SUMMARY OF SAFETY AND PROBABLE BENEFIT

I. GENERAL INFORMATION

Device Generic Name: Device, Fecal Incontinence, Implanted

Device Trade Name: Acticon Neosphincter (originally called the Artificial Bowel Sphincter Prosthesis)

Applicant's Name and Address:
American Medical Systems, Inc.
10700 Bren Road West
Minnetonka, Minnesota 55343
612-933-4666

Humanitarian Device Exemption (HDE) Number: H990003

Date of Humanitarian Use Device Designation: December 22, 1998
HUD 98-0028

Date of Panel Recommendation:
The Acticon Neosphincter was not submitted to the Gastroenterology and Urology Devices panel for review. (Refer to Section XI for discussion)

Date of Good Manufacturing Practices Inspection: The last FDA GMP/QS inspection was conducted on March 12, 1999. Although the firm was issued an FDA 483, the deviations are not considered significant enough to re-inspect for approval of the HDE. In addition, the contract sterilization facilities, Quality Sterilization Services and Griffith Micro Science, have both been inspected on March 1, 1999 and November 5, 1997, respectively.

Date of Notice of Approval to Applicant: SEP 20 1999

II. INDICATIONS FOR USE

The Acticon Neosphincter is an implantable device used to treat severe fecal incontinence in post-pubescent males and females who have failed, or are not candidates for, less invasive forms of restorative therapy. It is intended to mimic the natural process of bowel control and bowel movement.

III. DEVICE DESCRIPTION

The Acticon Neosphincter is an implantable, fluid filled, solid silicone elastomer device. The prosthesis consists of three interconnected components: an occlusive cuff, a pressure-regulating balloon and a control pump with a septum. The three components are connected with kink-resistant tubing. The device simulates normal anal sphincter function by allowing the anal canal to open at the control of the patient. In both males and females, the occlusive cuff is implanted around a segment of the anal canal. The cuff occludes the anal canal by applying pressure circumferentially.

To evacuate the bowel, the patient squeezes and releases the pump mechanism, located in the labium or scrotum, several times to move fluid from the cuff to the pressure-regulating balloon implanted in the abdomen. This movement of fluid empties and collapses the cuff, resulting in the release of the compressive force around the anal canal. Residual pressure within the balloon allows fluid to flow back into the cuff, automatically refilling the cuff within a few minutes. The balloon maintains pressure in the occlusive cuff.

IV. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

Contraindications

1. This device is contraindicated in patients whom the physician determines to be poor candidates for surgical procedures and/or anesthesia due to physical or mental conditions.

2. This device is contraindicated in patients with fecal incontinence complicated by an irreversibly obstructed proximal segment of bowel.

Warnings

1. Patients with urinary tract or gastrointestinal infections, diabetes, spinal cord injuries, open sores, or skin infections in the region of the surgery have an increased risk of infection associated with a prosthesis. Appropriate measures should be taken to reduce the likelihood of infection.

   Infection that fails to respond to antibiotic therapy may result in removal of the prosthesis. Infection followed by explantation of the device may result in scarring that may make subsequent reimplantation more difficult.

2. Erosion may be caused by infection, pressure on the tissue, improper cuff sizing, improper balloon selection, tissue damage, and component misplacement. The cuff may erode around the anal canal or the control pump may erode through the scrotal or labial skin. The pressure-regulating balloon can erode into the bladder.

Failure to evaluate and promptly treat the erosion may result in a substantial worsening of the condition leading to infection and/or loss of tissue.

3. This device is composed of a number of materials, including solid silicone elastomers. This device does not contain silicone gel. Scientific literature has included reports of adverse events in patients with implantable silicone devices. These adverse events, as reported, suggest allergic-like reactions or autoimmune-like symptoms. No causal relationship has been established between these events and solid silicone elastomer.

4. Surgical, physical, psychological, or mechanical complications, if they occur, may necessitate revision or removal of the prosthesis. Removal of the device without timely reimplantation of a new device may complicate subsequent reimplantation. The timing of reimplantation should be determined by the treating physician based on the patient's medical condition and history.

5. Receptive anal intercourse may damage the occlusive cuff and is not recommended for patients implanted with this prosthesis.

Precautions

Patient Related

1. Patient selection requires thorough preoperative consultation and evaluation by the physician.

2. Patients should be counseled in order to have a realistic expectation of the physical, psychological, and functional outcome of the implantation of an Acticon Neosphincter. Although the prosthesis is designed to restore bowel control, some patients continue to have a degree of incontinence after this procedure.

3. Patients may experience pain when the device is activated, in the postoperative period, and during periods of initial use. Cases of chronic pain associated with the device have been reported. Pain with a severity or duration beyond that which is expected may require medical or surgical intervention. Patients should be counseled on expected postoperative pain including severity and duration.

4. Tissue fibrosis or previous surgery in the area of the implant may preclude implantation of an occlusive cuff at the anal canal.

5. Acute pathological conditions of the bowel, e.g. diarrhea or constipation, can interfere with proper functioning of the device and may require the use of external pads or manipulations to assist defecation.

6. Any progressively degenerative disease, e.g., multiple sclerosis, may limit the future usefulness of the implanted prosthesis as a treatment of the patient's fecal incontinence.

7. Adequate manual dexterity, strength, and motivation are required for proper use of the device.

8. Trauma or injury to the pelvic, perineal or abdominal areas, such as impact injuries associated with sports, can result in damage to the implanted device and/or surrounding tissues. This damage may result in the malfunction of the device and may necessitate surgical correction including replacement of the prosthesis. The physician should advise patients of these possibilities and warn them to avoid trauma to these areas.

9. If a radiopaque solution is used instead of sterile isotonic saline to fill the device, ensure the patient is not allergic to the radiopaque solution.

10. Vaginal delivery of children may interfere with future proper functioning of the occlusive cuff.

Surgery Related

1. Improper cuff sizing, improper balloon selection, or other causes may result in tissue erosion, migration of components, or continued incontinence.

2. Component migration can occur if the cuff is sized improperly, if the pump or balloon are not positioned correctly, or if the tubing lengths are incorrect. Migration can result in, pain, complications, device malfunction and surgical revision.

3. Unsuccessful outcomes may result from improper surgical technique, anatomical misplacement of components, improper sizing and/or filling of components.

4. Although reinforced tubing has been designed to be more resistant to tubing kinks, tubing kinks may still result from tailoring the connecting tubing to an improper length during the implant procedure.

Device Related

1. As with any biomedical prosthesis this device is subject to wear and eventual failure over time. It is not feasible to predict how long the implanted prosthesis will function in a particular patient.

2. If the deactivation valve is closed when the cuff is inflated, fluid cannot transfer from the cuff to the balloon and sustained fecal obstruction may arise as a result:

    a) In the event of large pressures within the bowel, automatic pressure relief that normally occurs with the device would be prevented. The fecal obstruction can be relieved by cycling the device.

b) Cycling the device may be difficult if deactivation occurs when the pump bulb is deflated. If unable to cycle the prosthesis, squeezing the sides adjacent to the deactivation button will allow fluid to fill the pump bulb and then the pump can be cycled normally.

c) Release of the deactivation valve may require greater pressure than that used to cycle the device.

3. Use caution when passing any instrument through the anal canal. For certain procedures, e.g., anal ultrasound or colonoscopy, first deflate the cuff then deactivate the device prior to passing any instrument through the anal canal.

4. System pressure changes may occur over time.

V. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse effects data have been collected during two clinical studies. Adverse events reported in the first clinical study conducted in the United States (Investigational Device Exemption No. G880037) are presented in Table 1.

Table 1: Adverse Events Reported for G880037 (n=21)

Adverse Events	# of Patients
Infection	5
Mechanical	5*
Pain	2

*Two patients experienced multiple mechanical complications.

Adverse events reported as of December 31, 1999 in the ongoing study (IDE No. G960116) are presented in Table 2.

Table 2: AMS Acticon Neosphincter Adverse Device Effects (n=50)

Adverse Events	**# of Events**
Infection	18
Pain	14
Constipation	11
Impaction	8
Erosion	7
Surgical perforation	4
Wound dehiscence (separation)	4
Erythema	4
Difficult evacuation	3
Fecal incontinence	3
Difficult activation	2
Malposition	2
Fever	2
Hematoma	2
Wound drainage	1
Seroma	1
Edema	1
Other [1]	15

[1] Other events include: Report of fullness with difficulty sitting, slight discomfort at night, patient reports need to "pump" 60 times to open system, vaginal tear (5mm), insufficient cuff pressure, few episodes of stool leakage, unable to pump device, excessive bleeding during implant, urinary retention, discomfort cycling pump, perianal itching, eccymosis, drainage from posterior perineal area, patient cannot access pump secondary to arthritis in finger, and report of red incision.

Adverse events related to the Acticon Neosphincter fall into two basic categories mechanical/component failure, and patient/implant-related failure.

Mechanical failures include types of problems that are directly related to the device's failure to function correctly. Examples of this type of adverse event include the following:

- Fluid loss can result in the cuff only partially filling or not filling at all if sufficient fluid is lost. Fluid loss has been associated with damage to one of the silicone components of the system, damage to the system such as perforation of the device, and wear of the cuff.
- Pump failure can result in the device not functioning. Balloon problems range from leaks to decreases in the pressure of the balloon which may result in incontinence.
- Cuff failure can result in the device not functioning. Cuff problems are primarily related to leaks caused by wear, fatigue, or intra-operative damage.

Patient/implant related failure include the types of events that can be the result of the implantation surgery, or the patient's response to the presence of the device. The types of events that have been reported with use of the Acticon prosthesis include the following:

- Erosion and migration involve the movement of the prosthesis within the body or from the inside to the outside of the body.
- Implantation of the device involves the risk of infection. Infection has been the most serious of the adverse events reported to date.
- Pain is an expected occurrence; however, some patients experience an unacceptable amount of pain. Pain may be caused by the misplacement or missizing of the components, undiagnosed problems such as infection, erosion, migration, or factors not related to the implant.
- Patient dissatisfaction may be related to unrealistic expectations of the results, or to patient difficulty operating the device.
- Fibrous capsule formation of a silicone prosthesis is a normal physiologic process. This capsule is usually inconsequential to the functioning of the device. It is thought that the presence of the capsule will frequently support the prosthesis allowing it to function without migration or displacement.
- Iatrogenic complications result from poor surgical technique or lack of adequate care during surgery. These may include mechanical failure, perforation, cosmetic problems, or functional difficulties.
- Other reported complications associated with use of the Acticon Neosphincter include evacuation difficulties such as impaction or incontinence.

Each of these adverse events, except for fibrous capsule formation has necessitated removal of the device in some patients, with or without reimplantation.

Other Potential Risks

Risks associated with implantable bowel sphincters or their materials that have been reported in the medical literature but did not occur during the prospective studies include tubing kinks, tubing leaks, cuff tab tearing, and scrotal adhesion.

VI. ALTERNATIVE PRACTICES AND TREATMENTS

Fecal incontinence is the involuntary loss of flatus, liquid, or solid stool and presents in a range of severity. Although it is considered a benign disorder, severe fecal incontinence is a distressing and socially isolating medical condition that can have a devastating effect on a person's working life, social life, and emotional well being. Individuals, who suffer from the condition, often alter their lifestyle to minimize the likelihood of bowel accidents in public places. Over time, this can result in progressive social isolation and work incapacity. The vast majority of cases are mild to moderate and can be managed or resolved with medical interventions such as pharmacological therapy, biofeedback training and

dietary management. For some patients with a sphincter defect, surgical procedures such as sphincteroplasty, postanal repair, or total pelvic floor repair may be attempted.

For a limited number of individuals with severe fecal incontinence (the involuntary loss of solid stool or liquid stool on a weekly or more frequent basis) who have failed medical interventions and are not candidates for sphincter repair, the choices are limited.

An alternative surgical procedure, adynamic muscle transposition, may be used in patients where the anal sphincter is either denervated or anatomically absent. It involves the transposition of a muscle, usually the gracilis or gluteus maximus, to create a barrier to the passage of stool. The procedure, first introduced in the 1950s, has had limited success and is rarely used in current practice.

Finally, some patients are faced with a choice of a permanent ostomy, a surgically created passage to allow bodily wastes to be expelled from the body through the abdominal wall, or life-long management of incontinence with pads or diapers. Neither of these alternatives provides the kind of normalcy with respect to bowel function and fecal continence that patients desire.

VII. MARKETING HISTORY

Foreign Market Introduction
A CE mark for the Acticon was received in May of 1996. Limited marketing of the Acticon Neosphincter in select European countries and Australia began in July of 1996. During this limited launch 62 patients were implanted with the Acticon prosthesis. Based on these results, American Medical Systems, Inc., introduced the device outside of the United States in 1998. The Acticon Neosphincter has not been withdrawn from marketing for any reason related to safety or lack of benefit.

VIII. SUMMARY OF PRE-CLINICAL TESTING

Mechanical Testing
A risk analysis, including a failure modes and effects analysis (FMEA), was used to identify safety and reliability attributes considered applicable to the Acticon Neosphincter or its components. Bench testing was performed to characterize the device components attributes and functions. All bench testing was performed on finished, sterilized devices or components.

Performance Characteristics Testing
Performance characteristics of the device were evaluated by testing samples for the following performance characteristics:

- Squeeze force versus fluid displacement
- Fluid displacement per pump stroke
- Prevention of spontaneous inflation or deflation
- Pump output pressure produced by pump squeeze force
- Pump bulb refill time
- Pump deactivation force and activation pressure
- Pump valve leakage and maximum back pressure
- Tubing kink resistance
- Balloon capacity
- Cuff expansion and maximum pressure

Performance testing demonstrated acceptable prosthesis or component performance.

Reliability Testing
Device reliability attributes were evaluated in bench testing by subjecting samples to representative *in-vivo* conditions, where possible, and to a number of uses likely to exceed the number of uses over the estimated life of the device, for the following reliability attributes:

- Cuff deflation/inflation cycling
- Pump cycling
- Balloon inflation/deflation cycling
- Pump cycling and septum access
- Cuff fold wear resistance life cycling
- Prosthesis adhesive bond reliability

Reliability testing demonstrated acceptable prosthesis or component performance.

Component Strength Testing
Device strength attributes were evaluated by subjecting test samples to representative *in vivo* conditions, where possible, and to a number of uses likely to exceed the number of uses over the estimated life of the prosthesis for the following strength attributes:

- Cuff maximum pressure and expansion
- Cuff leakage or unbuckling under pressure
- Connector strength
- Tubing burst/leak pressure
- Connector/component leak pressure
- Subassembly bond strength
- Prosthesis material strength

Component strength testing demonstrated acceptable prosthesis or component performance.

Materials Safety and Toxicology Testing

The safety of the materials used in the Acticon Neosphincter were evaluated through a testing program that included chemical analysis of exhaustive extracts, infrared spectral analysis of surfaces having direct tissue contact, and a series of *in vitro* and *in vivo* biological studies. All biological nonclinical laboratory studies were conducted in compliance with the Good Laboratory Practice Regulations.

Chemical Analysis of Extractives

Testing was conducted on the AMS Model 800 Artificial Urinary Sphincter (AUS) and the AMS Dynaflex inflatable penile prosthesis because these devices use the identical materials and the design of the AUS is almost identical to the Acticon Neosphincter. Extractive analysis identified compounds that may leach from the Acticon Neosphincter and quantified the potential patient exposure to each extractive. These include polydimethylsiloxanes of varying molecular weights (296 to >150,000 daltons), water soluble silica (silicic acid), formaldehyde, and traces of platinum and tin catalysts. For each extractable compound known to produce some toxic or irritant effect(s) the total potential exposure from an Acticon Neosphincter was shown to be well below the exposures required to produce any observed effect based on published toxicity data for each extractive. Exposure to leachable components at the concentrations present in the Acticon Neosphincter was determined not to be a significant health risk for patients.

Infrared Spectra Surface Analysis

To document the principle chemical composition for each device component which could have direct tissue contact, infrared spectra of the outer device surfaces were collected using attenuated total reflectance Fourier transform infrared spectroscopy. Testing showed that only polydimethylsiloxane has direct tissue contact. No other materials or unusual spectral features were detected.

Biological Safety Tests

Finished products were subject to the complete spectrum of biological tests cited in the "Guidance for Manufacturers of Silicone Devices Affected by Withdrawal of Dow Corning Silastic Materials (July 6, 1993)." This included tests for *in vitro* cytotoxicity, acute systemic toxicity, intracutaneous irritation, sensitization, direct tissue contact (intramuscular implantation for 14 and 90 days) and three genetic toxicity tests.

Studies were also conducted in which substantial amounts of ground silicone elastomer were implanted subcutaneously in Sprague Dawley rats. The effects of the implanted material on the host system was evaluated and included an acute pharmacokinetic study (distribution and excretion of silicones), testing for effects on the immunological system (immunomodulation and adjuvanticity), and studies for sub-chronic and chronic toxicity, reproductive effects, and oncogenicity.

Test results indicate that the materials used in the Acticon Neosphincter do not produce localized or systemic toxic effects when implanted.

Shelf Life Testing
Shelf life was determined to be equivalent to the shelf life of AMS's inflatable penile prostheses products (700, Ultrex, CX, Ambicor) and the AMS 800 artificial urinary sphincter. The three product lines use very similar materials for device construction and use the same materials for packaging. An accelerated aging study was performed on the package configuration and showed the packaging would provide physical protection and a sterile barrier for a 5-year shelf life with a 2-year safety margin. The Acticon Neosphincter is labeled with a "use before date" which is 5 years from the date of manufacture.

IX. SUMMARY OF CLINICAL STUDIES

Two clinical studies were conducted in the United States on this device. The first study (IDE No. G880037) began in August 1988 and was closed in April of 1995. In the second study (IDE No. G960116) patient enrollment began in July 1996 and was ongoing at the time of HDE approval. In addition, the Acticon Neosphincter is currently available in Europe and several other countries.

G880037 was a multi-center, prospective study of the Artificial Bowel Sphincter (ABS), an earlier version of the Acticon Neosphincter. Patients selected for the study demonstrated severe fecal incontinence unresponsive or unlikely to respond to accepted medical or surgical alternatives. Patients with ongoing inflammatory bowel disease or active pelvic sepsis were excluded.

A total of 21 patients were enrolled at 3 sites. Patients enrolled included 10 males and 11 females ranging from 15 to 68 years of age. The reported causes of incontinence are provided in Table 3.

Table 3: Etiology of Incontinence

Etiology of Incontinence	**Total Number**	**Percent**
Major Trauma	6	28.6
Birthing Injury	5	23.8
Imperforate Anus	3	14.2
Spinal Cord Tumor	2	9.5
Laminectomies	2	9.5
Spina Bifida	1	4.8
Myasthenia Gravis	1	4.8
Prolapsed Intervertebral Disc	1	4.8
Total Patients	**21**	**100**

Seven (7) patients had a stoma at the time of enrollment, 5 patients had a temporary stoma created at the time of device implantation (it was believed this

would decrease the risk of infection). Patients were followed for periods ranging from 6 to 76 months. Functional outcomes were determined based on water perfusion and manometry testing and continence diaries. The investigators reported that 64% of patients achieved complete continence to liquid and solid stool. An additional 18% of patients achieved continence to solid stool but experienced occasional leakage of liquid stool.

Complications included infection (5 patients), mechanical malfunctions (5 patients, with 2 patients having multiple problems), and pain (2 patients). Of the 5 patients who developed an infection, 3 underwent permanent explantation of the device, 1 had an explantation with replacement of the device, and in 1 patient the infection resolved with antibiotics. All 5 patients who experienced mechanical problems underwent revision procedures. Three (3) of these patients achieved an acceptable level of continence but the other 2 underwent device removal. The 2 patients with pain had resolution of their pain.

Of the 12 patients who experienced complications during the study, 7 were successfully treated but 5 patients (24%) required permanent device removal. For the remaining 16 patients, 13 (82%) demonstrated either improvement or resolution of their fecal incontinence.

Study Conclusions (G880037)
Based on the promising results of this study the sponsor conducted additional product development, which included modifications to the device, in preparation for an expanded and modified clinical trial.

Differences between the ABS and the modified device, the Acticon Neosphincter, are (1) a longer cuff, (2) a larger (40cc) pressure regulating balloon used in the Acticon, and (3) a septum port added to the control pump for the Acticon.

G960116 was a multi-center, prospective, non-randomized, clinical trial which was on-going at the time of HDE approval. Each patient was his or her own control utilizing defined primary and secondary endpoints. Post-pubescent patients who had severe fecal incontinence without regard to etiology are considered for implantation of the device. To be enrolled in the study patients must have had fecal incontinence for at least six months, have tried at least one non-surgical treatment prior to enrollment, and have an Incontinence Score of ≥88 according to the Fecal Incontinence Scoring System. In addition, patients with ongoing inflammatory bowel disease or active pelvic sepsis are excluded.

As of December 31, 1998, 50 patients had been enrolled at the 11 sites in the United States and Canada. Forty-seven (47) patients had been implanted with the device, 10 males and 37 females. The average age was 47 years (range 18 to 81). The causes of the patients' incontinence is shown in Table 4.

Table 4: Etiology of Fecal Incontinence

Etiology	**Total Number**	**Percent**
Neurological	17	36.2%
Anorectal Trauma	8	17%
Obstetrical Trauma	9	19.1%
Congenital Abnormality	10	21.3%
Other [1]	3	6.4%
Total Patients	**47**	**100%**
[1]other includes rectal prolapse (2) and musculoskeletal (1)		

Safety

No deaths, life-threatening conditions, or unanticipated effects were reported.

Adverse Events

There were 122 adverse events reported, 20 of which were non-device related (e.g., diarrhea, chest pain, depression, COPD). One hundred and two (102) device-related events occurred in 38 patients (76%). The types of events and methods of intervention for all device-related events are provided in Table 7.

Table 7: Treatment for Adverse Events

			Methods of Intervention[3]			
Event Type	**Number of Patients[1]**	**Number of Events[2]**	**None Required**	**Medication**	**Surgery**	**Other[4]**
Constipation	6	11		11		2
Difficult Activation	2	2				2
Difficult Evacuation	3	3	1	2		1
Edema	1	1	1			
Erosion	7	7		2	7	1
Erythema	3	4	1	3		1
Fecal Incontinence	2	3			3	
Fever	2	2		2		
Hematoma	2	2	1			1
Impaction	8	8	1	1	1	5
Infection	14	18		7	15	3
Malposition	2	2			2	
Pain	10	14	1	7	2	7
Seroma	1	1				1
Surgical Perforation	4	4			4	
Wound Dehiscence	4	4	2	1		1
Wound Drainage	1	1				1
Other[5]	9	15	3	2	2	9

[1] Patients may have had more than one type of event.
[2] Patients may have had more than one event of the same type.
[3] There may have been more than one type of intervention for each event, and patients may have multiple events that are treated with the same intervention.
[4] Examples are enemas, wound packing/cleaning, and observation.
[5] Other events include report of fullness with difficulty sitting, slight discomfort at night, necessity to "pump" 60 times to open system, vaginal tear (5mm), insufficient cuff pressure, episodes of stool leakage, inability to pump device, excessive bleeding during implant, urinary retention, discomfort cycling pump, perianal itching, ecchymosis, drainage from posterior perineal area, patient inability to access pump secondary to arthritis in finger, and report of red incision.

- Surgical complications were encountered during 4 implantation procedures. Two (2) of the 4 cases were aborted due to inadvertent surgical perforation of either the rectum or the vagina. Intraoperative repair was performed with no further complications. Surgical perforation of the rectum occurred in the other

2 cases. In each case, the perforation was repaired intraoperatively and the implantation procedure proceeded.

- The majority of adverse events occurred as post-surgical complications. Approximately half of the events required medical intervention or resolved with no intervention. The remaining clinically significant events resulted in the need for revision surgery. Revision surgery is defined as any surgical procedure involving the Acticon Prosthesis, subsequent to the original implant procedure. Nineteen (19) patients experienced events that required surgical intervention. In 4 patients, surgical intervention was completed without device revision. Of the 38 patients who experienced an adverse device event, 15 patients have undergone 23 device revisions. Infection is the most frequent reason for revision with a total of 11 patients undergoing revision because of infection. Revision surgery for erosion was necessary in 7 patients, with infection being present in all but 1 of these patients. Revision surgery for malposition occurred in 2 patients, 1 of which also experienced infection and erosion. Recurring incontinence occurred in 2 patients.

Table 8: Reason for Revision by Patient

		Reason for Revision*					
Patient	# of Surgeries	Infection	Erosion	Malposition	Pain	Fecal incontinence	Surgical perforation
1	2	1					
2	1	1	1				
3	3	1	1				
4	2	1					
5	1	1	1				
6	2					2	
7	2			1		1	
8	1	1					
9	2	2	1	1			
10	1	1	1		1		
11	1	1	1		1		
12	1	1					
13	1	1					
14	2		1				
15	1						1
Total	23	12	7	2	2	3	1

*A single adverse event may require several surgeries for resolution.

- Of the 50 patients where an implant was attempted, 2 cases were aborted during the implant procedure due to perforation during surgery (rectal perforation and vaginal perforation). In a third patient, the cuff length was too short and the cuff sizer was left in place leading to infection followed by removal of the cuff sizer without implantation. A fourth patient had a cuff

sizer left in place at the time of surgery. This patient was subsequently implanted with a longer cuff.

- Of 50 patients enrolled into the study, 12 patients have not had any device related events reported (24%). For the other 38 patients, 19 patients experienced an adverse device event that did not require surgical intervention. Fifteen (15) patients (30%) required a device revision and 4 patients (8%) had the implantation procedure aborted.

Effectiveness

Endpoints

The Fecal Incontinence Scoring System (FISS) is the primary endpoint utilized to assess the effectiveness of the Acticon Prosthesis. The FISS is based on responses to a self-administered questionnaire regarding the frequency of the patient's symptoms. A clinically significant improvement is a reduction of ≥24 in scores from pre-implant to follow-up.

Table 5: Fecal Incontinence (FI) Score Definitions

FI Value	**Definition**
0-60	Continent to solid and liquids
61-72	Incontinent < monthly
73-84	Incontinent > monthly
85-96	Incontinent >weekly
97-108	Incontinent daily
109-120	Incontinent >daily

Secondary endpoints were also evaluated pre- and post-implantation to assess the safety, effectiveness and impact on patient quality of life with the Acticon Neosphincter. These endpoints include anorectal manometry, two Quality of Life Questionnaires, and adverse device effects.

Results

Device implantation was attempted in 50 patients, but in 3 patients device implantation was aborted (1 cuff sizer was left in place and later explanted, 1 rectal perforation, and 1 vaginal perforation). Discussion of the effectiveness of the device is based on the 47 patients, but analysis of safety is on the 50 patients. Of the 47 patients implanted with the device, 32 have had the device activated. Five (5) patients have had the device permanently explanted. Three (3) patients experienced erosion of a device component with or without concurrent infection and the other 2 patients had infections. Another 5 patients had undergone explantation of the device and may have undergone reimplantation at a later date. These 5 patients were still enrolled in the study at the time of HDE approval.

Table 6: Follow-up Compliance

	Activation	6 Months	1 Year
	Number of Patients		
Follow-up performed	32	13	6
Due for follow-up	2	4	1
Missed follow-up	1	3	2
Not eligible for follow-up	6	17	28
Explanted, not to be re-implanted	3	5	5
Explanted, possibly to be re-implanted	3	5	5
Total Patients	**47**	**47**	**47**

- Pre-implant fecal incontinence scores were not attainable from 7 patients due to a pre-existing stoma. The mean pre-implant score for patients without a pre-existing stoma was 108 (n=40, range 71-120). The average patient enrolled in the study was incontinent, at least daily, prior to Acticon Neosphincter implantation.

- Six-month post-device-activation fecal incontinence scores were collected from 13 patients with a mean score of 44 (range 0-108) for a mean reduction of 67 points in the fecal incontinence score. The 67-point drop signifies that patients, on average, went from complete incontinence at least daily to complete continence to solid and liquid stool at 6 month post-activation. Twelve (12) of the 13 patients with 6-month follow-up had a successful outcome. The remaining patient had good closure of the anal canal clinically and responded that the device was "manageable; no changes needed" to the question of patient satisfaction.

- Twelve-month post-device-activation fecal incontinence scores were collected from 6 patients with a mean score of 37 (range 0-67) for a mean reduction of 78 points in the fecal incontinence scores. Patients on average were taken from complete incontinence at least daily to complete continence to solid and liquid stool following implantation with the ABS. The 12-month follow-up success rate was 100%, although the number of patients was small.

- Normal anorectal manometry resting pressures range from 40 to 80 mm Hg. Average preoperative resting pressures were 27mm Hg, at activation the average increased to 51mm Hg. The 13 patients tested 6 months after activation had an average resting pressure of 56mm Hg. There is not a close correlation between manometric resting pressures and clinical outcomes.

- Fecal Incontinence Quality of Life was assessed by patient questionnaire. At baseline many patients reported altering their activities to avoid bowel accidents in public places. However, following implantation, patients reported markedly improved quality of life. Many patients reported less restriction on their activities and spent less time worrying about fecal incontinence.

- A Health Status Questionnaire analyzed scores for eight scales of health status, function, limitations and perceptions. Change in each of the scales between pre-

implantation and 12-month follow-up was compared. Social function showed a statistically significant improvement. Six of the other seven scales had changes in a "positive direction." However, the number of patients completing 12 months of follow-up is limited (n=6).

Study Conclusions (G960116)
Though the number of patients is small, results of the study to date have shown complete continence in at least 92% of patients who have completed 6-month or 12-month follow-up. The Acticon Neosphincter shows probable benefit as an alternative for treatment of severe fecal incontinence. The potential risks to the patient of multiple complications and having to undergo device revision is balanced by the benefit of complete or significantly improved continence.

Adverse Events Reported From Outside the United States
There were 16 adverse events related to the device voluntarily reported to the AMS Complaint System for the commercially available Acticon Neosphinter. For the period of July 1996 through December 31, 1998, according to the AMS Patient Information Form database, 152 patients had received Acticon devices. The 16 adverse events involved 11 patients and resulted in 15 surgical procedures including 9 revision surgeries, 2 replacement surgeries, and 4 removal surgeries.

Table 9: Summary of Adverse Effects reported to AMS Complaint System

Adverse Device Effect	Frequency
Infection	2
Erosion	3
Migration	0
Malposition	0
Mechanical	5
Pain	1
Recurring incontinence	3
Patient dissatisfaction	0
Other	9
Total	**16**

When calculated using a denominator of total devices implanted of n=152, 10.3% of devices were revised, removed, or replaced for reported adverse device effects. This rate is based only on surgery data voluntarily reported to AMS. The number of surgeries and the number of patients implanted may be greater than reported.

X. CONCLUSIONS DRAWN FROM STUDIES

Pre-clinical studies assessed the device design, mechanical properties, reliability and materials biocompatibility. Results of this testing provide assurance that the device design and materials are appropriate for the intended use.

Preliminary results from clinical trials indicate that, although the number of patients is limited, most (>90%) patients had a successful outcome (reduction in the number of incontinence episodes) six months and one year after implantation.

The adverse events profile associated with use of the American Medical System's Acticon Neosphincter shows a high (70%) number of adverse events most of which resolved without permanent sequelae but many (40%) of which require revision surgery.

These rates of adverse events for the Acticon Neosphincter are compared to other colorectal surgeries. In a study examining the overall mortality and morbidity for patients undergoing resection of the colon and rectum, 361 out of 971 patients (37%) undergoing elective surgery experienced at least one postoperative complication[1]. In another study examining the change in patterns in the morbidity and mortality following colorectal surgery, for 304 patients who underwent elective surgery for colorectal disease the overall complication rate ranged from 36% to 39%[2]. Both of these studies examined colorectal surgeries that did not include implantation of a prosthetic device.

The overall rate of infection following implantation of the Acticon Neosphincter is at least twice as high as the infection rate seen in the other studies, 27% compared to 10%. However, a larger infection rate could be expected due to the presence of a prosthetic device that may impair local host defenses. Most of these infections could only be resolved by removal of the implanted device[3].

In conclusion, the preclinical and clinical studies provide reasonable assurance that the probable benefit to health from use of the device outweighed the risks of injury or illness, taking into account the risks and benefits of currently available alternative forms of treatment for this specific patient population.

XI. PANEL RECOMMENDATIONS

The Acticon Neosphincter was not submitted to the Gastroenterology and Urology Devices panel.

XII CDRH RECOMMENDATION

CDRH has determined that, based on the data submitted, implantation of the Acticon Neosphincter will not expose patients to an unreasonable risk of serious illness or injury, and that the probable benefit to health from using the device outweighs the risk of illness or injury in those patients for whom the device is indicated, and issued an approval order on SEP 20 1999.

XIII APPROVAL SPECIFICATIONS

Professional Labeling

- Acticon Neosphincter Package Insert
- Acticon Neosphincter Operating Room Manual

Patient Labeling

- Important Information for Patients Considering an Acticon Neosphincter
- A Guide to Coping with Fecal Incontinence
- Learning to use Your New Prosthesis - Men
- Learning to Use Your New Prosthesis - Women

XIV. REFERENCES

1. Bokey, E.L., et al., Postoperative morbidity and mortality following resection of the colon and rectum for cancer. Dis Colon Rectum 1995, 38:480-487.

2. Nwiloh, J, et al., Changing patterns in the morbidity and mortality of colorectal surgery. Am J Surgery, 1991, 162:83-85.

3. Textbook of Surgery, Prosthetic Device-Associated Infections. Philadelphia, W.B. Saunders Company; 1997.