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DELIVERY VIA UNITED PARCEL SERVICE

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Re: Exploratory Study of the Gastrointestinal Environment in Patients with *Clostridium difficile*-Associated Disease (CDAD)

Dear Dr. Cox and Ms. Winkle:

Vancocin (vancomycin hydrochloride) capsules are approved to treat two serious and life-threatening infections of the gastrointestinal (GI) tract caused by the bacteria *Clostridium difficile* and *Staphylococcus aureus*. Most of the use of Vancocin capsules is in patients with *Clostridium difficile*-associated disease (CDAD). Vancocin capsules remain the only antibiotic approved by FDA for the treatment of this life-threatening condition.

As you know, the Office of Generic Drugs (OGD) has stated that waivers of *in vivo* bioequivalence (BE) testing can be requested in abbreviated new drug applications (ANDAs) for vancomycin hydrochloride capsules on the basis of *in vitro* dissolution testing. While FDA has not issued any specific Guidance regarding BE testing for Vancocin capsules, FDA's general Guidance on *in vitro* BE studies requires such studies to be suitably designed, and to be validated to correlate with *in vivo* effects¹.

Thus, the first step in an *in vitro* approach to BE is the development of an *in vitro* model. That model then must be correlated with important *in vivo* effects. We note that the *in vitro* model currently recommended by OGD is as follows²:

Apparatus:	USP Apparatus 1 (basket)
Rotation speed:	100 rpm
Medium:	0.1N HCl (or 0.1N HCl with NaCl at pH 1.2), pH 4.5 Acetate buffer, and pH 6.8 phosphate buffer
Volume:	900 mL
Temperature:	37°C

¹ Guidance, *Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations*, March 2003, at 20.

² OGD letter to Infinium Capital, March 1, 2006.

Sampling times: 5, 10, 15, 20, 25, 30, and 40 minutes or as needed for profile comparison”

OGD states that these *in vitro* test conditions significantly limit the risk of missing a bioINequivalent generic drug because they provide a close approximation of the *in vivo* environment in which the drug would be used. However, these conditions mimic the environment of the healthy human GI tract. Consequently, the assumptions and test conditions of this model have little relevance to the unhealthy GI tract of any patient that would receive Vancocin.

As mentioned, the primary use of Vancocin is in the treatment of CDAD. CDAD results in significant changes in the physiology of the GI tract including altered motility (ranging from ileus to hypermotility), pH and volume conditions, as well as the presence of various abnormal intraluminal constituents and inflammatory mediators. Consistent with FDA’s Guidance, an *in vitro* approach to BE for Vancocin capsules must mimic the GI environment in patients with CDAD. This, in turn, requires a better understanding of the diseased GI environment. Based on that understanding, per the Guidance, a “suitable” *in vitro* approach can be proposed and then “validated” to correlate with *in vivo* effects. Guidance at 20.

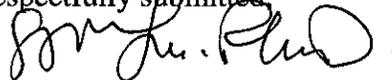
We have no information suggesting that OGD has undertaken any such effort. In the interests of patient safety, ViroPharma Incorporated has.

Specifically, we have initiated a study with the gastroenterology section of Temple University Hospital to compare the GI environment of patients with CDAD to a population of healthy subjects. A copy of the study protocol is attached. The specific aims of this study are to:

1. Compare the pH and temperature within the stomach, small intestine and colon in patients with CDAD and healthy volunteers. The FDA-approved Smartpill will be used to accomplish this objective.
2. Compare gastroenterocolonic motility in both study groups. To accomplish this, whole gut scintigraphy will be performed to define precisely gastric, small bowel, and colonic motility in patients experiencing CDAD.

Although we understand that FDA takes the position that we cannot discuss this with them, we would like to submit and discuss these data with the Agency once they are available. We believe that reviewing all available data is the best approach to ensuring patient safety. We again encourage FDA to follow its own Guidance and use only *in vitro* tests that are both suitably designed and validated to correlate with *in vivo* effects. We are prepared to assist FDA in these efforts in any way that we can.

Respectfully submitted,



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**Exploratory Study of the Gastrointestinal Environment in Patients with *Clostridium*
difficile-Associated Disease (CDAD)**

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1. OBJECTIVES

The purpose of this study is to examine the intestinal environment of patients with *C difficile*-associated diarrhea (CDAD) and compare the findings to a population of healthy subjects. These results are relevant in the medical management of patients with CDAD because there is little information on factors which may influence the bioavailability of vancomycin, a principle drug used in the treatment of CDAD.

Specific Aims of this study are to:

1. Compare the pH and temperature within the stomach, small intestine, and colon in both study groups. The FDA-approved Smartpill will be used to accomplish this objective.
2. Compare gastroenterocolonic motility in both study groups. To accomplish this aim whole gut scintigraphy will be performed.

2. BACKGROUND

Clostridium difficile (*C. difficile*) is an organism that is responsible for 15-20 percent of cases of antibiotic-associated diarrhea.(1,2) The association of *C. difficile* with antibiotics is due to their impact on the colonic microflora.(3,4) Older age and the patients' severity of illness are also important risk factors for *C. difficile* infection.(5-7) Infection with *C. difficile* can produce a wide range of clinical manifestations (otherwise known as *C. difficile*- associated diarrhea or CDAD) including asymptomatic carriage, mild to moderate diarrhea, and life threatening pseudomembranous colitis.(8)

In patients with mild CDAD, supportive care alone may be sufficient treatment. In more severe disease, specific therapy is required. Oral metronidazole (Flagyl, G.D. Searle, Chicago,

III) is the drug of choice in the treatment of CDAD and nearly all strains are inhibited by concentrations of 2 ug/ml or less.(9-11) Oral vancomycin capsules (Vancocin, ViroPharma Incorporated, Exton, PA) are the second-line agent for the treatment of CDAD.(10) Recently, with the emergence of an epidemic strain of *C. difficile* which causes severe disease, this paradigm may be shifting. More and more hospitals are using Vancocin earlier in CDAD management. Recently questions have arisen as to which factors may influence the bioavailability of Vancocin. This issue has become relevant recently as pharmaceutical companies are planning the development of generic equivalents to Vancocin. Because Vancocin's mechanism of action is as a topical antimicrobial, only in vitro solubility testing is required by the FDA for generic approval. In vivo comparison trials of Vancocin vs. generic vancomycin preparations are not required. However, the intestinal environment is complex and if in vitro testing is to be established as the standard for the determination of equivalence, factors which may influence solubility such core body temperature and pH need to be considered. In addition, Vancocin has proven effectiveness in CDAD even though colonic motility is suspected to be altered (rapid transit with only minimal surface contact time available). If this is confirmed by whole gut scintigraphy then the rate of solubility during in vitro testing as determined by standard testing, and accepted by the FDA, may need to be adjusted.

3. ELIGIBILITY CRITERIA

A. CDAD Case Patients

All inpatients at Temple University Hospital, regardless of gender or racial background, will be eligible for the study. The *C. difficile* – associated diarrhea patients must have both diarrhea and a positive *C. difficile* toxin by EIA in the stool. EIA results for all inpatients are available on a three times per week basis in our microbiology lab. Once it is established that patients have CDAD, they must meet the following eligibility criteria:

Inclusion Criteria

1. Age 18-75
2. Have no other potential etiology for diarrhea such as a malabsorptive disorder or inflammatory bowel disease.
3. Ability to voluntarily sign/date written informed consent to participate in this study.
4. Treated for CDAD for less than 24 hours prior to enrollment.
5. Able to safely swallow the study capsule and egg sandwich scintigraphic meal.

Exclusion Criteria

1. Pregnancy
2. Patients who underwent abdominal surgery within the previous 3 months
3. Estimated survival < 30 days
4. Use of medical devices such as pacemakers, infusion pumps, or insulin pumps
5. Patients with a history of gastric, small bowel, or colonic resection
6. Patients likely to be discharged within 5 days of enrollment.
7. Inability to verbally communicate

B. Healthy Subjects – healthy subjects will be recruited from a pool of healthy subjects known within the GI section. Patients who qualify for the study will initially sign consent and have the study reviewed as an outpatient. Prior to admission 5 patients will take 40 mg of esomeprazole (Nexium, Astra-Zeneca) for 5 days prior to admission to the Temple University Hospital GCRC. For the first 96 hours of the study they will stay in the GCRC of Temple University Hospital. On day 5 of the study they will be discharged from the GCRC and return to the hospital for outpatient visits if necessary.

Inclusion Criteria for Healthy Subjects

1. Age 18-75
2. Ability to voluntarily sign/date written informed consent to participate in this study.
3. No symptoms referable to the GI tract

Exclusion Criteria for Healthy Subjects

1. Pregnancy
2. Underwent abdominal surgery within the previous 3 months
3. Use of medical devices such as a pacemaker or insulin pump
4. History of gastric, small bowel, or colonic resection

Medication Restrictions for CDAD Patients and Healthy Controls

No medications that affect gastrointestinal motility will be permissible for 2 full days before the start of the study and during the 5 days of the study including but not limited to those drugs listed below.

A. Prokinetic agents

metoclopramide, tegaserod, domperidone, erythromycin

B. Narcotic analgesic agents

methadone, fentanyl, percocet, etc.

C. Anticholinergic agents for IBS

Hyoscyamine, dicyclomine

D. Medications for constipation

enemas, cathartics, polyethylene glycol solutions, lactulose, Milk of Magnesia, Mg citrate

E. 5HT3 antagonists

alosetron hydrochloride, ondansetron hydrochloride

F. Anti-diarrheal agents

attapulgate, donnagel, rheaban, bismuth subsalicylate, loperamide, and atropine diphenoxylate

4. STUDY PROTOCOL

A. CDAD Case Patients

We will enroll ten (10) eligible inpatients with diarrhea found to be positive for *C. difficile* confirmed by toxin EIA. After identification of a positive patient, the study coordinator will contact the patient after notification and approval by the patient's attending physician. To study covariates of interest, 5 of the patients must be on proton pump inhibitor therapy ≥ 5 days prior to study entry and 5 patients must be ≥ 60 years of age. Frequency matching will be used to fill the necessary quotas.

After obtaining informed consent the chart will be reviewed and the following data will be abstracted:

1. Age and gender of the patient
2. Place of residence prior to hospitalization (nursing home, skilled/rehab facility, home)

3. Comprehensive metabolic profile including serum albumin – if not performed in the previous 7 days then this will be requested by the investigators. If one or more has been performed, the values closest to the time of enrollment will be used.
4. Location in the hospital – ICU vs. floors
5. Oral temperature prior to starting therapy.
6. Number of episodes of vomiting in the previous 24 hours.

Patients will then complete a stool survey. Patients will estimate the number of stool passages in the prior 24 hours and assess the consistency using the following scale:

1. Solid – would not change shape if sitting in a waterless commode. May be hard or soft.
2. Loose – would conform to the shape of the commode
3. Watery – all liquid with minimal to no solid component

Patients will be asked if they are having abdominal discomfort and this will be graded on a 1 to 5 Lickert scale. The scale will be as follows:

1	2	3	4	5
No pain	Mild pain	Mild-moderate pain	moderate pain	severe pain

CDAD Disease Severity

Based on the above information only patients classified as having *moderate* CDAD will be enrolled. *Moderate* CDAD patients must satisfy all of the following criteria during the 24 hours prior to study entry:

- 3-6 loose or watery bowel movements per day
- Abdominal pain rated as 2-4
- ≤ 2 episodes of vomiting per day

Treatment: All patients will be treated for *C. difficile* colitis during the study using a regimen designated by their attending physician. The study protocol will specifically not interfere with treatment.

B. Healthy Subjects

Volunteers will undergo a complete physical exam including vital signs upon admission to the GCRC. Blood will be sent for comprehensive metabolic profile. Using frequency matching, as with CDAD patients, 5 subjects will be under the age of 60 years. As mentioned, 5 patients will be started on esomeprazole prior to admission to the GCRC.

Protocol Tests

Whole Gut Transit Scintigraphy (WGTS)

Within 24 hours of enrollment patients will begin whole gut transit scintigraphy. The purpose of this test will be to precisely define gastric, small bowel, and colonic motility in patients experiencing CDAD. WGTS is a 4-day test performed in the Nuclear Medicine department. Patients stop medications known to affect GI motility for 48 h before the test. A conventional dual isotope gastric emptying meal is used. The meal consists of two large scrambled eggs labeled with 500 μCi (18.5 MBq) of $^{99\text{m}}\text{Tc}$ sulfur colloid served between two pieces of toasted white bread. The subjects are asked to complete the meal ingestion with 5 min. Each subject then drinks 300 ml of water containing 125 μCi (4.6 MBq) of ^{111}In -DTPA.

Combined $^{99\text{m}}\text{Tc}$ and ^{111}In imaging begins immediately after consumption of the liquid and is repeated every 30 min for 2 h to record gastric emptying of liquids and solids. A large field of view camera (General Electric Medical Systems, Milwaukee, WI) with medium energy collimator and a nuclear medicine computer (Scientific Imaging, Denver, CO) are used.

The patient is positioned so that the entire abdomen is included in the field of view. The initial images from 0 to 120 min are upright, 128x128 byte mode, 30-s anterior and posterior images using a 140 Kev photopeak with a 20% window for 99 m-Tc. These are immediately followed by 60-s anterior and posterior images of the 111-In activity using the same matrix size but a 247 Kev photopeak and 20% window. Between all image sets, the subjects are permitted normal activity in the standing or sitting position.

After 120 minutes, sets of supine anterior and posterior, 60-s 128x128 byte mode images using the 247 Kev photopeak for 111-In with a 20% window are obtained every 30 min to characterize small bowel transit. Supine imaging is used to better define the terminal ileum (TI) and cecum-ascending colon (CAC). These are continued for up to 360 min or until all the abdominal activity seems to have passed through the small bowel and accumulated in the TI and/or CAC.

Supine anterior and posterior images of the 111-In activity in the colon are acquired at 24, 48, and 72 h after meal ingestion. These are 128X128 byte mode images acquired for 4 min using a 247 Kev photopeak with a 20% window. A cobalt marker is placed on the right iliac crest to serve as an anatomic reference.

Analysis of the gastric emptying data are performed as previously described. Images are recalled from computer disk and analyzed to determine gastric counts. Region of interests (ROIs) were manually drawn around the total stomach at each time interval. A geometric mean of the anterior and posterior values was used to correct for depth changes (geometric mean

counts = square root [anterior counts X [posterior counts]] and counts are corrected for radioisotope decay (12).

The average total small bowel counts between 2 and 6 h are used as the input value both for total counts available to fill the colon and to obtain the percentage in the TI-CAC at 6 h. Total small bowel indium-111 activity is calculated by subtracting any remaining gastric counts from counts from the entire abdomen. The percent (%) arrival of total small bowel activity at the terminal ileum-cecum/ascending colon (TI-CAC) at 6 h is used as an index of small bowel transit (12-14).

For the colonic images, counts are measured in regions of interest (ROI) corresponding to the ascending colon (region 1), hepatic flexure (region 2), transverse colon (region 3), splenic flexure (region 4), descending colon (region 5), and rectosigmoid (region 6) (13). Administered radioactivity that is unaccounted for in the images is assumed to have been eliminated with bowel movements and is assigned to region 7. The geometric center is calculated as the summation of counts at each region of interest as a fraction of the total counts, weighted by that region number. (13)

The WGTS studies are interpreted as a part of the daily routine clinical procedure performed in the Nuclear Medicine section. Normal values for gastric emptying, small bowel transit and colonic transit are established from results of prior studies in 28 normal volunteers (18 men and 10 women, mean age 26.2 yr, range 18-45 yr) (13). The mean \pm 2 SD are used as the normal range for the each test result. The normal upper limit of retained gastric activity

(mean \pm 2SD) for the test meal at Temple University is 50% at 2 h. Abnormal gastric emptying of solids was diagnosed if $> 50\%$ of technetium-99 m radioactivity is retained in the stomach at 2 h.

The accumulation of the In-111 DTPA activity in the TI-CAC at 360 min is used as an index of small bowel transit. Normal small bowel transit is for $>40\%$ accumulation of indium-111 radioactivity to have reached the terminal ileum and/or cecum-ascending colon at 6 h. Small bowel transit is diagnosed as delayed if $<40\%$ of total small bowel activity is accumulated in the TI-CAC at 6 h. Detection of rapid small bowel transit is based upon inspection of the In-111 DTPA images and a time of first visualization of activity in the CAC (cecal arrival time) at <90 min (mean $- 2$ SD).

For colonic transit, the normal values for the geometric center at 24 h is 2.0-7.0, at 48 h is 4.6-7.0, and at 72 h is 6.2-7.0. If the geometric center (GC) is <4.6 at 48 h, the study is terminated and a diagnosis of colonic inertia is made. (15). We use the term colonic inertia to imply slow transit throughout the colon (21). If the GC is ≥ 4.6 , the patient returns for additional CT imaging at 72 h. If GC is ≥ 4.6 at 48 h but <6.2 at 72 h, the scintigraphic “diagnosis” is functional rectosigmoid obstruction (FRSO).

SmartPill Capsule

During the time of WGTS we plan to perform simultaneous measurement of luminal pressure, temperature, and pH using the SmartPill. Fortunately these tests do not interfere with each other and can be performed simultaneously.

The SmartPill GI Monitoring System includes an ingestible capsule, a receiver, a receiver docking station and display software. The capsule houses sensors for pH, temperature, and pressure, and has the ability to transmit the sensed data at 434 MHz to a receiver worn by the subject. Shape and dimensions of the capsule (cylindrical, 26.8 mm long by 11.7 mm in diameter) are nearly identical to the ingestible imaging capsule from Given Imaging Ltd which is used clinically. The portable receiver worn by the subject receives and stores data; the MotiliGI software provides calculations and graphical displays to the physician. After activation and ingestion, the capsule signals are transmitted from within the GI tract and are captured by a receiving antenna incorporated into the receiver, which also provides an interface for data transmission to a PC as well as connections for battery charging. The capsule functions for at least 5 days after activation and has a pH range of 0.5 to 9 with an accuracy of ± 0.5 pH units. The pressure sensor has a pressure range of 0 to 350 mm Hg with an accuracy of 5 mmHg. The temperature sensor has a range of 25° to 49°C, with an accuracy of $\pm 0.8^\circ\text{C}$.

All study subjects will ingest the capsule with 120 cc of water after an overnight fast. The SmartPill capsule will be activated and calibrated. Intraluminal GI tract pH, pressure, temperature will be measured continuously with the SmartPill capsule. The capsule will be swallowed approximately 3 hours before the scintigraphic meal and recording will continue for 5 days. Six hours after the capsule has been ingested, all participants will undergo an abdominal x-ray to confirm that the capsule has completed transit through the upper GI tract and is present within the colonic lumen.

All study subjects will maintain a diary and will record times of bowel movements, meals, gastrointestinal symptoms (pain/discomfort, nausea, vomiting), and supine/sleeping times. Strenuous activities such as sit-ups, abdominal crunches, and prolonged aerobic activity (greater than 15 minutes) will be prohibited while the subject is being monitored. Subjects will resume their regular diet. The diary will contain the Bristol Stool Form Scale (Appendix I) which they will fill out for characterization of their stool caliber for each bowel movement during the entire 5 days of the study. The Bristol Stool Form Scale is a simple, patient-acceptable 7 point scale with apparently good correlation with intestinal transit. (16) Subjects will be instructed, if possible, to recover and return the SmartPill capsule. Bringing the capsule back confirms the capsule elimination. The investigators will dispose of the capsules according to standard hospital protocol for potentially infectious waste. Subjects will wear the SmartPill recorder until they have evacuated the SmartPill or for 5 days after which the study is downloaded. Twenty-one (21) days after capsule ingestion CDAD patients and healthy subjects will undergo a single abdominal x-ray to determine if the capsule spontaneously passed. CDAD patients who undergo an x-ray prior to day 21 for clinical purposes which demonstrates that the capsule has passed, will not need an x-ray at day 21. Subjects and patients who retrieve and return the capsule will also not need an x-ray.

5. RISKS AND BENEFITS

Risks of Venipuncture: There is potential for pain at the site. A hematoma may develop. Rarely there can be damage to venous, arterial, or neurologic structures.

Risks of the SmartPill: Risks of the ingestion and passage of the capsule through the GI tract are minimal. Currently, several other diagnostic capsules, the Given PillCam and the Heidelberg pH

capsule, are FDA released medical devices. The SmartPill is similar in size and shape to the Given capsule and, therefore, poses similar risk. The only reported complication has been non-passage of the Given capsule due to a stricture in patients with gastrointestinal disease where strictures can be a complication such as with inflammatory bowel disease. Such an event is rare and not documented in subjects with no significant GI surgical history – the types of individuals to be studied in this study. In the 435 healthy and 443 non-healthy individuals who have ingested the Heidelberg pH Capsule, there were no complications in the healthy subjects and one complication in the non-healthy subject. This complication involved a patient with pyloric stenosis, and the capsule was retrieved through endoscopy (17). In the 1712 non-healthy and 14 healthy individuals who ingested the Given Video Capsule, there were no complications in the healthy subjects and 25 complications in the non-healthy subjects. Eight subjects experienced delayed, but eventual spontaneous passage of the capsule. Six capsules failed to perform optimally but passed without complications. One capsule required retrieval through endoscopy due to small bowel stenosis and ten required surgical removal of the capsule due to strictures from Inflammatory Bowel Disease.

In a previous trial involving 148 subjects (61 gastroparetics and 87 healthy subjects), no serious adverse events occurred with the SmartPill GI Monitoring System. A total of ten adverse events were reported. Six of the ten were not related to the study device, and three were GI Symptom related adverse events. The remaining adverse event occurred in a gastroparetic patient who had ingested Citrucel, a bulk forming laxative, and subsequently developed a jelly-like, viscous mass that entrapped the capsule in the stomach and could not be retrieved by

endoscopy. Erythromycin IV was administered and the capsule subsequently emptied from the stomach.

The exit of the capsule from the GI tract will be confirmed for each subject. If the subject retrieves the SmartPill and returns it to the study site (which they will be encouraged to do), no further documentation will be needed. A single plain x-ray of the abdomen will be taken 21 days after ingestion if the CDAD patient or subject does not retrieve and return the capsule. There is a very small exposure to radiation related to this study x-ray. If the capsule has not passed in 21 days the principal investigator or other qualified gastroenterologist will clinically evaluate the study subject and intervene if necessary. Interventions could include use of a laxative to promote capsule transit through the GI tract, endoscopy to retrieve the capsule if within reach of an upper endoscope or colonoscope, or surgical consultation if the capsule appears to be lodged within the small intestine.

Other potential adverse events include technical issues with the function of the SmartPill GI Monitoring System and clinical events that may occur with subjects during the conduct of the study. Clinical adverse events possible include difficulty in device ingestion, vomiting, gastric sensations, and gastric distress. Technical issues that can occur include premature battery termination (failure) of either the capsule or receiver, signal loss within 6 hours or before the capsule emptying from the stomach, signal loss after 6 hours but before 48 hours, loss of capsular structural integrity, and failures to receiver or capsule electronics. Subjects ingesting the capsule or the meal may have nausea, vomiting, aspiration of capsule or meal, abdominal pain, diarrhea or constipation.

Risks of WGTS: The Total Effective Radiation Dose Equivalent (TEDE) for each scintigraphic test is 66 millirem, with a dose of 1165 millirad to the lower large intestine as the highest radiation dose to an internal organ. For the entire study the TEDE would be less than what an individual living in the United States receives from total average natural background radiation in a year. There is a potential for a reaction in patients allergic to egg products, however this will be screened for prior to study entry.

Risks of Esomeprazole: Esomeprazole is used widely for the treatment of acid-peptic diseases. Side-effects occurring in more than 2% of patients in clinical trials include bloating, flatulence, cramps, and diarrhea.

6. DATA COLLECTION AND STATISTICS

All data will be recorded and analyzed in SPSS v. 13.0 (SPSS, Inc., Chicago, Ill). Continuous variables will be compared using t-tests and, if not normally distributed, will be analyzed using non-parametric techniques. Discrete variables will be analyzed using Pearson chi-square or the Fisher's Exact test. To compare multiple groups one-way analysis of covariance will be used or the Kruskal-Wallis test depending on data distribution. 95% confidence intervals will be presented as needed. A p value $\leq .05$ will be considered significant and all comparisons will be considered 2-tailed.

7. MEDICAL RADIATION SUBCOMMITTEE APPROVAL – approval pending

8. IND/IDE NUMBER – N/A

9. BIBLIOGRAPHY

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Appendix I. Bristol Stool Form Scale

THE BRISTOL STOOL FORM SCALE		
Type 1		Separate hard lumps, like nuts
Type 2		Sausage-like but lumpy
Type 3		Like a sausage but with cracks in the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces

Bristol stool form scale is a general measure of stool consistency or form. Using this scale, you can help your physician sort out patterns or changes in bowel habit. Remember, this is intended as a general, not exact, measure. Use this guide to complete your diary and worksheet, and share the information with your physician.