potential GpR 2 participants for DNA collection. However, you must continue to complete and key the CG - Genetic Consent and Blood Collection Documentation form, answering No in items 10, 11, 12, and 14; then skip to item 20 and complete the form.
- The CG form must be entered in the data system to allow the Enrollment Check.
- All remaining DNA shipping kits supplied by the Genetics Repository should be destroyed/recycled at each clinic center.

6.33. Adverse event reporting (AE form)

Purpose: To document any event (e.g., abnormal laboratory findings, symptom exacerbations, Emergency Room visits, hospitalizations, upper endoscopy or gastric emptying scintigraphy complications, surgical interventions for symptom management, and complications of these interventions or study procedures) that occurs after a patient has consented to participate in the Gastroparesis Registry 2 study.

When: Complete the AE form at all GpR 2 visits

Definitions

- **Adverse event** is defined as any unfavorable sign, symptom, state, condition, or laboratory finding in a Gastroparesis Registry 2 patient. Adverse events may result from appropriate application of the protocol in relation to the processes of enrolling, studying, or following Gastroparesis Registry 2 participants, as well as from mistake or misadventure.
- **Life-threatening adverse event** is defined as an adverse event that in the view of either the investigator or sponsor, places the patient or subject at immediate risk of death. It does not include an adverse event that, had it occurred in a more severe form, might have caused death
- **Serious adverse event** is defined as any event that suggests a significant hazard, contraindication, side effect, or precaution. Serious adverse event includes any event that is fatal or life-threatening, is permanently disabling, requires or prolongs inpatient hospitalization, or is a congenital anomaly, cancer, or overdose. This includes any event that may jeopardize the participant and may require medical or surgical intervention to prevent a serious event.
- **Unexpected adverse event** is defined as any adverse event that is not identified in nature, severity, or frequency in the risk information included in the Gastroparesis Registry 2 protocol and other relevant sources of information such as product labeling and package inserts of research procedures.

Reportable Gastroparesis Registry events

- All adverse events thought to be associated with a Gastroparesis Registry2 study or procedure are reportable and should be documented on the Adverse Event Report (AE) form.
- Any event threatening the integrity or well-being of the Gastroparesis Registry 2 (e.g., suspected fraud) is a reportable Gastroparesis Registry 2 event. We recognize that this category is not well-defined; however, it is included as a reminder that reportable events can have a broader scope than events that happen to a patient. Some examples include:
  (1) Abnormal laboratory values
  (2) Events that impact the patient's treatment or participation

(2) Events that are recorded on the Follow-Up Medical History (FH) form
(3) Events that may or may not be related to the study
(4) Other events that clinical center staff feel should be reported

- Deciding whether an event is reportable to the Gastroparesis Registry 2 (i.e., is in either of these categories) will be the responsibility of the Principal Investigator (PI) of the center.
- The Scientific Data Research Center will maintain a list of serious adverse events for reporting and review at Steering Committee meetings.

CTCAE v3.0

- The GpCRC uses the Common Terminology Criteria for Adverse Events, (CTCAE v3.0) to specify and grade adverse events.
- This document is posted on the GpCRC website (www.gpcrc.us – click on Documents)
- Use the CTCAE v3.0 to specify the Short Name for the adverse event and the severity grade for the adverse event.
- **Adverse events Grade 3 or higher, should be faxed the form to the SDRC (Attention: Ivana Vaughn) for review by Dr. Linda Lee, the Safety Officer.**

Local reporting requirements

- Your institution's IRB has reporting requirements of its own regarding events occurring in the course of conduct of a study. These reporting requirements may be more stringent than those adopted by the Gastroparesis Registry 2. Regardless of what the Gastroparesis Registry 2 requires, you must continue to meet your local IRB's requirements. If the local requirements are more stringent than the Gastroparesis Registry's, you may report events locally that you do not report to Gastroparesis Registry.
- Since the Gastroparesis Registry 2 is an observational study, few adverse events related to the study are expected. Potential adverse events are those related to blood draws for the study or study procedures.
- If such an event occurs, appropriate medical care should be provided immediately in the clinic.
- If a suspected adverse event is reported by telephone several days later, the participant should be evaluated in the clinic by medical staff (preferable) or referred to an appropriate facility for evaluation and management.
- All such events should be documented in the study chart and reported on the Adverse Event (AE) form.
- For more information please refer to FDA Guidance for Clinical Investigators, Sponsors, and IRB: Adverse Event Reporting to IRBs – Improving Human Subject Protection.

6.34. Procedures for missed or incomplete visits (MV form)

Purpose

- Record data about missed or incomplete visits

Form

- Missed or Incomplete Visit (MV) form

When

- At close of a visit window for any missed follow-up visit or for any follow-up visit with specific forms not completed

By whom

- Clinical Coordinator

Procedures for missed or incomplete in-person visits

- For a missed visit:
  - Date of missed visit is the last date of the visit window
  - Indicate reason(s) for missed visit
- For an incomplete visit:
  - Date of incomplete visit is the date on which a partial set of procedures was performed
  - Indicate reason(s) for missed procedures

6.35. Procedures for patients lost to follow-up

Purpose

- Ascertain vital status of patient
- Document reason(s) patient did not attend visit
- Ascertain if patient is lost to follow-up

When

- Whenever patient misses a study visit and is difficult to contact

By whom

- Clinical coordinator

Search strategies

- Contact all persons identified on the Patient Location (PL) form
  - Telephone different times during the day/evening
  - Send letter via regular or certified registered mail to determine if patient is still at listed address
- Check current telephone directory for listings both for the patient and the patient's contacts specified on the PL form, eg., next of kin, health care professionals
- Check post office for forwarding address; ask patient's contacts for forwarding address
- Check obituaries
- Check state vital records

6.36. Procedures for mortality closeout (DR form)

Purpose

- Record participant death

Forms

- Complete the Death Report (DR) form

By whom

- Study Physician and Clinical Coordinator

6.37. Medical management of patients (standard of care)

Since the Gastroparesis Registry 2 is an observational study, it will not be the role of study investigators to prescribe or prohibit use of medications as part of the study. Nevertheless, to keep recommendations and care for participants in the study as uniform as possible, investigators should generally discuss with participants what is laid out in the SOP IV: Standards of Care for Patients with Gastroparesis document.

6.38. Gastroparesis Registry 2 Study Closeout (CO form)

Purpose

- To temporarily close out a patient's participation in the Gastroparesis Registry 2 if they are being enrolled into GLUMIT-DG, APRON or another GpCRC main study.

Form

- Closeout (CO) form

When

- The Closeout form should be completed upon enrollment of the GpR 2 patient into another GpCRC study.

By whom:

- Clinical coordinator

Instructions

- Complete and key this form for patients enrolled in the Gastroparesis Registry 2 who are subsequently enrolled in another GpCRC study. All GpR 2 visits will be due until this form is keyed. The keying of this form will turn off the visit windows for the Gastroparesis Registry 2.

- If the patient is not enrolled in a new study, this form should not be keyed.

- If the form has already been keyed, it should be deleted.

7. Forms management

7.1. Clinical center ID codes

Alphabetic IDs

- Alphabetic clinic IDs are used on forms, lists, and tables
- Alphabetic clinical center IDs are based on the name of the institution with which the clinical center is affiliated
- Assigned IDs

Johns Hopkins Bayview Medical Center	JHU
Massachusetts General Hospital	MGH
Temple University	TU
Texas Tech University	TTU
University of Louisville	UL
Wake Forest University Health Sciences	WFU

*Legacy sties:

California Pacific Medical Center*	CPMC
Stanford University	SU
University of Michigan	UMI

California Pacific Medical Center (CPMC) was a satellite of Stanford University and will used SU's alphabetic and numeric IDs

Numeric site IDs

- The NIDDK Repository uses numeric IDs to identify the GpCRC clinical centers
- These will be used on the specimens (whole blood, plasma, and serum samples sent to the Biosample Repository)
- Assigned IDs

Baylor College of Medicine (Pediatric)	647
*California Pacific Medical Center**	*613*
Johns Hopkins Bayview Medical Center	643
Massachusetts General Hospital	649
Stanford University	*613*
Temple University	610
Texas Tech University	637
University of Louisville	644
University of Michigan	*611*
Wake Forest University Health Sciences	614
Johns Hopkins University- SDRC	61

7.2. Patient identifiers

What

- Patient ID number
- Patient code

Patient ID number

- 4 characters, all numeric
- ID number labels will be distributed to clinics by the Scientific Data Research Center
- The ID number for a patient will remain the same for the duration of the GpCRC, even if the patient enters another GpCRC study or if the patient fails screening and is subsequently re-evaluated – the ID never changes

Ranges of patient IDs assigned to clinics

Baylor College of Medicine	BCM	0001	-	0999
Johns Hopkins Bayview Medical Center	JHU	8001	-	8999
Massachusetts General Hospital	MGH	9001	-	9999
Temple University	TU	1001	-	1999
Texas Tech Medical Center	TTU	6001	-	6999
University of Louisville	UL	7001	-	7999
Wake Forest University Health Sciences	WFU	5001	-	5999

- Legacy centers:

California Pacific Medical Center	*CPMC*	*4001*	-	*4999 (odd)*
Stanford University	*SU*	*4001*	-	*4999 (even)*
University of Michigan	*UMI*	*2001*	-	*2999*

- *California Pacific Medical Center (CPMC) was a satellite of Stanford University and will use SU's range of patient IDs*

Patient code

- 3 character alpha code assigned by the Scientific Data Research Center and printed on the ID number label
- Each patient code is unique across the GpCRC

7.3. Visit ID code

- 1 to 4 character alpha-numeric code
- Determined by purpose of visit and timing with respect to visit windows
- Visit ID codes

s	Screening, baseline data collection, and enrollment
s2	Used for second PAGI-SYM completed during screening at the time of the EGG and Nutrient Test
f024	24 weeks follow-up visit (approximately 6 months)
f048	48 weeks follow-up visit (approximately 1 year)
f072	72 weeks follow-up visit (approximately 1 year, 5 months)
f096	96 weeks follow-up visit (approximately 2 years)
f120	120 weeks follow-up visit (approximately 2 years, 4 months)
f144	144 weeks follow-up visit (approximately 3 years)
f168	168 weeks follow-up visit (approximately 3 years, 3 months)
f192	192 weeks follow-up visit (approximately 4 years)
f216	216 weeks follow-up visit (approximately 4 years, 4 months)
f240	240 weeks follow-up visit (approximately 5 years)
n	Unscheduled follow-up visit

7.4. General guidelines for forms completion

Ink

- Forms should be completed in ink that is dark enough to photocopy legibly; do not use pencil or colors (e.g., red, green, light blue, or purple) that do not photocopy well

Changing responses on forms

- If an error is made on the form, correct the response by marking through the response with one or two lines and writing the correct response next to or above the original response. The staff member making the correction should put their initials and the date in the margin by the correction. A brief explanation for the change should also be written in the margin; e.g., 'error', 'pt changed mind', 'wrong response checked'.
- **Do not obliterate, erase, or white-out incorrect responses**
- The idea is to preserve an audit trail of the original response and subsequent changes to it

Multi-page forms

- The patient ID number should be written on the top right of every page of every form or MACO label applied in the space provided -- protect yourself against ineffective staples, lost paperclips, and photocopying mishaps

Miscellaneous

- All written responses should be printed legibly so the responses can be keyed to the database
- Do not use abbreviations or short-hand, medical jargon (i.e., bid, pt, rx, etc) that may not be easily understood or keyed in the written responses
- Numeric data should be recorded in the units prescribed on the form and to the level of precision (number of digits) indicated on the form
- All numbers should be right justified and leading and trailing zeroes should be recorded on the form where applicable (e.g., an age of 8 would be written and keyed as "08").
- All letter codes should be left justified with the remaining spaces left blank (e.g., a visit ID for the screening visit at baseline would be completed and keyed as "s").
- The clinical coordinator should review all responses for completeness and accuracy before signing off on the form
- Wherever possible, forms should be completed in real time, not retroactively. Interviews and questionnaires should be completed on the actual data form.
- The data on some forms, such as the Laboratory Results (LR) form, will be transcribed from worksheets or lab reports, but the visit date on the form should correspond to the date the form was initiated
- Staple relevant lab reports and worksheets to the data form; if your lab reports are transferred to you electronically, print a paper copy of the report and staple the copy to the GpR 2 data collection form.

Calculations

- All calculations should be performed using a calculator
- Values should be rounded according to the GpCRC data rounding rule (see section on data rounding rule, later in chapter 7.12 of this SOP)

7.5. Instruction box

- Each form includes an instruction box at the top of the first page. This instruction box gives the purpose of the form, when it should be completed, who administers the form, the respondent, and specific instructions for the form

7.6. Form skips, stops, caution ineligibility symbols

Skip pattern

- Form navigation (skip pattern) instructions are indicated in **boldface**. Skips are designated by an arrow from that response to a box with the number of the next item to be completed.

Stop sign

- Stops are indicated with an arrow from the response to a stop sign – instructions are given that must be fulfilled in order to continue with the form. For example, Form RG (Registration) asks if the patient has signed the consent form; if the response is "no", the form is stopped with the instructions that *'the consent form must be signed prior to continuing with screening'*.

Caution sign

- Items that require further review are indicated with an arrow from the response to a caution sign

Instructions are given regarding completion of the form when a caution is encountered

Ineligibility sign

- Ineligible conditions are designated by an arrow from the response to the symbol:

Other

- Other special instructions are indicated on the form in *italics*. Some examples are:
  – *check only one*: only one of the listed responses should be checked
  – *check all that apply*: one or more of the listed responses may be checked
  – *specify*: a response should be printed on the line(s) provided

7.7. Headers and footers

- Each page of each form includes headers and footers which identify the form and the patient. The top right of the first page of each form has a space to check when the form is keyed [( )keyed]. The top right of subsequent pages is reserved for the patient ID number. For example:

Gastroparesis Registry 2 Patient ID: __ _____

- The keyed box should be ed when the form is keyed; the person keying the form should also date and initial the form by the keyed box
- The patient ID number should be written on each page of the form (or apply a MACO label if directed)
- The footers identify the form name and study in the first line, the revision version, the date of the revision, full form name and the page numbers in the second line. For example:

Form RG GpR 2

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7.8. Key fields

- The first 7 items of each form include the key fields which identify the clinical center, patient, visit and study

A. Clinical center, patient and visit identification
1. Center ID: ___ _____
2. Patient ID: ___ _____
3. Patient code: ___ ___

4. Date form completed:___ -___-___-___
day mon year
5. Visit code: ___ _____
6. Form & revision: ___ ___

7. Study: Gastroparesis Registry 2 5

- The form and revision number will be printed on the forms in item 6; if a form is only used for one specific visit, the visit code will also be printed on the forms
- When a form revision affects the data that are collected, the form revision number and date will change; if this occurs, older revisions of that form should no longer be used for data collection
- If the form is revised without affecting the data collection - i.e., the wording of an item is

7.9. Missing data

- If a data item is missing and cannot be obtained when the form is completed or reviewed, write the appropriate code in the first left hand space of the empty data field:

  ? = data temporarily missing or inconsistent; to be collected or resolved in the near future; items keyed with a ? will need to be followed up on and resolved
  d = patient does not know the answer
  n = not applicable in this situation
  m = data missing
  r = patient refused

- When using any of the above codes, the entire data field does not need to be filled with the code (e.g., a missing height would be completed as m .).

- If data are missing on the form, an explanation for the missing values should be written on the form and keyed to the database in the General Comments section of the keying.

- It is very important to keep the number of missing data items at a minimum, especially at baseline, since many future papers will depend on having a good set of baseline values. If an item is missing at the time the form is filled out, but is expected to be collected in the near future, use a '?' rather than the 'm' code for the item on the form. The 'm' missing code is for items that are truly missing. Coordinators are discouraged from using the 'm' code as a way to get through the data entry checks and enroll a patient; the screening windows should be broad enough to allow you to collect all data within the allotted time window. Also, if the data system will not accept a value because it is out of range, please contact the SDRC, so we can make a determination as to whether the range checks need to be adjusted. In the meantime, use a '?' rather than an 'm' on the form. If there is a valid reason that a required baseline laboratory value is missing, please fax the Laboratory Results (LR) form to the SDRC along with the reason for the missing value.

7.10. Administrative sign off

- Each form contains a section for administrative sign off
- These items include the Clinical Coordinator PIN and signature and the date the form was reviewed.
- Depending on the form, they may also include the PIN and signature of other staff

7.11. Handling forms

Form duplication

- The individual forms and form sets specific to a particular visit are available on the GpCRC website here: https://jhuccs1.us/gpcrc/closed/forms/dataforms.htm
- You can print master copies from the website and then photocopy as needed or print as needed from the website– if you print copies ahead of time, do not print huge quantities as forms may be revised, especially in the early days of a study
- If a master copy gets frayed or faded, print a new master — always use clear copies for reproduction masters.

Form storage

- Forms for patients registered but not enrolled (ineligibles)in the Gastroparesis Registry 2 should be kept in a single folder in a locked room in a locked filing cabinet.
- Each patient who is enrolled in the Gastroparesis Registry 2 will have a patient file – either a notebook or file folder which is kept in a locked room or locked filing cabinet. The patient file should contain all Gastroparesis Registry 2 study documents for the patient – consents, forms, appointment schedule, labels, enrollment materials. The forms should be arranged in the notebook or folder chronologically by visit. Tabs can be used to separate the visits.

7.12. Data rounding rules

To round data, examine the digits following the last position required on the data form:

- If the first digit following the last data position required for the response is less than 5, leave the digit in the last data position required for the response unchanged, e.g., if you need to round to _._, then 4.73 rounds to 4.7 and 1.44 rounds to 1.4
- If the first digit following the last data position required for the response is 5 or more, round up the digit in the last data position required for the response, e.g., if you need to round to _._, then 4.78 rounds to 4.8 and 4.75 rounds to 4.8

When completing a calculation for the Gastroparesis Registry 2, apply the rounding rule only at the last step, when required to record a quantity on the Gastroparesis Registry 2 data form.

Examples for ST and WL forms:

- If the first digit following the last data position required for the response is less than 5, leave the digit in the last data position required for the response unchanged, e.g., if you need to round to _._ _ , then 1.4232 rounds to 1.42 and 1.443 rounds to 1.44

- If the first digit following the last data position required for the response is 5 or more, round up the digit in the last data position required for the response, e.g., if you need to round to _._ _ , then 1.4252 rounds to 1.43 and 4.756 rounds to 4.76

Data form response: **a.** _ . _ _ e+ _ _ _
Report says: 3.3086e + 010
Correct data form entry is: **a.** 3.31 e+ 010

7.13. Data audits and edits

Data audits

- The Scientific Data Research Center will serve as the site monitor
- The Scientific Data Research Center will conduct periodic data audits as a quality control measure
- Audits may be done by mail or on-site
- During an audit, the forms will be reviewed to see if they were completed and keyed correctly; the forms will also be checked against the source documents to be sure that values were transcribed correctly.

Source documents include but are not limited to:

- Gastric emptying scintigraphy reports
- Upper endoscopy reports
- Gastric imaging study reports
- Laboratory test result reports
- Medical records for archival information
- There are no source documents for questionnaires (the questionnaires are the original documents for the data collection)

Data edits

- Computerized data edits will be sent to the clinics periodically
- The data edits check for consistency and questionable values in the database.

Changes resulting from audits or edits

- Changes made to the forms as a result of an audit or an edit should be marked "per audit" or "per edit" and should be dated and initialed.

8. Quality assurance

8.1. Site visits

Purpose

- Conduct an audit of selected patient data
- Review documentation and procedures for the Gastroparesis Registry 2
- Tour facilities
- Discuss with clinical center personnel any problems that have occurred or that are expected to occur in conducting the study

The following regulatory and study documents should be available or accessible:

- IRB communications organized with original approval letters, revision approvals, annual renewals, serious adverse event forms, and any communications regarding concerns or special requests from clinical center review board
- Signed and dated consent forms for all participants including the date and signature of a witness
- Documents including Gastroparesis Registry 2 Protocol, PPMs, and SOPs
- Study forms for participants should be available for data audit

Participants

- At least two SDRC personnel will attend the site visit. One person from another Gastroparesis Registry 2 clinical center may also attend. Representatives from other resource centers associated with the GpCRC may also attend
- GpCRC certified staff from the clinical center

Reviewed during site visit

- IRB documentation
  - Original approval
  - Annual renewals (if applicable)
  - IRB submissions
  - Approval for updated consent forms and protocol

- Gastroparesis Registry 2 Documents
  - Directory
  - SOPs
  - Forms Book
  - PPMs
  - Protocol

- Enrollment and retention
  - Status
  - Recruitment and retention strategies

  - Problems
  - Losses to follow-up

- Personnel
  - Certification status
  - Personnel changes
  - Backup plans for personnel in event of absence

- Clinical management
  - Adverse event reporting procedures
  - Study procedures
  - Clinical center coordination
  - Scheduling
  - Clinical center concerns or problems

- Participant files
  - Security
  - Organization
  - Consent statements
  - Each patient's Gastroparesis Registry 2 forms and their source documents:
    - laboratory test results: clinical chemistries, ANA, HbAlc, hs-CRP, Vitamin D, etc
    - gastric emptying reports and scintigraphies on CD
    - upper endoscopy report
    - electrogastrogram with nutrient bar report
    - electrogastrogram with water load report
    - wireless motility capsule report
    - autonomic function testing report

- Specimen shipment
  - Comparison of specimens expected and received
  - Shipping procedures and problems
  - Shipping supplies

- Protocol performance
  - Protocol deviations

- Forms and data management
  - Monthly form status reports

  - Batch edits for form values
  - Source documentation
  - Data audit (selected patients)
  - Eligibility criteria
  - Adverse events
  - Death reports

- Previous site visit report
  - Action items follow-up
  - Data audit follow-up

Site visit follow-up

- A list of action items is compiled at the end of the site visit to identify items which require further action. The procedure for site visit action item follow-up is:
  - Action items will be listed at the end of the site visit report
  - Clinical centers will be required to respond to action items within 30 days of receipt of the site visit report. Responses should be in writing and sent to the SDRC.
  - The SDRC will be required to respond to the action items within 30 days of the completion of the site visit report. The SDRC will send a written report to the clinical center.

8.2. Performance monitoring

- The SDRC will generate enrollment reports that will provide a count of participants enrolled at each clinical center

- On approximately a monthly basis, the SDRC will generate reports summarizing the performance of all clinical centers. These reports will include information on enrollment and the percentage of expected visits for which documentation has been entered into the Gastroparesis Registry 2 data system. Also, for those visits for which data have been entered, the report will show the percentage of missed visits, the completeness of data collection, the timeliness of data entry, results of edits and audits and protocol deviations. Performance reports will be reviewed by the Steering Committee, and the Steering Committee will make decisions regarding actions to be taken in the event that a clinical center is performing poorly.

8.3. Data quality surveillance

General procedures

- Quality assurance of data accuracy will occur routinely through three main procedures: data entry checks, monthly checks for completeness and edits, and form audits

- In addition, detection of problems may occur during data analysis. For example, in preparing reports for Steering Committee meetings, problems may be discovered. Outliers and unusual variations or patterns in the data are examined and may reveal problems.

- Quality assurance of data analysis is achieved by independent replication of key analyses within the SDRC and review of reports by multiple individuals before distribution

Data entry checks

- The data system will contain checks during the data entry process of range, logic, and consistency of items within forms

- The data system will perform checks between forms to ensure that the same fields entered on different forms match

- A double data entry system will be used for all forms

Monthly check for completeness and edits

- On a monthly basis, SDRC will generate a database report of:
  - number of participants enrolled
  - missed visits
  - incomplete visits (missing or pending forms)
  - missed specimen collection or shipment
  - edits (see below)

- Edits are run on the database of the keyed forms monthly. Checks for missing, out-of-range, unusual and inconsistent values, cross-form checks and arithmetic errors are some of the types of checks performed. A listing of edits is sent to each clinical center for resolution. The clinical center must respond to each edit on the listing, make appropriate changes to the forms and database, compute documentation of each change, and file the documentation with the edited data collection form. Items that cannot be corrected (e.g., missing values, unusual measures) are entered into a database at the SDRC. These items are excluded from future edits. A hard copy of the edits, with each resolution should be kept in a notebook located at the clinical center.

8.3. Data quality surveillance

Forms audits

On a periodic (approximately monthly) basis the SDRC selects and requests copies of forms for specific participants be sent by each clinical center to the SDRC for auditing

- Audited forms are compared with the database; discrepancies are noted and queried
- Audited paper forms are also inspected for other problems, which are noted and queried
- Each clinical center will be required to resolve discrepancies from the audit report and fax the resolutions to the SDRC within 7 days
- The SDRC will generate a summary report of the audit discrepancies by clinical center to be distributed to all Gastroparesis Registry 2 centers
- Discrepancy rates over time by clinical center are reported to the Steering Committee