

K011812

NOV 0 8 2001

9 510(K) SUMMARY

Merry Lee Bain
Vice President/Director Regulatory Affairs
& Clinical Services
Cook Incorporated
925 South Curry Pike
Bloomington, Indiana, 47402
(812) 339-2235

Trade Name: SPECTRUM® Ventricular Catheter
Common/Usual Name: Ventricular Catheter, External Drainage Catheter
Proposed Classification: Central Nervous System Fluid Shunt and Components
21 CFR Part 882.5550 (84JXG)
Class II

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

The SPECTRUM® Ventricular Catheter is comparable in terms of intended use and technological characteristics to predicate Ventricular catheters, including Cook Incorporated's Ventricular Catheter. Like the Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter and the Cook SPECTRUM®/ABRM Catheter for intravascular use, the SPECTRUM® Ventricular Catheter has an antimicrobial component comprised of a combination of minocycline and rifampin.

The SPECTRUM® Ventricular Catheter is a 9 Fr catheter nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. The SPECTRUM® Ventricular Catheter is impregnated with an antimicrobial combination of minocycline and rifampin which may reduce the risk of catheter-related infection during use. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 Φ g/cm), and the average amount of rifampin on the catheter is approximately 4 mg (116 Φ g/cm). Components supplied with the SPECTRUM® Ventricular Catheter include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

The SPECTRUM® Ventricular Catheter is similar with respect to indications for use, materials and physical construction to predicate devices in terms of section 510(k) substantial equivalency, and has undergone testing to support substantial equivalence. The substantially equivalent determination under the Federal Food, Drug, and Cosmetic Act is not intended to have any bearing whatsoever on the resolution of patent infringement suits or other patent matters.

The device will be manufactured according to specified process controls, undergoing processing, sterilization and packaging procedures similar to predicate devices currently manufactured and marketed by Cook Incorporated.

The SPECTRUM® Ventricular Catheter has undergone biocompatibility testing (Dermal Sensitization, Cytotoxicity, 7 Day Muscle Implantation with Histopathology, Intracutaneous Toxicity, Systemic Toxicity, Hemolysis, Genotoxicity, and a Two Week Brain Implantation Study), physical performance testing, HPLC analysis, zone of inhibition testing, susceptibility testing, and clinical evaluation. Results of this testing provide reasonable assurance of device performance for its intended use.

Clinical Study

To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of catheter-related infection, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The average duration of catheter placement was 8.5 ± 5.8 days in the treatment group, and 8.2 ± 6.9 days in the control group. Results showed that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of catheter-related infection than those receiving the control catheter (1.3% versus 9.4%, respectively).



**Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850**

NOV 0 8 2001

Ms. April Lavender, RAC
Vice President, Regulatory Affairs
Cook, Inc.
925 South Curry Pike
P.O. Box 489
Bloomington, Indiana 47402

Re: K011812

Trade/Device Name: SPECTRUM® Vectricular Catheter
Regulation Number: 21 CFR 882.4100
Regulation Name: Ventricular Catheter
Regulatory Class: Class II
Product Code: NHC
Dated: September 5, 2001
Received: September 10, 2001

Dear Ms. Lavender:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

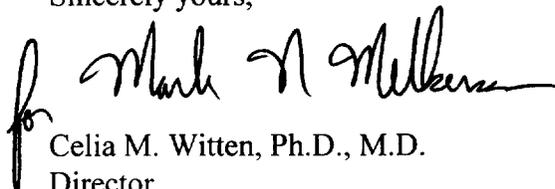
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Page 2 – Ms. April Lavender, RAC

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4659. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>

Sincerely yours,

A handwritten signature in black ink, appearing to read "for Celia M. Witten". The signature is written in a cursive style and is positioned to the left of the typed name.

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

NOV 08 2001

510(k) Number (if known): K01XXXX

K011812

Device Name: SPECTRUM® Ventricular Catheter

Indications For Use:

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Susan Walker

(Division Sign-Off)
Division of General, Restorative
and Neurological Devices

510(k) Number K011812

Prescription Use

OR

Over-The-Counter Use



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 08 2001

Ms. April Lavender, RAC
Vice President, Regulatory Affairs
Cook, Inc.
925 South Curry Pike
P.O. Box 489
Bloomington, Indiana 47402

Re: K011812

Trade/Device Name: SPECTRUM® Ventricular Catheter
Regulation Number: 21 CFR 882.4100
Regulation Name: Ventricular Catheter
Regulatory Class: Class II
Product Code: NHC
Dated: September 5, 2001
Received: September 10, 2001

Dear Ms. Lavender:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Page 2 – Ms. April Lavender, RAC

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4659. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>

Sincerely yours,

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

NOV 08 2001

510(k) Number (if known): K01XXXX

K011812

Device Name: SPECTRUM® Ventricular Catheter

Indications For Use:

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Susan Walker
(Division Sign-Off)
Division of General, Restorative
and Neurological Devices

510(k) Number K011812

Prescription Use

OR

Over-The-Counter Use 3

Memorandum

From: Reviewer(s) - Name(s) Dwight Yen

Subject: 510(k) Number K 011812 / S1

To: The Record - It is my recommendation that the subject 510(k) Notification:

- Refused to accept.
- Requires additional information (other than refuse to accept).
- Is substantially equivalent to marketed devices.
- NOT substantially equivalent to marketed devices.

De Novo Classification Candidate? YES NO

Other (e.g., exempt by regulation, not a device, duplicate, etc.)

- Is this device subject to Postmarket Surveillance? YES NO
- Is this device subject to the Tracking Regulation? YES NO
- Was clinical data necessary to support the review of this 510(k)? YES NO
- Is this a prescription device? YES NO
- Was this 510(k) reviewed by a Third Party? YES NO
- Special 510(k)? YES NO
- Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers YES NO

This 510(k) contains:

- Truthful and Accurate Statement Requested Enclosed
(required for originals received 3-14-95 and after)
- A 510(k) summary OR A 510(k) statement
- The required certification and summary for class III devices
- The indication for use form (required for originals received 1-1-96 and after)
- Material of Biological Origin YES NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

- No Confidentiality
- Confidentiality for 90 days
- Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

84 NHC Class II (982.4102)

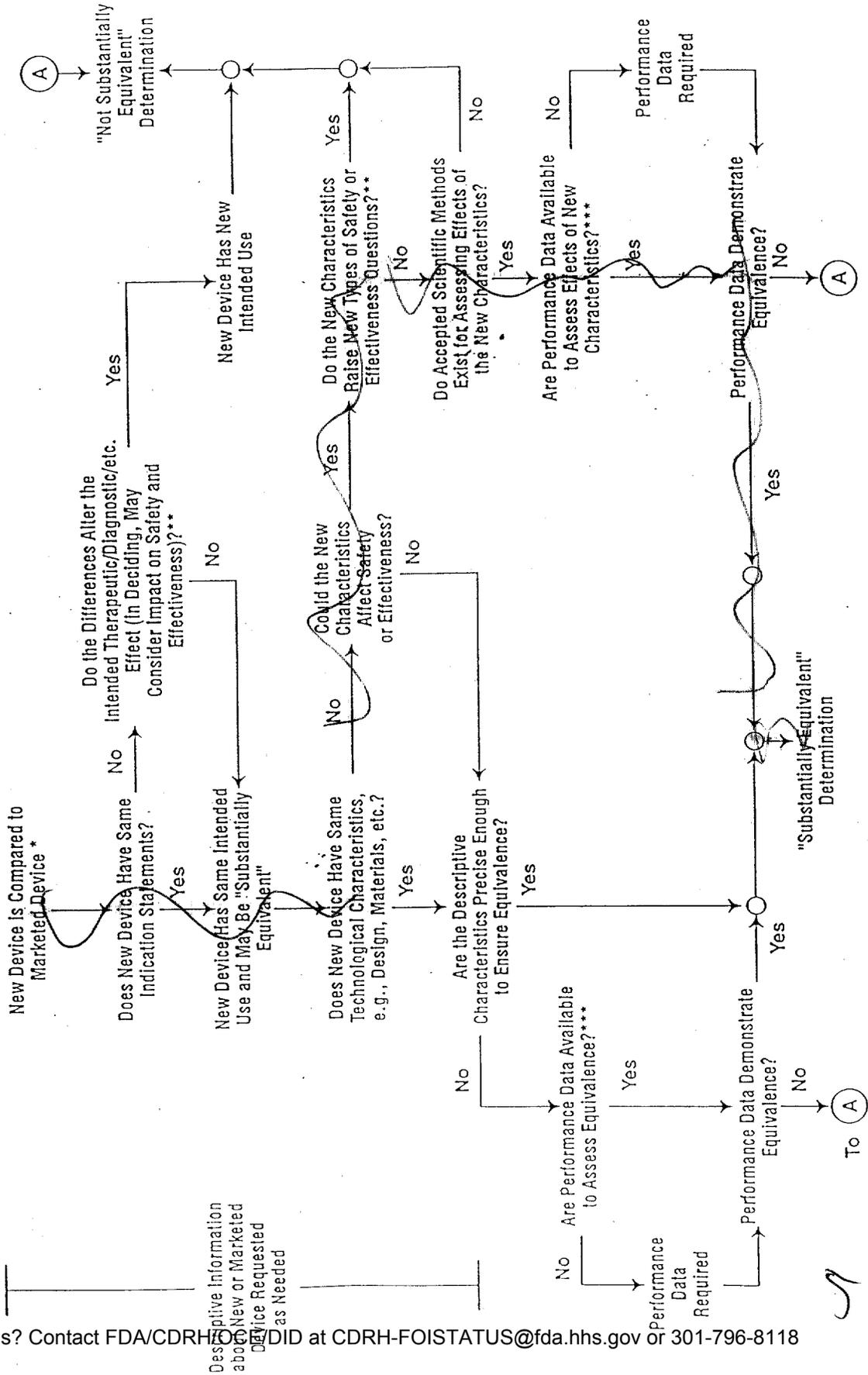
Review: Nick R. Dyden GSAB 11/2/01
(Branch Chief) (Branch Code) (Date)

Final Review: Susan Wall 11/8/01
(Division Director) (Date)

Revised: 8/17/99

4

510(k) "Substantial Equivalence" Decision-Making Process (Detailed)



Questions? Contact FDA/CDRH FOIA at CDRH-FOI STATUS@fda.hhs.gov or 301-796-8118

* 510(k) Submissions Compare New Devices to Marketed Devices. FDA Requests Additional Information if the Relationship Between Marketed and "Predicate" (Pre-Amendment or Reclassified Post-Amendments) Devices Is Unclear.
 ** This Decision is Normally Based on Descriptive Information Alone, But Limited Technical Information is Sometimes Required.
 *** Data May Be Required for the 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

510K Memo Record

Date: 31 October 2001

To: The record K011812

From: Dwight Yen, Electronics Engineer (HFZ 410)

Subject: Premarket notification from Cook, Inc. for the Spectrum Ventricular Catheter

Contact: April Lavender, VP Regulatory Affairs (812) 339-2235

Description: The Cook Spectrum Ventricular Catheter is a modification to Cook's ventricular catheter (K962097) currently on the market. The modification involves impregnating the catheter with a combination of antimicrobial agents (minocycline and rifampin). Cook Inc. currently markets two catheters with same combination antimicrobial agents. They are the Spectrum Silicone Foley Catheter (K000251) and the ABRM Central Venous Catheter (K950118). The Codman's Bactiseal ventricular catheter (K003322) impregnated with Rifampin and Clindamycin HCL was cleared for neurological shunt applications. A comparison table of devices with antibiotics or antimicrobial, which were reviewed as part of this submission, is attached.

Antimicrobial impregnation of Cook's catheter is accomplished through a controlled dipping process in which catheters are placed in a manifold and the manifold is placed in a tank containing well-defined concentrations of the required solutions. Both inner and outer surfaces of the catheters are exposed to the solution and the antimicrobial impregnates the entire catheter wall, throughout the catheter radius. After removal from the tank, the catheters undergo a series of flushes with filtered compressed air and with distilled water. To confirm the uniformity of impregnation and batch-to-batch consistency, the catheters undergo visual inspection for evidence of physical damage, non-uniformity of color and presence of particulate. A zone of inhibition testing against *S. epidermidis* is performed using proximal, middle and distal catheter segments taken from the first hour, middle hour and last hour of the impregnation process. The zones obtained serve as the basis for batch release of the catheters, with a zone of 15-mm constituting the minimum threshold for release. This 15-mm zone is the same release specification for the intravascular catheter.

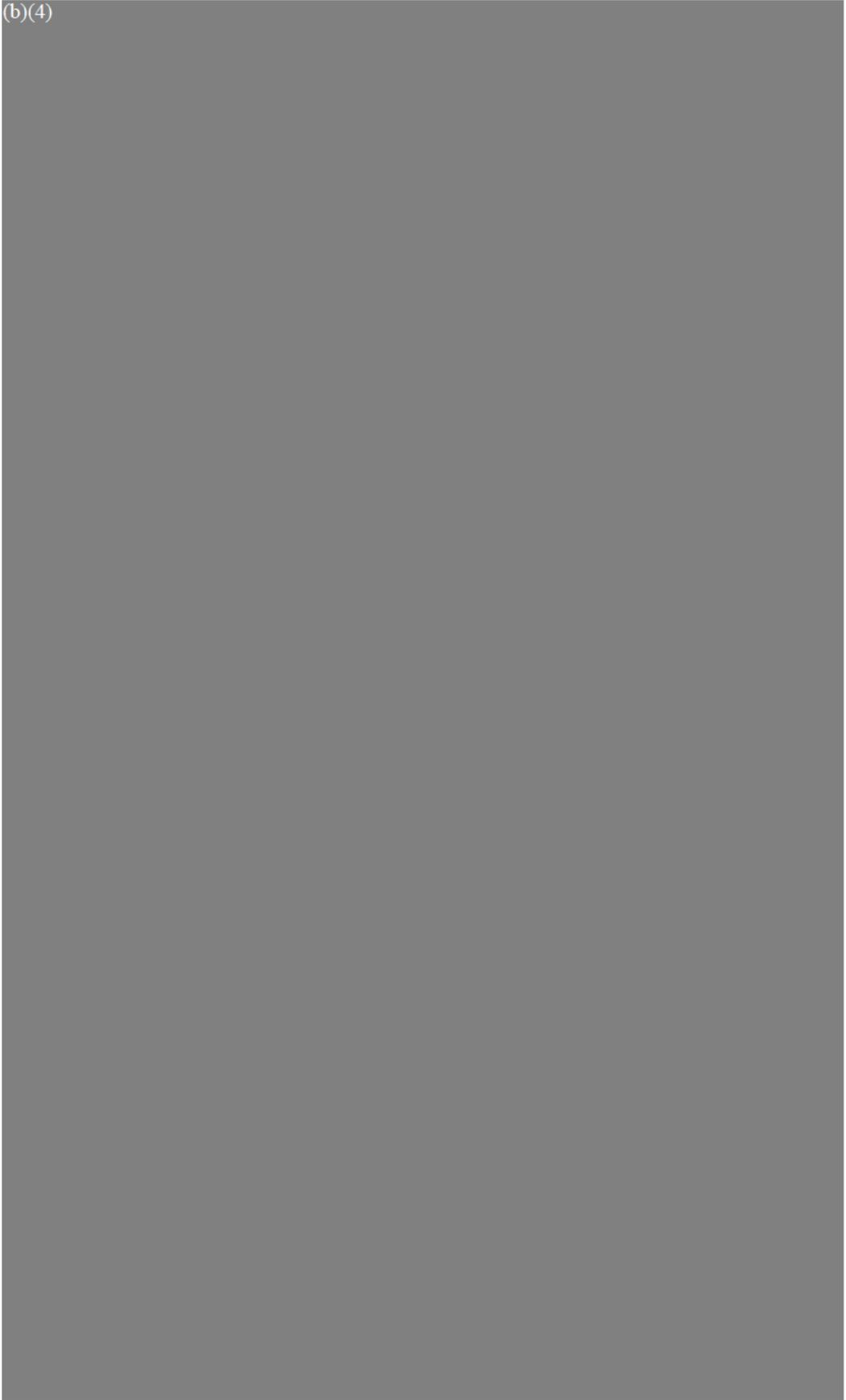
(b)(4)



(b)(4)



(b)(4)



(b)(4)



- Intended Use:** The device is used for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. This intended use is SE to predicate Cook Ventricular catheter (K962097). The additional claims with the antibiotic impregnated catheter is that the antimicrobial agents may reduce the risk of catheter colonization and catheter-related infection during use.
- Predicates:** The antimicrobial impregnated ventricular catheter is comparable to Cook's untreated ventricular catheter (K962097) currently on the market in terms of intended use. The antimicrobial agents and the method of impregnation are identical to Cook's foley catheter (K000251) and ABRM central venous catheter (K950118).
- Labeling:** Revised draft package labels are provided. The labeling include claims that the antimicrobial agents minocycline and rifampin may reduce the risk of catheter colonization and catheter-related infection during use. The label also contains clinical information, which summarized the clinical study design and the results of the study.
- Sterility:** The device is provided sterile for single use. EtO sterilization method will be used to provide sterility to an SAL of 10^{-6} . Sterilization validation is consistent with the half cycle method as described in ANSI 11135:1994. EtO residuals will be verified to be less than the maximum allowable limits as defined in ISO 10993-7: 1995 which are 20 mg for EtO and 12 mg for ethylene chlorohydrin. Device will be packaged in a molded tray sealed within a Tyvek-Poly pouch.

Manufacture:

(b)(4)



Shelf Life determination based on zone of inhibition testing were performed and results were used to support a 2 year expiration date on the package labeling.

Materials:

Testing to assess biocompatibility was conducted in accordance with ISO 10993 standards. Testing included (b)(4)

(b)(4)



(b)(4)

(b)(4)

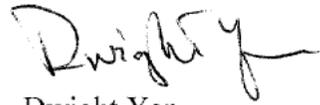
Summary of test results was provided. Test results support biocompatibility of the materials used in the device.

Technical:

(b)(4)

An Indication for use, a 510K Summary, a Truthful and Accurate Statement are provided.

RECOMMENDATION: SE to predicates, 84 NHC Class II (882.4100).



Dwight Yen

o.k.
Neil 11/2/01

Comparison Table of Devices with Antibiotics or Antimicrobial

Device	Manufacturer K#	Drug Combination	Claims	Status
Central Venous Catheter	Cook K950118	Rifampin and Minocycline	To decrease the incidence of bacteria colonization along the catheter and to decrease the incidence of catheter related bacteremia.	Cleared
Foley Catheter	Rochester Medical K971627	Nitrofurazone	Shown to provide statistically significant reduction in the incidence of catheter acquired bacterial urinary tract infection during the first 5 days of catheterization.	Cleared
Central Venous Catheter	Arrow K993691	Chlorhexidine acetate and silver sulfadiazine	The technology is intended to provide protection against catheter Related bloodstream infections.	Cleared
Hemodialysis Catheter	Arrow K993933	Chlorhexidine acetate and silver sulfadiazine	Antimicrobial surface catheter is intended to help provide protection Against catheter related infections resulting from microorganisms Migrating the subcutaneous tract along the exterior surface of the catheter.	Cleared
Foley Catheter	Cook K000251	Rifampin and Minocycline	Catheter is impregnated with the antimicrobial agents minocycline And rifampin, which may reduce the risk of gram positive bacterial Colonization of the catheter and catheter-related bacteriuria during use	Cleared
Surgical Mesh	AMS K002721	Rifampin and Minocycline	To be Determined	Pending
Ventricular Catheter	Codman K003322	Rifampin and Clindamycin HCL	Catheters have been shown in laboratory studies to reduce the colonization of gram positive bacteria on the tubing surface.	Cleared
<i>Ventricular Catheter</i>	<i>Cook K011812</i>	<i>Rifampin and Minocycline</i>	<i>Catheter is impregnated with the antimicrobial agents minocycline and rifampin which may reduce the risk of catheter colonization and catheter-related infection during use.</i>	<i>Pending</i>
Penile Prosthesis	AMS D970012	Rifampin and Minocycline	In-vitro studies with the antibiotic treated device ... show a microbial "zone of inhibition" around the test material. A limited animal model study suggests that this surface treatment may reduce the potential for bacterial colonization on the treated device.	Approved

COMPLETED AUG 30 2001

-MEMORANDUM

**DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration**

**Division of Neuropharmacological Drug Products (HFD-120)
Center for Drug Evaluation and Research**

Date: 7/16/01

From: Russell Katz, M.D., Division Director

Subject: Spectrum Antibiotic-Impregnated Ventricular Catheter, Cook, Inc.

To: Dwight Yen
CDRH HF 410

Document type: Consultative Review

ODE1 number:

8-30-01
James P. Lynch, M.D.
JR

Division of Neuropharmacological Drug Products, HFD-120

See the attached review for the Division's comments.

Consultative Review and Evaluation of Clinical Data

Consult (Serial Number)	6467
Sponsor:	Cook
Device:	Antibiotic Impregnated Ventricular Catheter
Proposed Indication:	Intraventricular Drainage of CSF
Material Submitted:	510 (k) Submission
Consult Date:	11 July 2001
Date Received / Division:	7/16/01/DNDP
Date Review Completed:	7/16/01
Reviewer:	Rob Harris, M.D., Ph.D.

1. Introduction

The Cook Group intends to market an external ventricular catheter for CSF drainage, monitoring and antibiotic instillation. Coating of catheters with antimicrobial agents has been demonstrated both in vitro and in vivo to decrease adherence and colonization of microbes to catheter surfaces. The Spectrum Catheter is coated with minocycline and rifampin and is comparable to other Cook Spectrum catheters currently employed in urology. This premarket notification submission contains the results of a clinical trial of 288 evaluated patients out of 306 enrollees. The results indicate the product is safe and reduces intraventricular CSF catheter microbial colonization, a laboratory finding.

CDRH requests clinical neurosurgical/neurological opinion for the submission.

2. Comments

(b)(4)



(b)(4)



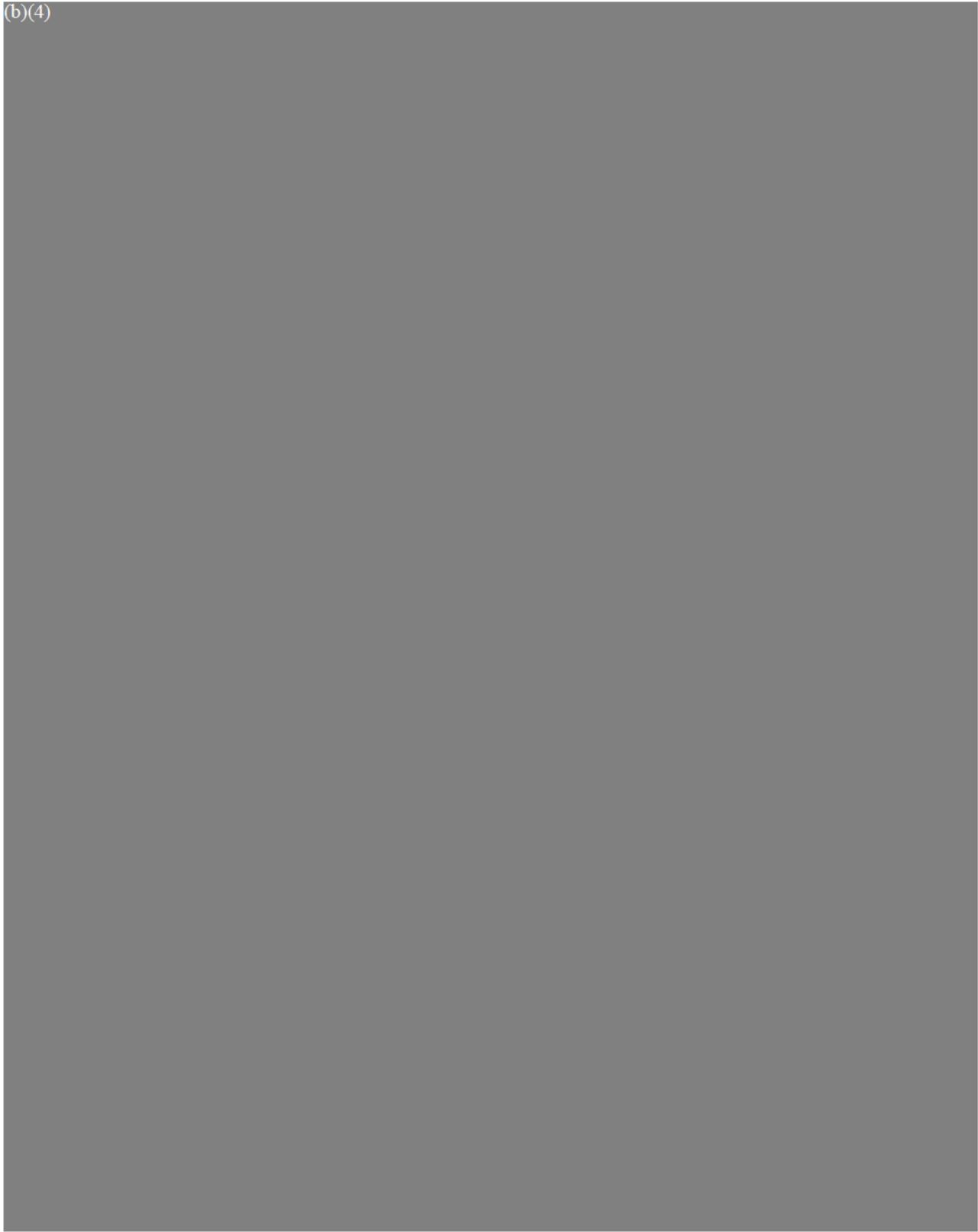
Data Summary

(b)(4)

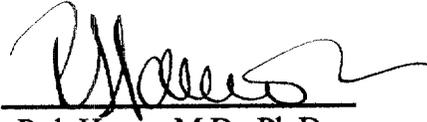


15

(b)(4)



16



Rob Harris, M.D., Ph.D.
Medical Reviewer

J. Feeney, MD


8/23/01

rdh
cc:
HFD-120
CON

Yen, Dwight

From: Bushar, Harry F.
nt: Tuesday, July 17, 2001 5:08 PM
: Yen, Dwight
Cc: Ogden, Neil; Witten, Celia; Dawisha, Sahar; Campbell, Gregory; Roberson, Helen W.
Subject: Statistical Review of 510(k) K011812 for Cook SPECTRUM Ventricular Catheter

As requested, I have reviewed 510(k) K011812 for Cook SPECTRUM Ventricular Catheter, an external ventricular drainage catheter impregnated with a combination of anti-microbial agents (minocycline and rifampin), which is intended to obtain access to a ventricular cavity of the brain for relieving elevated intra-cranial pressure or fluid volume. The sponsor has conducted a prospective, randomized, multi-center clinical trial "to evaluate the efficacy of the SPECTRUM Ventricular Catheter in preventing ventriculitis". (See page 18.) My comments are the following:

(b)(4)



Please contact me for any further review of this submission.

Harry F. Bushar, Ph.D.
Mathematical Statistician
Phone: (301) 827-4361

Yen, Dwight

From: Bushar, Harry F.
At: Thursday, October 25, 2001 1:24 PM
To: Yen, Dwight
Cc: Ogden, Neil; Campbell, Gregory; Roberson, Helen W.
Subject: RE: DC #K011812 SPECTRUM Ventricular Catheter

(b)(4)

Harry F. Bushar, Ph.D.

Mathematical Statistician
Phone: (301) 827-4361
FAX: (301) 443-8559

-----Original Message-----

From: Yen, Dwight
Sent: Thursday, October 18, 2001 9:42 AM
To: Bushar, Harry F.
Cc: Ogden, Neil
Subject: FW: DC #K011812 SPECTRUM Ventricular Catheter

Hi Harry,

The data for Fig 2 is provided below.
Dwight

-----Original Message-----

From: Merry Lee Bain [SMTP:mbain@cook-inc.com]
Sent: Thursday, October 18, 2001 9:09 AM
To: Yen, Dwight
Subject: Fw: DC #K011812 SPECTRUM Ventricular Catheter

> Good Morning!
> As per your request, attached is the data in Excel. Please note that as
> stated in the 510k (page 32), the day used to signify occurrence of
> ventriculitis is the calculated midpoint between the day on which the CSF
> culture was positive and the day on which the previously obtained CSF
> culture was negative, designated in the file column heading as DUR'. I
hope
> this resolves the discrepancy, and will wait to hear from you!
>

<< File: survival.xls >>

> Best regards-
> Merry Lee
> Merry Lee Bain
> V.P./Director Regulatory Affairs & Clinical Services
> Chief Compliance Officer
> COOK INCORPORATED
> 925 S. Curry Pike, P.O. Box 489
> Bloomington, Indiana 47402

MEMORANDUM

Date: 9/5/2001

To: File K011812

Fr: Dwight Yen

cc:

Re: Cook's Spectrum Ventricular Catheter with Rifampin and Minocycline

The memo to file is specifically addressing remaining issues of:

1. Development of resistance to these antibiotics,
2. Safety of these antibiotics coated catheters for neurological use,
3. Appropriateness of these antibiotics for the types of organisms that cause shunt infections.

Development of resistance to these antibiotics:

This issue was discussed with the sponsor during a pre-IDE meeting held on February 26, 1998 (see attached Meeting Minutes). The sponsor cited results from a previous clinical study (Darouiche, 1997) for central venous catheter in which a polyurethane catheter similarly impregnated with minocycline and rifampin was compared with a catheter coated with chlorhexidine gluconate and silver sulfadiazine. The study saw no evidence suggesting emergence of resistance to either minocycline or rifampin.

Consultative review from Dr. James King, Microbiologist in the Division of Anti-Infective Drug also addressed the issue of resistance (see Review Memo Dated June 15, 1998). In this review, he states that colonization of the catheters occurs in intimate contact with the surface of the catheter where the small total amount of rifampin and minocycline is concentrated. The constant strengths of the antibiotics at the surface of the catheters should mitigate against resistance development.

Safety of these antibiotics coated catheters for neurological use:

I believe the sponsor has adequately addressed the safety of the antibiotic coated catheter for neurological use based on the successful completion of their study of 306 patients. One hundred and forty-nine (149) patients received the treatment catheters with an average duration of catheter placement of 8.5 ± 5.8 days. As Dr. Rob Harris's review indicated, the complication rate within both study groups was what was expected in a population requiring ventricular catheter placement. No complication could be attributed to the presence or absence of a chemical on the catheter.

Appropriateness of these antibiotics for the types of organisms that cause shunt infections:

This issue was also discussed with the sponsor during the pre-IDE meeting. The sponsor's reasons included: 1) the agents' broad spectrum and synergistic activity against most organisms; 2) the agents have been in use for more than 30 years; 3) the combination allows decreased reliance of first choice drugs of treatment; 4) the agents have separate mechanisms of action, which decreases the likelihood of resistance to develop; and 5) although the agents elute from the catheter, residual levels of both remain on the catheter. Results from the previously described venous catheter study showed that in matched patient arms, patients having the minocycline and rifampin impregnated catheters were twelve times less likely to have catheter related bloodstream infection, and the catheter was three times less likely to be colonized than the catheter coated with chlorhexidine gluconate and silver sulfadiazine.

A study of the sources of infection in early colonized shunts (Bayston 1974) showed that most of these organisms involved in early shunt colonization are present on the patient at operation and do not come from the theatre environment or personnel as some have speculated. It has been suggested that colonization of vascular catheters may also be due to organisms entering the blood stream during the operation and migrating to the shunt by way of the venous catheter (Holt 1970). Central venous catheter coated with minocycline and rifampin, which has been cleared by FDA (K950118), has shown to significantly reduce the risk for catheter-related colonization and bloodstream infections.

COOK®

Cook Incorporated
P.O. Box 489
Bloomington, IN 47402-0489
Phone: 812 339-2235
Fax: 812-339-5369
www.cookgroup.com

October 29, 2001

ATTN: Dwight Yen (HFZ-410)
Office of Device Evaluation
Document Mail Center (HFZ-401)
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

RECEIVED

OCT 30 2 53 PM '01

FDA/CDRH/OCE/DID

RE: D.C. #K011812
SPECTRUM® Ventricular Catheter

Dear Mr. Yen,

As requested, attached is a hard copy of the revised draft labeling for the SPECTRUM® Ventricular Catheter (e-mailed to you earlier today) which is expected to allow completion of review for substantial equivalency. Please amend the 510(k) accordingly.

As always, thank you for your communications and efforts during review of this premarket notification.

Sincerely,
Cook Incorporated



Merry Lee Bain
Vice President/Director Regulatory Affairs & Clinical Services

Enclosure

22

DRAFT LABELING

These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

SPECTRUM® VENTRICULAR DRAINAGE CATHETER SET

DESCRIPTION

The SPECTRUM® Ventricular Drainage Catheter Set allows external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain. The SPECTRUM® Ventricular Drainage Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of catheter colonization and catheter-related infection during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of ventriculitis.

The SPECTRUM® Ventricular Drainage Catheter is available in a 9 Fr diameter and is nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 µg/cm), and the average amount of rifampin on the catheter is approximately 4 mg (116 µg/cm). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The minocycline and rifampin antimicrobial agents contain yellow/orange pigments, therefore, some coloration of the catheter is normal. Components supplied with the SPECTRUM® Ventricular Catheter Set include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

INDICATIONS FOR USE

The SPECTRUM® Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.

CONTRAINDICATIONS

This device is contraindicated in patients having allergy or history of allergy to tetracyclines or rifampin. **Note:** Because the SPECTRUM® Ventricular Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physician's Desk Reference*) should be considered when using this device, although there have been no reports of detected systemic levels of minocycline or rifampin in patients receiving a SPECTRUM® Catheter.

WARNINGS

- This device is not intended for permanent implantation.

23

- This device should not be used if dermatitis or scalp infection is present at the catheter insertion site.
- Care must be taken when using this device in patients receiving anticoagulants or those who are known to have a bleeding diathesis.
- Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headache, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may pre-dispose development of a subdural hematoma or hydrooma, or collapse of the lateral ventricular walls leading to obstruction of the ventricular catheter.
- Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally raised or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.
- The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.
- Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. **Under no circumstances should the catheter be forcefully removed.** If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.
- Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTIONS

- Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be initiated after implantation.
- Inspect contents of this set for damage. If product is damaged, do not use.
- Refer to manufacturer's instructions when using accessory components other than Cook products.
- Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.
- Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions. **The catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.**
- Kinking of catheter tubing may result in restricted flow or damage to the catheter.

- Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.
- Use rubber shod forceps when handling the catheter to prevent tearing or cutting the catheter.

CLINICAL STUDY INFORMATION

•To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of catheter-related infection, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). The study was stopped at an interim analysis. Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The patient characteristics (gender, age, ethnicity, indication for placement, receipt of systemic antibiotics, complications, duration of catheter placement, and reason for catheter removal) were comparable in the two groups. The average duration of catheter placement was 8.2 ± 6.9 days for patients in the control arm, and 8.5 ± 5.8 days for patients in the treatment arm. Results of the clinical study show that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of catheter-related infection (defined as a true positive microbiological culture of CSF) than those receiving the control catheter. The rate of catheter-related infection was 9.4% (13 of 139 patients) in the control arm as compared to 1.3% (2 of 149 patients) in the treatment arm ($p=0.0022$, Chi-square). Organisms isolated from CSF cultures from the 13 patients in the control group included: coagulase negative *Staphylococcus*, *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Corynebacterium*, *Klebsiella pneumonia*, coagulase positive *Staphylococcus* species, and diptheroids. Organisms isolated from CSF cultures from patients in the treatment group included *Enterobacter aerogenes*, *Enterococcus faecalis*, and *Staphylococcus aureus*. The proportions of patients free of catheter-related infection as a function of the duration of placement of the catheter in each group were compared using a log-rank test on the Kaplan-Meier estimates; the conditional rates of infection per 100 catheter days were 2.6% for treatment devices as compared to 17% for control devices ($p=0.00095$ by log-rank test).

J o.k.

SUGGESTED INSTRUCTIONS FOR USE

1. Determine the site of insertion and aseptically prepare and drape.
2. Open the periosteum, skull, and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
3. Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
4. Carefully withdraw the stylet and check for free flow of fluid.
5. Verify proper positioning of catheter using CT or other imaging modality.
6. After verifying proper placement, position the barbed end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the

tunneling device into the incision used for catheterization.

7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
8. After exiting the skin, pull catheter through the subcutaneous tunnel until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.
9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped or damaged. Slide snap-fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub of Luer lock adapter by sliding the snap-fit cap over the barbed portion of the adapter. **Avoid cutting or occluding tubing.**
10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie-down. Provide some slack in the catheter when securing the silicone winged tie-down to offer strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
11. Cap the catheter with the red sterile Luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

9 510(K) SUMMARY

Merry Lee Bain
Vice President/Director Regulatory Affairs
& Clinical Services
Cook Incorporated
925 South Curry Pike
Bloomington, Indiana, 47402
(812) 339-2235

Trade Name: SPECTRUM® Ventricular Catheter
Common/Usual Name: Ventricular Catheter, External Drainage Catheter
Proposed Classification: Central Nervous System Fluid Shunt and Components
21 CFR Part 882.5550 (84JXG)
Class II

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

The SPECTRUM® Ventricular Catheter is comparable in terms of intended use and technological characteristics to predicate Ventricular catheters, including Cook Incorporated's Ventricular Catheter. Like the Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter and the Cook SPECTRUM®/ABRM Catheter for intravascular use, the SPECTRUM® Ventricular Catheter has an antimicrobial component comprised of a combination of minocycline and rifampin.

The SPECTRUM® Ventricular Catheter is a 9 Fr catheter nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. The SPECTRUM® Ventricular Catheter is impregnated with an antimicrobial combination of minocycline and rifampin which may reduce the risk of catheter-related infection during use. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 Φ g/cm), and the average amount of rifampin on the catheter is approximately 4 mg (116 Φ g/cm). Components supplied with the SPECTRUM® Ventricular Catheter include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

The SPECTRUM® Ventricular Catheter is similar with respect to indications for use, materials and physical construction to predicate devices in terms of section 510(k) substantial equivalency, and has undergone testing to support substantial equivalence. The substantially equivalent determination under the Federal Food, Drug, and Cosmetic Act is not intended to have any bearing whatsoever on the resolution of patent infringement suits or other patent matters.

The device will be manufactured according to specified process controls, undergoing processing, sterilization and packaging procedures similar to predicate devices currently manufactured and marketed by Cook Incorporated.

The SPECTRUM® Ventricular Catheter has undergone biocompatibility testing (Dermal Sensitization, Cytotoxicity, 7 Day Muscle Implantation with Histopathology, Intracutaneous Toxicity, Systemic Toxicity, Hemolysis, Genotoxicity, and a Two Week Brain Implantation Study), physical performance testing, HPLC analysis, zone of inhibition testing, susceptibility testing, and clinical evaluation. Results of this testing provide reasonable assurance of device performance for its intended use.

Clinical Study

To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of catheter-related infection, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The average duration of catheter placement was 8.5 ± 5.8 days in the treatment group, and 8.2 ± 6.9 days in the control group. Results showed that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of catheter-related infection than those receiving the control catheter (1.3% versus 9.4%, respectively).

September 12, 2001

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

COOK, INC.
925 SOUTH CURRY PIKE
P.O. BOX 489
BLOOMINGTON, IN 47402
ATTN: APRIL LAVENDER

510(k) Number: K011812
Product: SPECTRUM
VENTRICULAR
CATHETER

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official.

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural or policy questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301) 443-6597 or at their toll-free number (800) 638-2041, or contact me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

COOK®

Cook Incorporated

P.O. Box 489
Bloomington, IN 47402-0489
Phone: 812 339-2235
Fax: 812 339-5369
www.cookgroup.com

September 5, 2001

Office of Device Evaluation
Document Mail Center (HFZ-401)
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

Attn: Dwight Yen

Re: 510(k) Supplement - for the SPECTRUM® Ventricular Catheter
D.C.# K011812

Dear Mr. Yen:

This 510(k) supplement is submitted to provide additional information requested during a telephone conference between personnel from the Food and Drug Administration, Cook Incorporated, and MED Institute on September 4, 2001.

Cook Incorporated requests that the additional information provided in this communication be considered as company confidential for an indefinite time period. Unless prior permission from Cook Incorporated has been obtained, release to the public of any information that has been noted as company confidential will be considered a violation of company rights.

It is hoped that the additional information provided herein will allow completion of review for substantial equivalence.

Sincerely,



[Handwritten signature electronically reproduced with permission]

April Lavender, RAC
Vice President, Regulatory Affairs

AL:twh
Enclosures

SL-32
30

TABLE OF CONTENTS

	<u>Page No.</u>
RESPONSE TO QUESTIONS	1
EXHIBIT I. REVISED LABELING	I.1

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

EXHIBIT I

REVISED LABELING

DRAFT LABELING

These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

SPECTRUM® VENTRICULAR DRAINAGE CATHETER SET

DESCRIPTION

The SPECTRUM® Ventricular Drainage Catheter Set allows external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain. The SPECTRUM® Ventricular Drainage Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of catheter colonization and ventriculitis during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of ventriculitis.

The SPECTRUM® Ventricular Drainage Catheter is available in a 9 Fr diameter and is nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 $\mu\text{g}/\text{cm}$), and the average amount of rifampin on the catheter is approximately 4 mg (116 $\mu\text{g}/\text{cm}$). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The minocycline and rifampin antimicrobial agents contain yellow/orange pigments, therefore, some coloration of the catheter is normal. Components supplied with the SPECTRUM® Ventricular Catheter Set include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

INDICATIONS FOR USE

The SPECTRUM® Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.

CONTRAINDICATIONS

This device is contraindicated in patients having allergy or history of allergy to tetracyclines or rifampin. **Note:** Because the SPECTRUM® Ventricular Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physician's Desk Reference*) should be considered when using this device, although there have been no reports of detected systemic levels of minocycline or rifampin in patients receiving a SPECTRUM® Catheter.

WARNINGS

- This device is not intended for permanent implantation.
- This device should not be used if dermatitis or scalp infection is present at the catheter insertion site.
- Care must be taken when using this device in patients receiving anticoagulants or those who are known to have a bleeding diathesis.
- Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headache, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may pre-dispose development of a subdural hematoma or hydroma, or collapse of the lateral ventricular walls leading to obstruction of the ventricular catheter.
- Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally raised or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.
- The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.
- Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. **Under no circumstances should the catheter be forcefully removed.** If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.
- Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTIONS

- Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be initiated after implantation.
- Inspect contents of this set for damage. If product is damaged, do not use.
- Refer to manufacturer's instructions when using accessory components other than Cook products.
- Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.
- Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions. **The catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.**

- Kinking of catheter tubing may result in restricted flow or damage to the catheter.
- Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.
- Use rubber shod forceps when handling the catheter to prevent tearing or cutting the catheter.

CLINICAL STUDY INFORMATION

•To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of ventriculitis, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The patient characteristics (gender, age, ethnicity, indication for placement, receipt of systemic antibiotics, complications, duration of catheter placement, and reason for catheter removal) were comparable in the two groups. The average duration of catheter placement was 8.2 ± 6.9 days for patients in the control arm, and 8.5 ± 5.8 days for patients in the treatment arm. Results of the clinical study show that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of ventriculitis (defined as a true positive microbiological culture of CSF) than those receiving the control catheter. The rate of ventriculitis was 9.4% (13 of 139 patients) in the control arm as compared to 1.3% (2 of 149 patients) in the treatment arm ($p=0.0022$, Chi-square). Organisms isolated from CSF cultures from the 13 patients having ventriculitis in the control group included: coagulase negative *Staphylococcus*, *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Corynebacterium*, *Klebsiella pneumonia*, coagulase positive *Staphylococcus* species, and diphtheroids. Organisms isolated from CSF cultures from patients having ventriculitis in the treatment group included *Enterobacter aerogenes*, *Enterococcus faecalis*, and *Staphylococcus aureus*. The proportions of patients free of ventriculitis as a function of the duration of placement of the catheter in each group were compared using a log-rank test on the Kaplan-Meier estimates; the conditional rates of ventriculitis per 100 catheter days were 2.6% for treatment devices as compared to 17% for control devices ($p=0.00095$ by log-rank test).

SUGGESTED INSTRUCTIONS FOR USE

1. Determine the site of insertion and aseptically prepare and drape.
2. Open the periosteum, skull, and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
3. Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
4. Carefully withdraw the stylet and check for free flow of fluid.
5. Verify proper positioning of catheter using CT or other imaging modality.

6. After verifying proper placement, position the barbed end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the tunneling device into the incision used for catheterization.
7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
8. After exiting the skin, pull catheter through the subcutaneous tunnel until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.
9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped or damaged. Slide snap-fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub of Luer lock adapter by sliding the snap-fit cap over the barbed portion of the adapter. **Avoid cutting or occluding tubing.**
10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie-down. Provide some slack in the catheter when securing the silicone winged tie-down to offer strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
11. Cap the catheter with the red sterile Luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

September 10, 2001

COOK, INC.
925 SOUTH CURRY PIKE
P.O. BOX 489
BLOOMINGTON, IN 47402
ATTN: APRIL LAVENDER

510(k) Number: K011812
Product: SPECTRUM
VENTRICULAR
CATHETER

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefax material as part of your official premarket notification submission unless specifically requested of you by an FDA official.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: <http://www.fda.gov/cdrh/modact/leastburdensome.html>

If after 30 days the requested information, or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural or policy questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301) 443-6597 or at their toll-free number (800) 638-2041, or contact me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Supervisor Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health



Memorandum

Reviewer(s) - Name(s) DWIGHT YEN

Subject: 510(k) Number K011812

To: The Record - It is my recommendation that the subject 510(k) Notification:

- Refused to accept.
- Requires additional information (other than refuse to accept). *Phone hold.*
- Accepted for review _____.
- Is substantially equivalent to marketed devices.
- NOT substantially equivalent to marketed devices.

De Novo Classification Candidate? YES NO

Other (e.g., exempt by regulation, not a device, duplicate, etc.)

- Is this device subject to Postmarket Surveillance? YES NO
- Is this device subject to the Tracking Regulation? YES NO
- Was clinical data necessary to support the review of this 510(k)? YES NO
- Is this a prescription device? YES NO
- Was this 510(k) reviewed by a Third Party? YES NO
- Special 510(k)? YES NO
- Abbreviated 510(k)? YES NO

This 510(k) contains:

- Truthful and Accurate Statement Requested Enclosed
(required for originals received 3-14-95 and after)
- A 510(k) summary OR A 510(k) statement
- The required certification and summary for class III devices
- The indication for use form (required for originals received 1-1-96 and after)
- Material of Biological Origin YES NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

- No Confidentiality Confidentiality for 90 days Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

84 HCA Class I (982.460)

[Signature] QSDB 9/7/01
(Branch Chief) for (Branch Code) (Date)

Final Review: _____
(Division Director) (Date)

42

510K Memo Record

Date: 7 September 2001

To: The record K011812

From: Dwight Yen, Electronics Engineer (HFZ 410)

Subject: Premarket notification from Cook, Inc. for the Spectrum Ventricular Catheter

Contact: April Lavender, VP Regulatory Affairs (812) 339-2235

Description: The Cook Spectrum Ventricular Catheter is a modification to Cook's ventricular catheter (K962097) currently on the market. The modification involves impregnating the catheter with a combination of antimicrobial agents (minocycline and rifampin). Please see memo dated August 29 and September 5 for additional description and review.

During our most recent communication on September 4, 2001 the sponsor was asked to address two issues. First, to clarify the inconsistency in the number of patients in the treatment arms who experienced infection. Second, to revise their draft label with regards to the use of the term ventriculitis. The sponsor provided an explanation that resulted in the inconsistency. This issue was addressed satisfactorily. Dr. Rob Harris reviewed their revised draft labeling and provided further corrections (see attachment). These changes were forwarded to the sponsor on September 6. The sponsor has not been able to respond to our labeling recommendation. On September 7, I told the sponsor I would put this submission on hold (phone hold) pending their response.

An Indication for use, a 510K Summary, a Truthful and Accurate Statement are provided.

RECOMMENDATION: Phone hold pending sponsor's response with acceptable labeling claim.

Dwight Yen

DRAFT LABELING

These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

SPECTRUM[®] VENTRICULAR DRAINAGE CATHETER SET

DESCRIPTION

The SPECTRUM[®] Ventricular Drainage Catheter Set allows external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain. The SPECTRUM[®] Ventricular Drainage Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of ~~catheter colonization and ventriculitis~~ microbial CSF colonization during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of clinical syndrome of ventriculitis.

The SPECTRUM[®] Ventricular Drainage Catheter is available in a 9 Fr diameter and is nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 µg/cm), and the average amount of rifampin on the catheter is approximately 4 mg (116 µg/cm). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The minocycline and rifampin antimicrobial agents contain yellow/orange pigments, therefore, some coloration of the catheter is normal. Components supplied with the SPECTRUM[®] Ventricular Catheter Set include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

INDICATIONS FOR USE

The SPECTRUM[®] Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.

CONTRAINDICATIONS

This device is contraindicated in patients having allergy or history of allergy to tetracyclines or rifampin. **Note:** Because the SPECTRUM[®] Ventricular Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physician's Desk Reference*) should be considered when using this device, although there have been no reports of detected systemic levels of minocycline or rifampin in patients receiving a SPECTRUM[®] Catheter.

WARNINGS

⚠ This device is not intended for permanent implantation.

⦿ This device should not be used if dermatitis or scalp infection is present at the catheter insertion site.

⦿ Care must be taken when using this device in patients receiving anticoagulants or those who are known to have a bleeding diathesis.

⦿ Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headache, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may pre-dispose development of a subdural hematoma or hydroma, or collapse of the lateral ventricular walls leading to obstruction of the ventricular catheter.

⦿ Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally raised or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.

⦿ The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.

⦿ Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. **Under no circumstances should the catheter be forcefully removed.** If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.

⦿ Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTIONS

⦿ Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be initiated after implantation.

⦿ Inspect contents of this set for damage. If product is damaged, do not use.

⦿ Refer to manufacturer's instructions when using accessory components other than Cook products.

⦿ Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.

⦿ Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions. **The catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.**

⦿ Kinking of catheter tubing may result in restricted flow or damage to the catheter.

⦿ Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.

- Use rubber shod forceps when handling the catheter to prevent tearing or cutting the catheter.

CLINICAL STUDY INFORMATION

To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of ~~ventriculitis~~ CSF microbial growth (a non-clinical, laboratory finding), a prospective, unblinded, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). The study was stopped at the first interim analysis. Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The patient characteristics (gender, age, ethnicity, indication for placement, receipt of systemic antibiotics, complications, duration of catheter placement, and reason for catheter removal) were comparable in the two groups. The average duration of catheter placement was 8.2 ± 6.9 days for patients in the control arm, and 8.5 ± 5.8 days for patients in the treatment arm. Results of the clinical study show that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of ~~ventriculitis~~ csf microbial growth (defined as a true positive microbiological culture of CSF, not correlated with clinical infection) than those receiving the control catheter. The rate of ~~ventriculitis~~ csf microbial growth was 9.4% (13 of 139 patients) in the control arm as compared to 1.3% (2 of 149 patients) in the treatment arm ($p=0.0022$, Chi-square). Organisms isolated from CSF cultures from the 13 patients having ~~ventriculitis~~ CSF microbial growth in the control group included: coagulase negative *Staphylococcus*, *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Corynebacterium*, *Klebsiella pneumonia*, coagulase positive *Staphylococcus* species, and diphtheroids. Organisms isolated from CSF cultures from patients having ~~ventriculitis~~ CSF microbial growth in the treatment group included *Enterobacter aerogenes*, *Enterococcus faecalis*, and *Staphylococcus aureus*. The proportions of patients free of ~~ventriculitis~~ CSF microbial growth as a function of the duration of placement of the catheter in each group were compared using a log-rank test on the Kaplan-Meier estimates; the conditional rates of ~~ventriculitis~~ csf microbial growth per 100 catheter days were 2.6% for treatment devices as compared to 17% for control devices ($p=0.00095$ by log-rank test). There were no cases of clinical ventriculitis encountered in placebo or control groups.

SUGGESTED INSTRUCTIONS FOR USE

- Determine the site of insertion and aseptically prepare and drape.
- Open the periosteum, skull, and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
- Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
- Carefully withdraw the stylet and check for free flow of fluid.
- Verify proper positioning of catheter using CT or other imaging modality.
- After verifying proper placement, position the barbed end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the tunneling device into the incision used for catheterization.

7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
8. After exiting the skin, pull catheter through the subcutaneous tunnel until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.
9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped or damaged. Slide snap-fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub of Luer lock adapter by sliding the snap-fit cap over the barbed portion of the adapter. **Avoid cutting or occluding tubing.**
10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie-down. Provide some slack in the catheter when securing the silicone winged tie-down to offer strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
11. Cap the catheter with the red sterile Luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

COOK®**MED Institute, Incorporated**

1400 Cumberland Ave.
West Lafayette, IN 47906
Phone: 765 463-7537
Fax: 765 497-0641
www.cookgroup.com

Fax Transmission

Date: 06 SEP 2001
To: DWIGHT YEN
Fax: 301-827-4350
From: TED HEISE

Number of Pages: COVER + 10

RE: K011812 - SPECTRUM VENTRICULAR
CATHETER

DEAR MR. YEN,

HERE IS THE RESPONSE TO THE
QUESTIONS YOU HAD DURING OUR PHONE
CONVERSATION ON SEPTEMBER 4, 2001.
A HARD COPY WILL BE SENT TODAY AND
SHOULD ARRIVE AT THE DOCUMENT MAIL
CENTER TOMORROW. PLEASE FEEL FREE
TO CALL IF YOU HAVE ANY QUESTIONS!

BEST REGARDS,

TED HEISE

ty

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

COOK®

Cook Incorporated

P.O. Box 489
Bloomington, IN 47402-0489
Phone: 812 339-2235
Fax: 812 339-5369
www.cookgroup.com

September 5, 2001

Office of Device Evaluation
Document Mail Center (HFZ-401)
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

Attn: Dwight Yen

Re: 510(k) Supplement - for the SPECTRUM® Ventricular Catheter
D.C.# K011812

Dear Mr. Yen:

This 510(k) supplement is submitted to provide additional information requested during a telephone conference between personnel from the Food and Drug Administration, Cook Incorporated, and MED Institute on September 4, 2001.

Cook Incorporated requests that the additional information provided in this communication be considered as company confidential for an indefinite time period. Unless prior permission from Cook Incorporated has been obtained, release to the public of any information that has been noted as company confidential will be considered a violation of company rights.

It is hoped that the additional information provided herein will allow completion of review for substantial equivalence.

Sincerely,



[Handwritten signature electronically reproduced with permission]

April Lavender, RAC
Vice President, Regulatory Affairs

AL:tw
Enclosures

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification

i

D.C. #K011812

TABLE OF CONTENTS

	<u>Page No.</u>
RESPONSE TO QUESTIONS	1
EXHIBIT I. REVISED LABELING	I.1

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification
D.C. #K011812

I.1

EXHIBIT I

REVISED LABELING

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification

L2

D.C. #K011812

DRAFT LABELING

These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

SPECTRUM® VENTRICULAR DRAINAGE CATHETER SET

DESCRIPTION

The SPECTRUM® Ventricular Drainage Catheter Set allows external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain. The SPECTRUM® Ventricular Drainage Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of catheter colonization and ventriculitis during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of ventriculitis.

The SPECTRUM® Ventricular Drainage Catheter is available in a 9 Fr diameter and is nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 $\mu\text{g}/\text{cm}$), and the average amount of rifampin on the catheter is approximately 4 mg (116 $\mu\text{g}/\text{cm}$). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The minocycline and rifampin antimicrobial agents contain yellow/orange pigments, therefore, some coloration of the catheter is normal. Components supplied with the SPECTRUM® Ventricular Catheter Set include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

INDICATIONS FOR USE

The SPECTRUM® Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.

CONTRAINDICATIONS

This device is contraindicated in patients having allergy or history of allergy to tetracyclines or rifampin. **Note:** Because the SPECTRUM® Ventricular Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physician's Desk Reference*) should be considered when using this device, although there have been no reports of detected systemic levels of minocycline or rifampin in patients receiving a SPECTRUM® Catheter.

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification
D.C. #K011812

I.3

WARNINGS

- This device is not intended for permanent implantation.
- This device should not be used if dermatitis or scalp infection is present at the catheter insertion site.
- Care must be taken when using this device in patients receiving anticoagulants or those who are known to have a bleeding diathesis.
- Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headache, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may pre-dispose development of a subdural hematoma or hydroma, or collapse of the lateral ventricular walls leading to obstruction of the ventricular catheter.
- Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally raised or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.
- The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.
- Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. **Under no circumstances should the catheter be forcefully removed.** If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.
- Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTIONS

- Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be initiated after implantation.
- Inspect contents of this set for damage. If product is damaged, do not use.
- Refer to manufacturer's instructions when using accessory components other than Cook products.
- Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.
- Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions. **The catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.**

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification
D.C. #K011812

1.4

- Kinking of catheter tubing may result in restricted flow or damage to the catheter.
- Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.
- Use rubber shod forceps when handling the catheter to prevent tearing or cutting the catheter.

CLINICAL STUDY INFORMATION

•To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of ventriculitis, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The patient characteristics (gender, age, ethnicity, indication for placement, receipt of systemic antibiotics, complications, duration of catheter placement, and reason for catheter removal) were comparable in the two groups. The average duration of catheter placement was 8.2 ± 6.9 days for patients in the control arm, and 8.5 ± 5.8 days for patients in the treatment arm. Results of the clinical study show that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of ventriculitis (defined as a true positive microbiological culture of CSF) than those receiving the control catheter. The rate of ventriculitis was 9.4% (13 of 139 patients) in the control arm as compared to 1.3% (2 of 149 patients) in the treatment arm ($p=0.0022$, Chi-square). Organisms isolated from CSF cultures from the 13 patients having ventriculitis in the control group included: coagulase negative *Staphylococcus*, *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Corynebacterium*, *Klebsiella pneumonia*, coagulase positive *Staphylococcus* species, and diphtheroids. Organisms isolated from CSF cultures from patients having ventriculitis in the treatment group included *Enterobacter aerogenes*, *Enterococcus faecalis*, and *Staphylococcus aureus*. The proportions of patients free of ventriculitis as a function of the duration of placement of the catheter in each group were compared using a log-rank test on the Kaplan-Meier estimates; the conditional rates of ventriculitis per 100 catheter days were 2.6% for treatment devices as compared to 17% for control devices ($p=0.00095$ by log-rank test).

SUGGESTED INSTRUCTIONS FOR USE

1. Determine the site of insertion and aseptically prepare and drape.
2. Open the periosteum, skull, and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
3. Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
4. Carefully withdraw the stylet and check for free flow of fluid.
5. Verify proper positioning of catheter using CT or other imaging modality.

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

SPECTRUM® Ventricular Catheter - 510(k) Premarket Notification
D.C. #K011812

1.5

6. After verifying proper placement, position the barbed end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the tunneling device into the incision used for catheterization.
7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
8. After exiting the skin, pull catheter through the subcutaneous tunnel until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.
9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped or damaged. Slide snap-fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub of Luer lock adapter by sliding the snap-fit cap over the barbed portion of the adapter. **Avoid cutting or occluding tubing.**
10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie-down. Provide some slack in the catheter when securing the silicone winged tie-down to offer strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
11. Cap the catheter with the red sterile Luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

MEMORANDUM

Date: 9/5/2001

To: File K011812

Fr: Dwight Yen

cc:

Re: Cook's Spectrum Ventricular Catheter with Rifampin and Minocycline

The memo to file is specifically addressing remaining issues of:

1. Development of resistance to these antibiotics,
2. Safety of these antibiotics coated catheters for neurological use,
3. Appropriateness of these antibiotics for the types of organisms that cause shunt infections.

Development of resistance to these antibiotics:

This issue was discussed with the sponsor during a pre-IDE meeting held on February 26, 1998 (see attached Meeting Minutes). The sponsor cited results from a previous clinical study (Darouiche, 1997) for central venous catheter in which a polyurethane catheter similarly impregnated with minocycline and rifampin was compared with a catheter coated with chlorhexidine gluconate and silver sulfadiazine. The study saw no evidence suggesting emergence of resistance to either minocycline or rifampin.

Consultative review from Dr. James King, Microbiologist in the Division of Anti-Infective Drug also addressed the issue of resistance (see Review Memo Dated June 15, 1998). In this review, he states that colonization of the catheters occurs in intimate contact with the surface of the catheter where the small total amount of rifampin and minocycline is concentrated. The constant strengths of the antibiotics at the surface of the catheters should mitigate against resistance development.

Safety of these antibiotics coated catheters for neurological use:

I believe the sponsor has adequately addressed the safety of the antibiotic coated catheter for neurological use based on the successful completion of their study of 306 patients. One hundred and forty-nine (149) patients received the treatment catheters with an average duration of catheter placement of 8.5 ± 5.8 days. As Dr. Rob Harris's review indicated, the complication rate within both study groups was what was expected in a population requiring ventricular catheter placement. No complication could be attributed to the presence or absence of a chemical on the catheter.

Appropriateness of these antibiotics for the types of organisms that cause shunt infections:

This issue was also discussed with the sponsor during the pre-IDE meeting. The sponsor's reasons included: 1) the agents' broad spectrum and synergistic activity against most organisms; 2) the agents have been in use for more than 30 years; 3) the combination allows decreased reliance of first choice drugs of treatment; 4) the agents have separate mechanisms of action, which decreases the likelihood of resistance to develop; and 5) although the agents elute from the catheter, residual levels of both remain on the catheter. Results from the previously described venous catheter study showed that in matched patient arms, patients having the minocycline and rifampin impregnated catheters were twelve times less likely to have catheter related bloodstream infection, and the catheter was three times less likely to be colonized than the catheter coated with chlorhexidine gluconate and silver sulfadiazine.

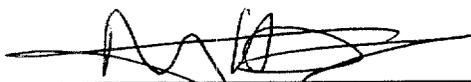
A study of the sources of infection in early colonized shunts (Bayston 1974) showed that most of these organisms involved in early shunt colonization are present on the patient at operation and do not come from the theatre environment or personnel as some have speculated. It has been suggested that colonization of vascular catheters may also be due to organisms entering the blood stream during the operation and migrating to the shunt by way of the venous catheter (Holt 1970). Central venous catheter coated with minocycline and rifampin, which has been cleared by FDA (K950118), has shown to significantly reduce the risk for catheter-related colonization and bloodstream infections.

FDA and INDUSTRY
Meeting Minutes
for
The Division of General and Restorative Devices
(DGRD)

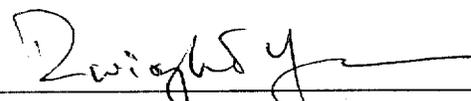
The following meeting minutes represent a record/summary of the issues and concerns raised during an interactive meeting between the DGRD and Industry. The sponsor has made the first attempt to draft their version of the meeting minutes which the DGRD has reviewed and made revisions to the minutes as deemed necessary. This process is also an attempt to verify and solidify the understandings between DGRD and Industry.

These minutes are not meant to represent written agreements between the DGRD and sponsor. Instead, their purpose is to serve as a record/summary of the issues and potential solutions with respect to the sponsor's request of the agency's opinions and guidance on a particular subject or subjects.

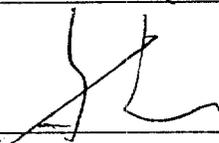
The attached minutes represent a consolidated final version of a meeting between FDA and Med Institute and took place on March 26, 1998.



Michael A. Eudy, CSO, DGRD
Date: 5-1-98



Dwight Yen, Lead Reviewer, GSDB
Date: 6/19/98



George Jan, Chief, GSDB/DGRD
Date: 6/27/98

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Memorandum**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

DATE: 16 June 1998

TO: Dwight Yen, Reviewer
CDRH/ODE/DGRD/GSDB

FROM: Rigoberto Roca, M.D. *PAR 6-17-98*
Medical Officer, DSPIDP
HFD-590

THROUGH: Marc Cavallé-Coll, M.D., Ph. D. *MJ 6-17-98*
Medical Team Leader, DSPIDP
HFD-590

SUBJECT: IDE #G980122
Cook® Incorporated Ventricular Coated (M/R) Catheter
Re: Drug Consult

The above referenced IDE is for a silicone ventricular catheter that is impregnated with minocycline and rifampin. The consultation is for a safety evaluation of the use of rifampin in this situation.

The proposed catheter is a ⁹6.5 Fr, 35 cm long catheter that will be used identically to that of standard external ventricular drainage catheters: to obtain access to a ventricular cavity in the brain for the purpose of externally draining fluid in order to relieve intracranial pressure.

The applicant indicates that the impregnation of the catheter is accomplished through a dipping process, providing a protective coating to the catheter, which will theoretically minimize the likelihood of catheter colonization. It is specifically stated that the impregnation of the catheter is meant to be for the protection/preservation of the catheter surface, and *not* for a therapeutic benefit. It is noted that for a 9 Fr catheter of 33 cm length, there is approximately 2.5 mg and 4.3 mg of rifampin and minocycline, respectively.

The applicant also provided a protocol that described the proposed patient population, the inclusion/exclusion criteria, and the safety monitoring that will be performed. Additional information regarding the preclinical animal studies and the impregnated catheter is also provided.

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Impression/Recommendation

It is believed that the rifampin, in the concentrations described, should not pose a significant clinical safety concern for the patient population that will be studied.

The issue of resistance development by the prolonged use of low doses of rifampin was discussed with Dr. James King, microbiologist reviewer from the Division of Anti-Infective Drug Products, HFD-520. It is believed that this should also not be a problem.

cc;

HFD-590/Dir/MGoldberger
HFD-590/MTL/Cavaille-Coll
HFD-590/MO/RRoca

510K Memo Record

Date: 29 August 2001

To: The record K011812

From: Dwight Yen, Electronics Engineer (HFZ 410)

Subject: Premarket notification from Cook, Inc. for the Spectrum Ventricular Catheter

Contact: April Lavender, VP Regulatory Affairs (812) 339-2235

Description: The Cook Spectrum Ventricular Catheter is a modification to Cook's ventricular catheter (K962097) currently on the market. The modification involves impregnating the catheter with a combination of antimicrobial agents (minocycline and rifampin). Cook Inc. currently markets two catheters with same combination antimicrobial agents. They are the Spectrum Silicone Foley Catheter (K000251) and the ABRM Central Venous Catheter (K950118). The antimicrobial agents are not present in a pharmacological dose in any of these catheters as shown in the table below. A penile prostheses was also recently cleared through the PDP process.

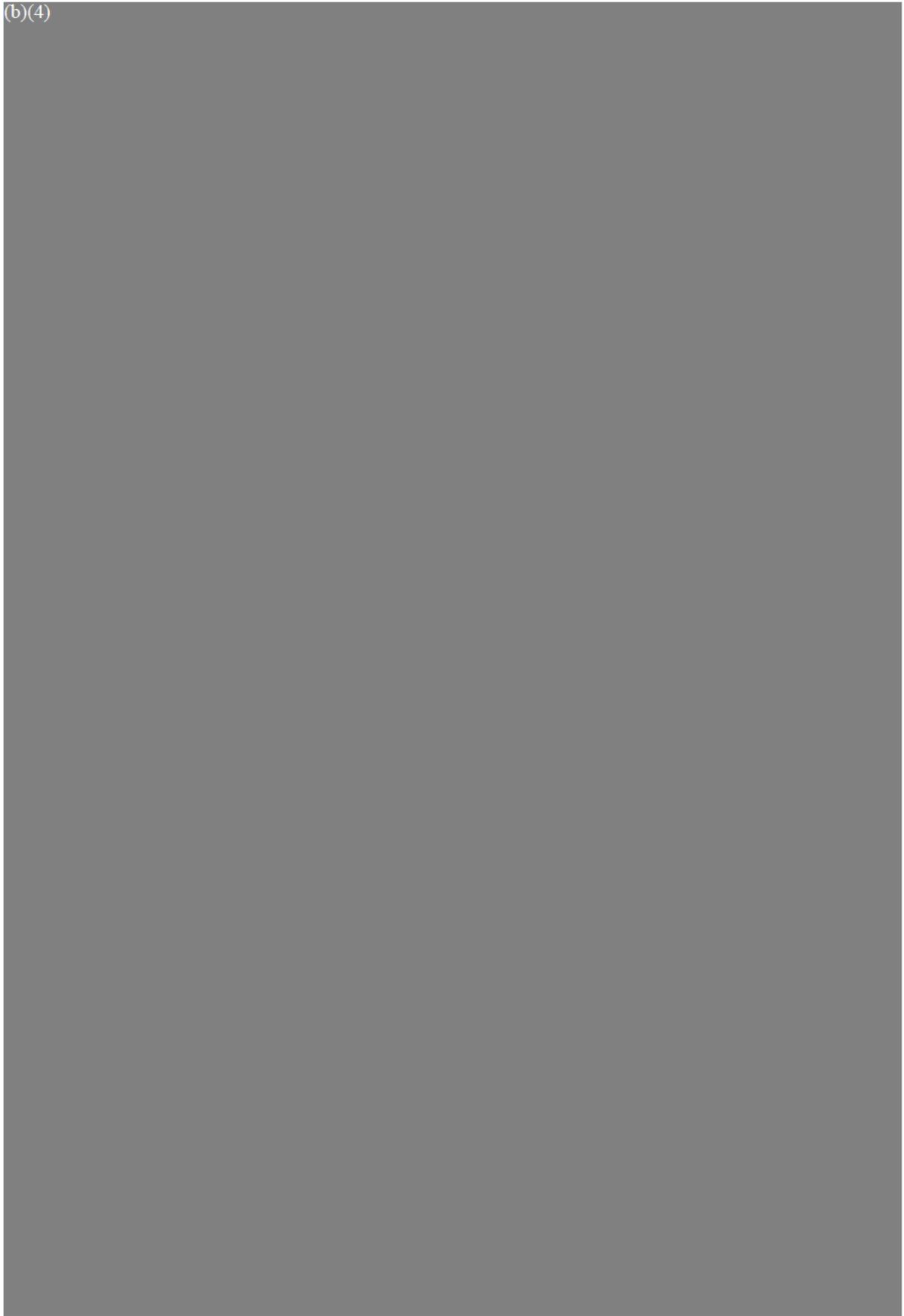
(b)(4)



(b)(4)



(b)(4)



Intended Use: The device is used for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. This intended use is SE to predicate Cook Ventricular catheter (K962097).

Predicates: The antimicrobial impregnated ventricular catheter is comparable to Cook's untreated ventricular catheter (K962097) currently on the market in terms of intended use. The antimicrobial agents and the method of impregnation are identical to Cook's foley catheter (K000251) and ABRM central venous catheter (K950118).

Labeling: Draft package labels are provided. **Dr. Harris recommends that labeling must clearly reflect that the study showed only reduction in the incidence of positive CSF cultures (a laboratory outcome). The pertinent clinical outcome, reduction in the incidence of clinical ventriculitis was not studied.**

Sterility: The device is provided sterile for single use. EtO sterilization method will be used to provide sterility to an SAL of 10^{-6} . Sterilization validation is consistent with the half cycle method as described in ANSI 11135:1994. EtO residuals will be verified to be less than the maximum allowable limits as defined in ISO 10993-7: 1995 which are 20 mg for EtO and 12 mg for ethylene chlorohydrin. Device will be packaged in a molded tray sealed within a Tyvek-Poly pouch.

Manufacture: (b)(4)



(b)(4)



Materials:

Technical:

An Indication for use, a 510K Summary, a Truthful and Accurate Statement are provided.

RECOMMENDATION: SE to predicate, 84 HCA Class II (882.4100)


Dwight Yen

COMPLETED AUG 30 2001

-MEMORANDUM

**DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration**

**Division of Neuropharmacological Drug Products (HFD-120)
Center for Drug Evaluation and Research**

Date: 7/16/01

From: Russell Katz, M.D., Division Director
*8-30-01
James R. Lytle, M.D.,
for*

Division of Neuropharmacological Drug Products, HFD-120

Subject: Spectrum Antibiotic-Impregnated Ventricular Catheter, Cook, Inc.

To: Dwight Yen
CDRH HF 410

Document type: Consultative Review
ODE1 number:

See the attached review for the Division's comments.

Consultative Review and Evaluation of Clinical Data

Consult (Serial Number)	6467
Sponsor:	Cook
Device:	Antibiotic Impregnated Ventricular Catheter
Proposed Indication:	Intraventricular Drainage of CSF
Material Submitted:	510 (k) Submission
Consult Date:	11 July 2001
Date Received / Division:	7/16/01/DNDP
Date Review Completed:	7/16/01
Reviewer:	Rob Harris, M.D., Ph.D.

1. Introduction

The Cook Group intends to market an external ventricular catheter for CSF drainage, monitoring and antibiotic instillation. Coating of catheters with antimicrobial agents has been demonstrated both in vitro and in vivo to decrease adherence and colonization of microbes to catheter surfaces. The Spectrum Catheter is coated with minocycline and rifampin and is comparable to other Cook Spectrum catheters currently employed in urology. This premarket notification submission contains the results of a clinical trial of 288 evaluated patients out of 306 enrollees. The results indicate the product is safe and reduces intraventricular CSF catheter microbial colonization, a laboratory finding.

CDRH requests clinical neurosurgical/neurological opinion for the submission.

2. Comments

(b)(4)



(b)(4)

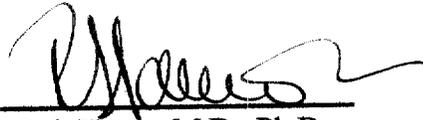


79

(b)(4)



80



Rob Harris, M.D., Ph.D.
Medical Reviewer

J. Feeney, MD


8/23/01

rdh
cc:
HFD-120
CON

Yen, Dwight

From: Bushar, Harry F.
nt: Tuesday, July 17, 2001 5:08 PM
to: Yen, Dwight
Cc: Ogden, Neil; Witten, Celia; Dawisha, Sahar; Campbell, Gregory; Roberson, Helen W.
Subject: Statistical Review of 510(k) K011812 for Cook SPECTRUM Ventricular Catheter

As requested, I have reviewed 510(k) K011812 for Cook SPECTRUM Ventricular Catheter, an external ventricular drainage catheter impregnated with a combination of anti-microbial agents (minocycline and rifampin), which is intended to obtain access to a ventricular cavity of the brain for relieving elevated intra-cranial pressure or fluid volume. The sponsor has conducted a prospective, randomized, multi-center clinical trial "to evaluate the efficacy of the SPECTRUM Ventricular Catheter in preventing ventriculitis". (See page 18.) My comments are the following:

(b)(4)



Please contact me for any further review of this submission.

Harry F. Bushar, Ph.D.
Mathematical Statistician
Phone: (301) 827-4361

82

Screening Checklist

For all Premarket Notification 510(k) Submissions

3-30-01

Device Name:						K					
Submitter (Company):											
Items which should be included (circle missing & needed information)						✓ IF ITEM IS NEEDED AND IS MISSING					
						SPECIAL	ABBREVIATED	TRADITIONAL			
						YES	NO	YES	NO	YES	NO
1. Cover Letter clearly identifies Submission as:											
a) "Special 510(k): Device Modification"											
b) "Abbreviated 510(k)"											
c) Traditional 510(k)						GO TO # 2,3		GO TO # 2,4,5		GO TO #2, 5	
2. GENERAL INFORMATION: REQUIRED IN ALL 510(K) SUBMISSIONS								✓ IF ITEM IS NEEDED AND IS MISSING			
Financial Certification or Disclosure Statement for 510(k)s with a Clinical Study 807.87(i) including forms 3454 and/or 3455						NA		YES		NO	
						SPECIALS		ABBREVIATED		TRADITIONAL	
						YES	NO	YES	NO	YES	NO
a) trade name, classification name, establishment registration number, device class											
b) OR a statement that the device is not yet classified						FDA-may be a classification request; see coordinator					
c) identification of legally marketed equivalent device						NA					
d) compliance with Section 514 - performance standards						NA					
e) address of manufacturer											
f) Truthful and Accurate Statement											
g) Indications for Use enclosure											
h) SMDA Summary or Statement (FOR ALL DEVICE CLASSES)											
i) Class III Certification & Summary (FOR ALL CLASS III DEVICES)											
j) Description of device (or modification) including diagrams, engineering drawings, photographs, service manuals											
k) Proposed Labeling:											
i) package labeling (user info)											
ii) statement of intended use											
iii) advertisements or promotional materials											
i) MRI compatibility (if claimed)											
l) Comparison Information (similarities and differences) to named legally marketed equivalent device (table preferred) should include:											
i) Labeling											
ii) intended use											
iii) physical characteristics											
iv) anatomical sites of use											
v) performance (bench, animal, clinical) testing						NA					
vi) safety characteristics						NA					
m) If kit, kit certification											
3. "SPECIALS" - ONLY FOR MODIFICATIONS TO MANUFACTURER'S OWN CLASS II, III OR RESERVED CLASS I DEVICE											
a) Name & 510(k) number of legally marketed (unmodified) predicate device											
b) STATEMENT - INTENDED USE AND INDICATIONS FOR USE OF MODIFIED DEVICE AS DESCRIBED IN ITS								* If no - STOP not a special			

83

LABELING HAVE NOT CHANGED*				
c) STATEMENT - FUNDAMENTAL SCIENTIFIC TECHNOLOGY OF THE MODIFIED DEVICE HAS NOT CHANGED*				* If no - STOP not a special
d) Design Control Activities Summary				
i) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis				
ii) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied				
iii) A declaration of conformity with design controls. The declaration of conformity should include:				
1) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met				
2) A statement signed by the individual responsible, that manufacturing facility is in conformance with design control procedure Requirements as specified in 21 CFR 820.30 and the records are available for review.				

	SPECIALS		ABBREVIATED		TRADITIONAL		✓ IF ITEM IS NEEDED AND IS MISSING
	YES	NO	YES	NO	YES	NO	
4. ABBREVIATED 510(K): SPECIAL CONTROLS/CONFORMANCE TO RECOGNIZED STANDARDS - PLEASE FILL OUT THE STANDARDS ABBREVIATED FORM ON THE H DRIVE							
a) For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type							
b) If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.							
c) For a submission, which relies on a recognized standard, a declaration of conformity to the standard. The declaration should include the following:							
i) An identification of the applicable recognized consensus standards that were met							
ii) A specification, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below							
iii) An identification, for each consensus standard, of							

84

any way(s) in which the standard may have been adapted for application to the device under review, e.g., an identification of an alternative series of tests that were performed			
iv) An identification, for each consensus standard, of any requirements that were not applicable to the device			
v) A specification of any deviations from each applicable standard that were applied			
vi) A specification of the differences that may exist, if any, between the tested device and the device to be marketed and a justification of the test results in these areas of difference			
vii) Name/address of test laboratory/certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations			
d) Data/information to address issues not covered by guidance documents, special controls, and/or recognized standards			

5. Additional Considerations: (may be covered by Design Controls)									
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:									
i) component & material									
ii) identify patient-contacting materials									
iii) biocompatibility of final sterilized product									
b) Sterilization and expiration dating information:									
i) sterilization method									
ii) SAL									
iii) packaging									
iv) specify pyrogen free									
v) ETO residues									
vi) radiation dose									
c) Software validation & verification:									
i) hazard analysis									
ii) level of concern									
iii) development documentation									
iv) certification									

Items shaded under "NO" are necessary for that type of submission. Circled items and items with checks in the "Needed & Missing" column must be submitted before acceptance of the document.

Passed Screening _____ Yes _____ No
 Date: _____

Reviewer: _____
 Concurrence by Review Branch: _____

85

REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENC" (SE) DECISION MAKING DOCUMENTATION

K _____

Reviewer: _____

Division/Branch: _____

Device Name: _____

Product To Which Compared (510(K) Number If Known): _____

	YES	NO	
1. Is Product A Device			If NO = Stop
2. Is Device Subject To 510(k)?			If NO = Stop
3. Same Indication Statement?			If YES = Go To 5
4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If YES = Stop NE
5. Same Technological Characteristics?			If YES = Go To 7
6. Could The New Characteristics Affect Safety Or Effectiveness?			If YES = Go To 8
7. Descriptive Characteristics Precise Enough?			If NO = Go To 10 If YES = Stop SE
8. New Types Of Safety Or Effectiveness Questions?			If YES = Stop NE
9. Accepted Scientific Methods Exist?			If NO = Stop NE
10. Performance Data Available?			If NO = Request Data
11. Data Demonstrate Equivalence?			Final Decision:

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

1. Intended Use:
2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device over-the-counter or prescription use? Does the device contain drug or biological product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:
2. Explain why not subject to 510(k):
3. How does the new indication differ from the predicate device's indication:
4. Explain why there is or is not a new effect or safety or effectiveness issue:
5. Describe the new technological characteristics:
6. Explain how new characteristics could or could not affect safety or effectiveness:
7. Explain how descriptive characteristics are not precise enough:
8. Explain new types of safety or effectiveness questions raised or why the questions are not new:
9. Explain why existing scientific methods can not be used:
10. Explain what performance data is needed:
11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		
2. Did we grant expedited review?		
3. Have you verified that the Document is labeled Class III for GMP purposes?		
4. If, not, has POS been notified?		
5. Is the product a device?		
6. Is the device exempt from 510(k) by regulation or policy?		
7. Is the device subject to review by CDRH?		
8. Are you aware that this device has been the subject of a previous NSE decision?		
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		
10. Are you aware of the submitter being the subject of an integrity investigation?		
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		

88

COOK®

K011812-A

Cook Incorporated
P.O. Box 489
Bloomington, IN 47402-0489
Phone: 812 339-2235
Fax: 812-339-5369
www.cookgroup.com

July 10, 2001

Office of Device Evaluation
Document Mail Center (HFZ-401)
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

RECEIVED
JUL 11 2 45 PM '01
FOIA/CDRH/OCE/DID

RE: 510(k) Premarket Notification for the SPECTRUM® Ventricular Catheter
D.C.# K011812

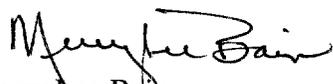
Dear Sir or Madam:

The purpose of this letter is to provide additional information for the 510(k) Premarket Notification for the SPECTRUM® Ventricular Catheter (D.C. #K011812) submitted to the Food and Drug Administration on June 11, 2001.

Please refer to Exhibit IV (attached) for financial disclosure information on the investigators participating in the clinical study of the SPECTRUM® Ventricular Catheter. Also included is additional information regarding results of the clinical evaluation of the SPECTRUM® Ventricular Catheter. Please amend the premarket notification accordingly.

Cook Incorporated requests that the additional information provided in this communication be considered as company confidential for an indefinite time period, as requested for the information contained in the original premarket notification submission.

Sincerely,
Cook Incorporated



Merry Lee Bain
Sr. Vice President Regulatory Affairs/QA

twh:MLB

Enclosure

SK23 89

TABLE OF CONTENTS

	<u>Page No.</u>
ADDITIONAL INFORMATION REGARDING RESULTS OF THE CLINICAL EVALUATION OF THE SPECTRUM® VENTRICULAR CATHETER	1
EXHIBIT IV FINANCIAL DISCLOSURE INFORMATION	IV.1

**COMPANY
CONFIDENTIAL**

**Additional Information Regarding Results of the Clinical
Evaluation of the Spectrum® Ventricular Catheter**

(b)(4)

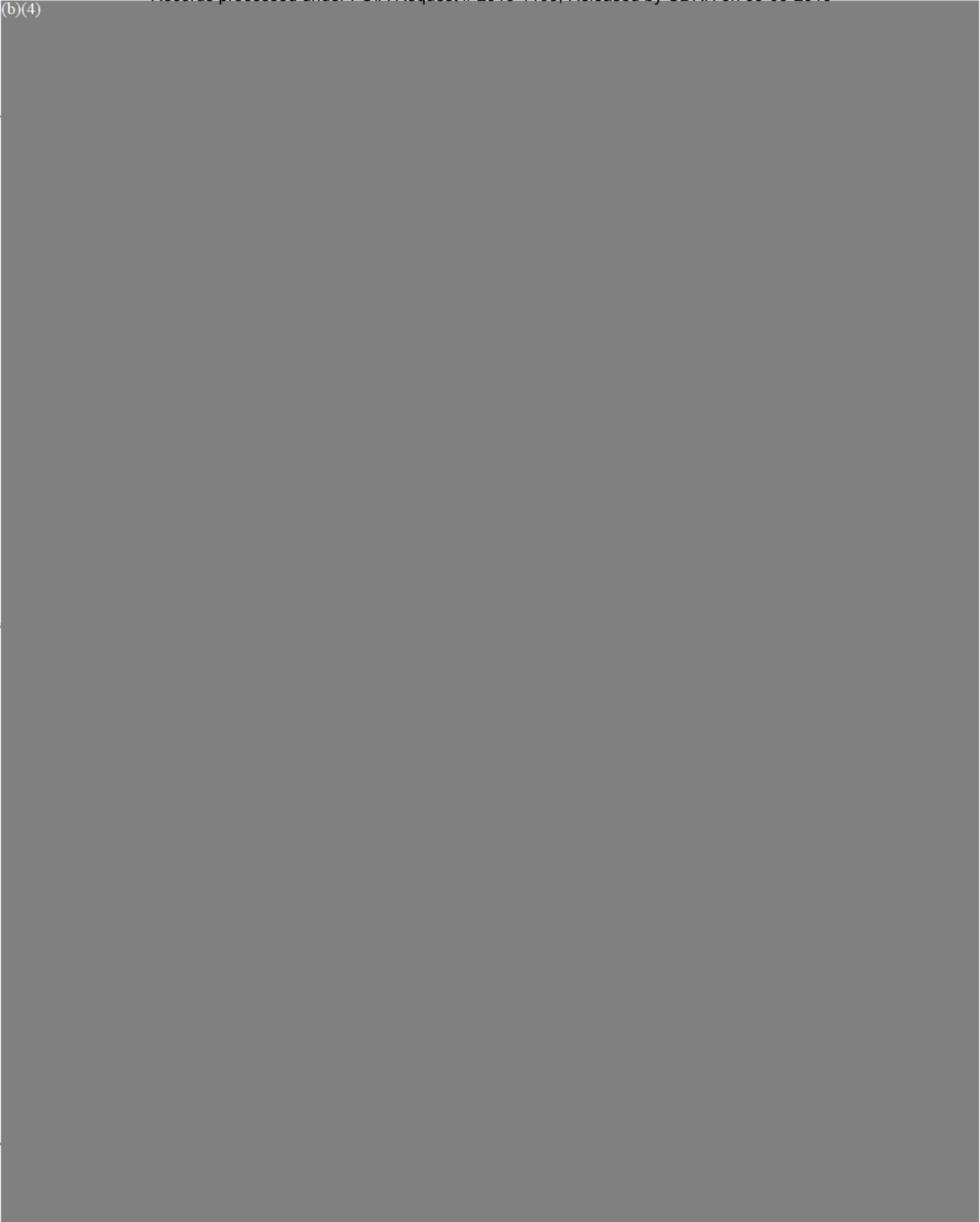


91

EXHIBIT IV

FINANCIAL DISCLOSURE INFORMATION

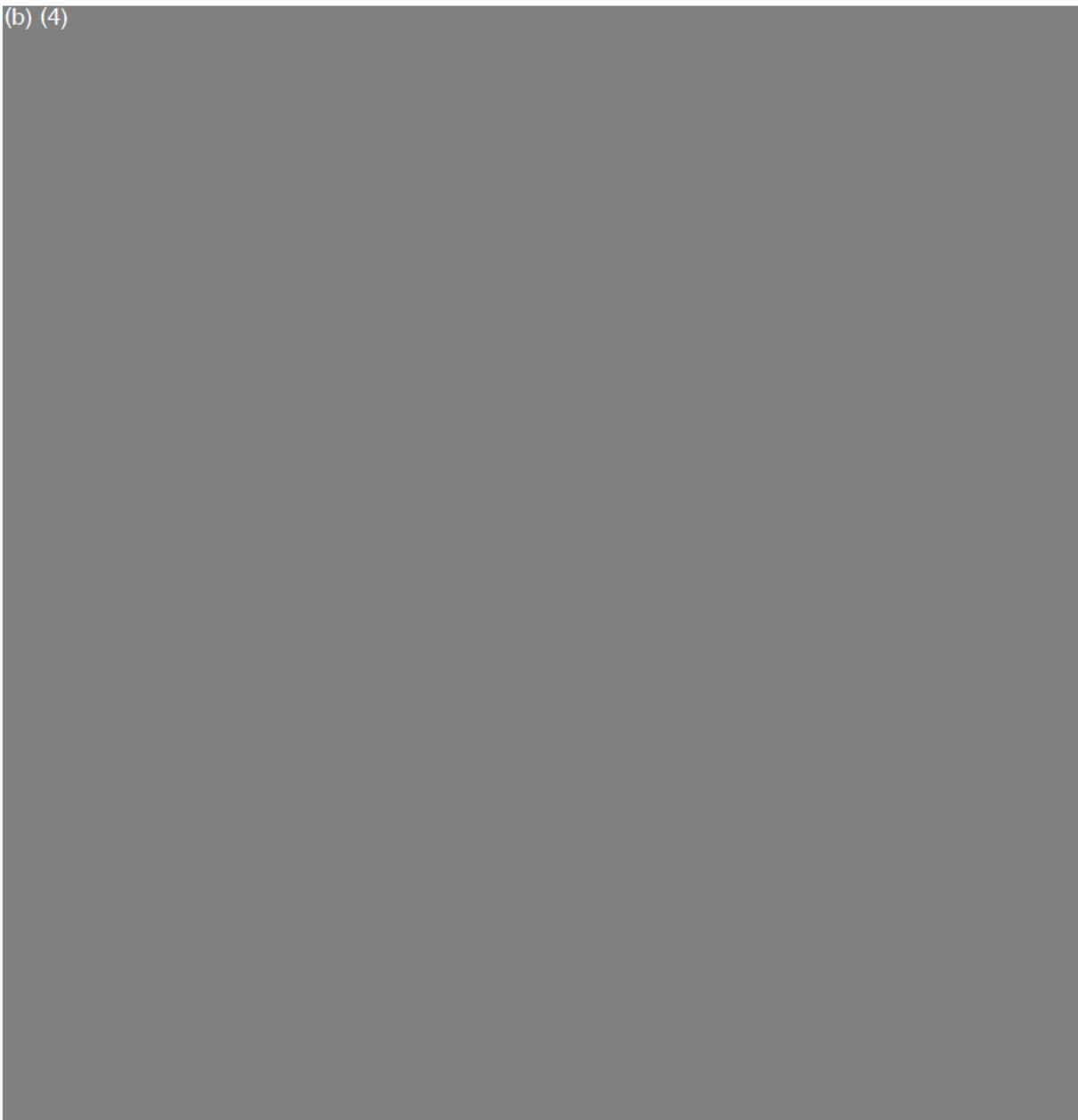
(b)(4)



Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

(b) (4)



**COMPANY
CONFIDENTIAL**

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

June 11, 2001

COOK, INC.
925 SOUTH CURRY PIKE
P.O. BOX 489
BLOOMINGTON, IN 47402
ATTN: APRIL LAVENDER

510(k) Number: K011812
Received: 11-JUN-2001
Product: SPECTRUM VENTRICULAR
CATHETER

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

On January 1, 1996, FDA began requiring that all 510(k) submitters provide on a separate page and clearly marked "Indication For Use" the indication for use of their device. If you have not included this information on a separate page in your submission, please complete the attached and amend your 510(k) as soon as possible. Also if you have not included your 510(k) Summary or 510(k) Statement, or your Truthful and Accurate Statement, please do so as soon as possible. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers Assistance (DSMA) at the telephone or web site below for more information.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the Document Mail Center will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the Document Mail Center (HFZ-401).

You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMA. If you have other procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact DSMA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address <http://www.fda.gov/cdrh/dsmamain.html> or me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Staff
Office of Device Evaluation

COOK®

Cook Incorporated
P.O. Box 489
Bloomington, IN 47402-0489
Phone: 812 339-2235
Fax: 812 339-5369
www.cookgroup.com

June 8, 2001

Office of Device Evaluation
Document Mail Center (HFZ-401)
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

RECEIVED
JUN 11 2 52 PM '01
FDA/CDRH/OCE/DID

RE: 510(k) Premarket Notification for the SPECTRUM® Ventricular Catheter
With Request for Expedited Review

Dear Sir or Madam:

The purpose of this letter is to notify the Food and Drug Administration, pursuant to Section 510(k) of the Federal Food, Drug and Cosmetic Act, that Cook Incorporated intends to manufacture, market and distribute the SPECTRUM® Ventricular Catheter. This external ventricular drainage catheter has the same intended use as the predicate Cook Ventricular Catheter, which is to obtain access to a ventricular cavity of the brain for relieving elevated intracranial pressure or fluid volume. An added feature is catheter impregnation with a combination of antimicrobial agents (minocycline and rifampin), which makes the device similar to predicate Cook SPECTRUM® catheters with respect to technology. The antimicrobial agents are not present in a pharmacological dose. Results from a randomized clinical study of the SPECTRUM® Ventricular Catheter, described herein, show patients receiving this catheter are significantly less likely to develop ventriculitis than those receiving a standard, non-coated catheter. Because of the significance shown and the fact that no other antimicrobial-coated ventricular drainage catheters are currently commercially available, we are hereby requesting expedited review of this premarket notification.

The following information pertaining to the SPECTRUM® Ventricular Catheter is submitted:

1. Trade/Proprietary Name: SPECTRUM® Ventricular Catheter
Common/Usual Names: Ventricular Catheter, External Drainage Catheter
2. Establishment Name: Cook Incorporated
Establishment Registration Number: 1820334

WE II

SK26

98

3. Proposed Classification: Central Nervous System Fluid Shunt and Components
21 CFR Part 882.5550 (84JXG)
Class II

Ventricular drainage catheters have been classified into Class II by the Center for Devices and Radiological Health with concurrence of the Neurological Devices Panel.

4. No performance standards have been established under Section 514 of the Federal Food, Drug, and Cosmetic Act applicable to external ventricular drainage catheters.
5. Draft labeling for the SPECTRUM® Ventricular Catheter includes outer package labeling and suggested instructions for use, which are enclosed as Exhibit I.
6. The SPECTRUM® Ventricular Catheter is comparable to the predicate devices listed below. Please refer to Section 8 and Exhibit II for product information on these devices.

MANUFACTURER

DEVICE

Cook Incorporated

Ventricular Catheter
Order #HVDC-110-33
D.C. #K962097 (84JXG)

Cook Urological, Inc. and
Cook OB/GYN™

SPECTRUM® Silicone Foley Catheter
Order #FSC-200037-05-CE-ABRM
D.C. #K000251 (78MJC,EZL)

Cook Incorporated

Cook SPECTRUM® Catheter (ABRM Catheter)
Order #C-UTLM-701J-RSC-ABRM
D.C. #K950118 (80FOZ)

7. See Sections 1 through 8 as enclosed for information describing the SPECTRUM® Ventricular Catheter including intended use, device description (materials of composition and device specifications), packaging and sterilization information, method of use, performance information including *in vitro* and *in vivo* testing and clinical evaluation, and comparison to predicate devices.
8. Refer to Section 9 for the 510(k) summary.

Cook Incorporated's intent to market this device is confidential commercial information and we request that it be considered as such by the FDA and not available through Freedom of Information except where required by law. Cook Incorporated requests that the contents of the premarket notification submission be considered as company

confidential for an indefinite time period. Unless prior permission from Cook Incorporated has been obtained, release to the public of any information which has been noted as company confidential will be considered a violation of the company's rights.

Please refer to Exhibit IV for financial disclosure information on the investigators participating in the clinical study of the SPECTRUM® Ventricular Catheter.

It is hereby certified, to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been knowingly omitted.

Sincerely,
Cook Incorporated



[Handwritten signature electronically reproduced with permission]

April Lavender, RAC
Vice President
Regulatory Affairs

AL:mlb

Enclosure

100

510(k) Number (if known): K01XXXX

Device Name: SPECTRUM® Ventricular Catheter

Indications For Use:

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _____ OR Over-The-Counter Use _____

(Per 21 CFR 801.109)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118 (Optional Format 1-2-96)

TABLE OF CONTENTS

	<u>Page No.</u>
1 INTENDED USE	1
2 MATERIALS OF COMPOSITION	1
3 DEVICE DESCRIPTION/SPECIFICATIONS	2
4 PACKAGING INFORMATION	4
5 STERILIZATION INFORMATION	5
6 METHOD OF OPERATION	5
7 PERFORMANCE INFORMATION	7

(b)(4)



. 7
. 8
. 9
. 9
. 9
10

10
12
13

13

15
16
16

17
18
20
22
22
25
27
37
38
39

102

8	COMPARISON TO PREDICATE DEVICES	40
9	510(K) SUMMARY	42

FIGURES

FIGURE 1	SPECTRUM® VENTRICULAR CATHETER	2
FIGURE 2	KAPLAN-MEIER SURVIVAL CURVES FOR FREEDOM FROM VENTRICULITIS	33

TABLES

TABLE 1	HPLC ANALYSIS	12
TABLE 2	HPLC ANALYSIS FROM ELUTION STUDY	13
TABLE 3	ZONE OF INHIBITION TESTING	15
TABLE 4	ZONE OF INHIBITION TESTING RESULTS FROM ELUTION STUDY	16
TABLE 5	ZONE OF INHIBITION TESTING RESULTS TO DETERMINE SHELF LIFE STABILITY	17
TABLE 6	DISTRIBUTION OF PATIENT ENROLLMENT AMONG THE SIX SITES	23
TABLE 7	PATIENT CHARACTERISTICS	24
TABLE 8	COMPLICATIONS REPORTED IN THE CLINICAL STUDY ...	25
TABLE 9	SYSTEMIC ANTIBIOTICS ADMINISTERED	30
TABLE 10	ORGANISMS ISOLATED FROM CSF CULTURES	31
TABLE 11	COLONIZATION OF CATHETERS WITH RESPECT TO DURATION OF PLACEMENT	34
TABLE 12	ORGANISMS CULTURED FROM VENTRICULAR CATHETERS	34
TABLE 13	RESULTS OF SUSCEPTIBILITY TESTING OF CATHETER ISOLATES	36
TABLE 14	SPECTRUM® VENTRICULAR CATHETER AND COMPARABLE PREDICATE DEVICES	41

EXHIBITS

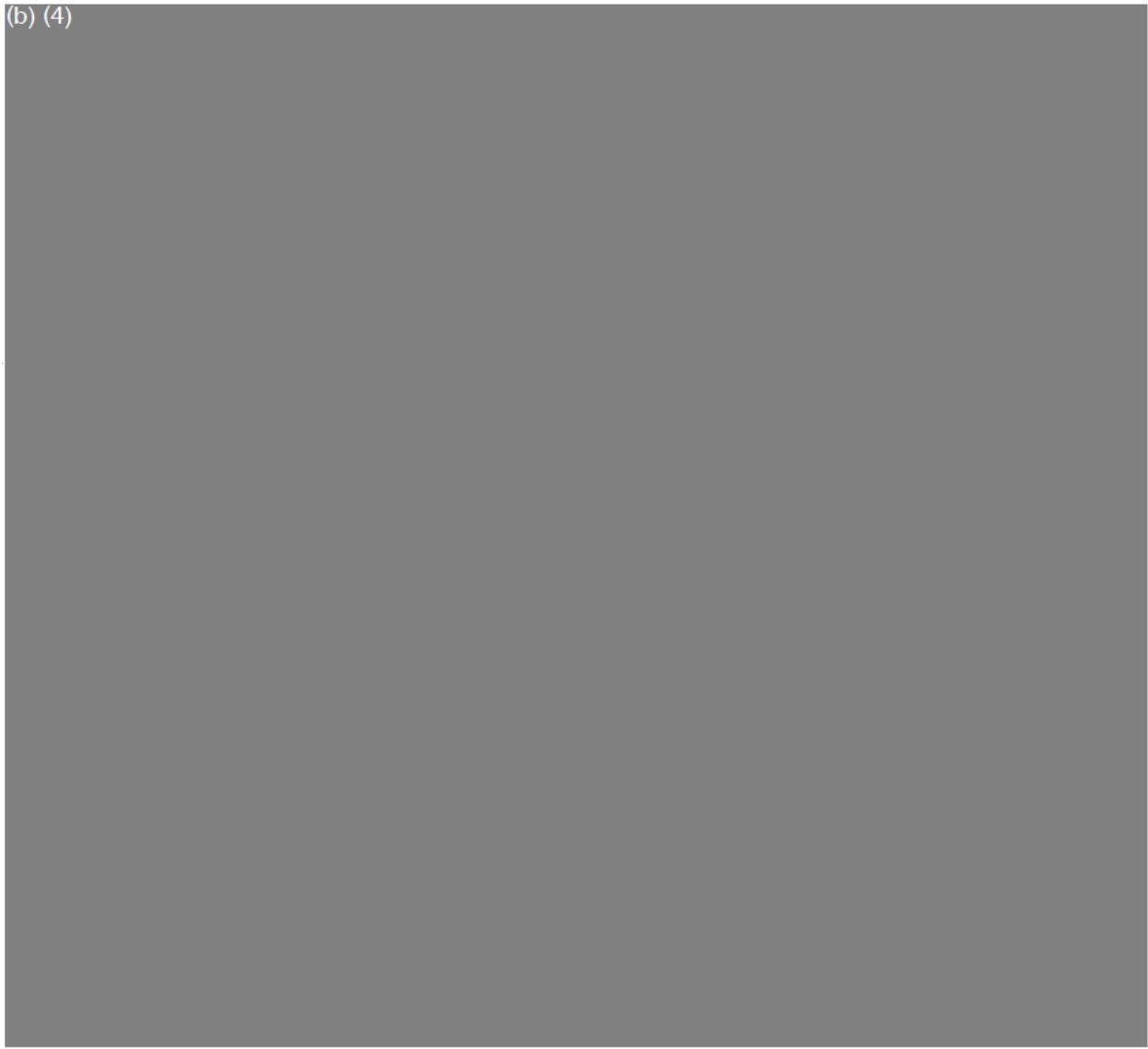
EXHIBIT I	DRAFT LABELING	I.1
EXHIBIT II	PRODUCT SHEETS FOR PREDICATE DEVICES	II.1
EXHIBIT III	BIOCOMPATIBILITY TESTING	III.1

1 INTENDED USE

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

2 MATERIALS OF COMPOSITION

(b) (4)

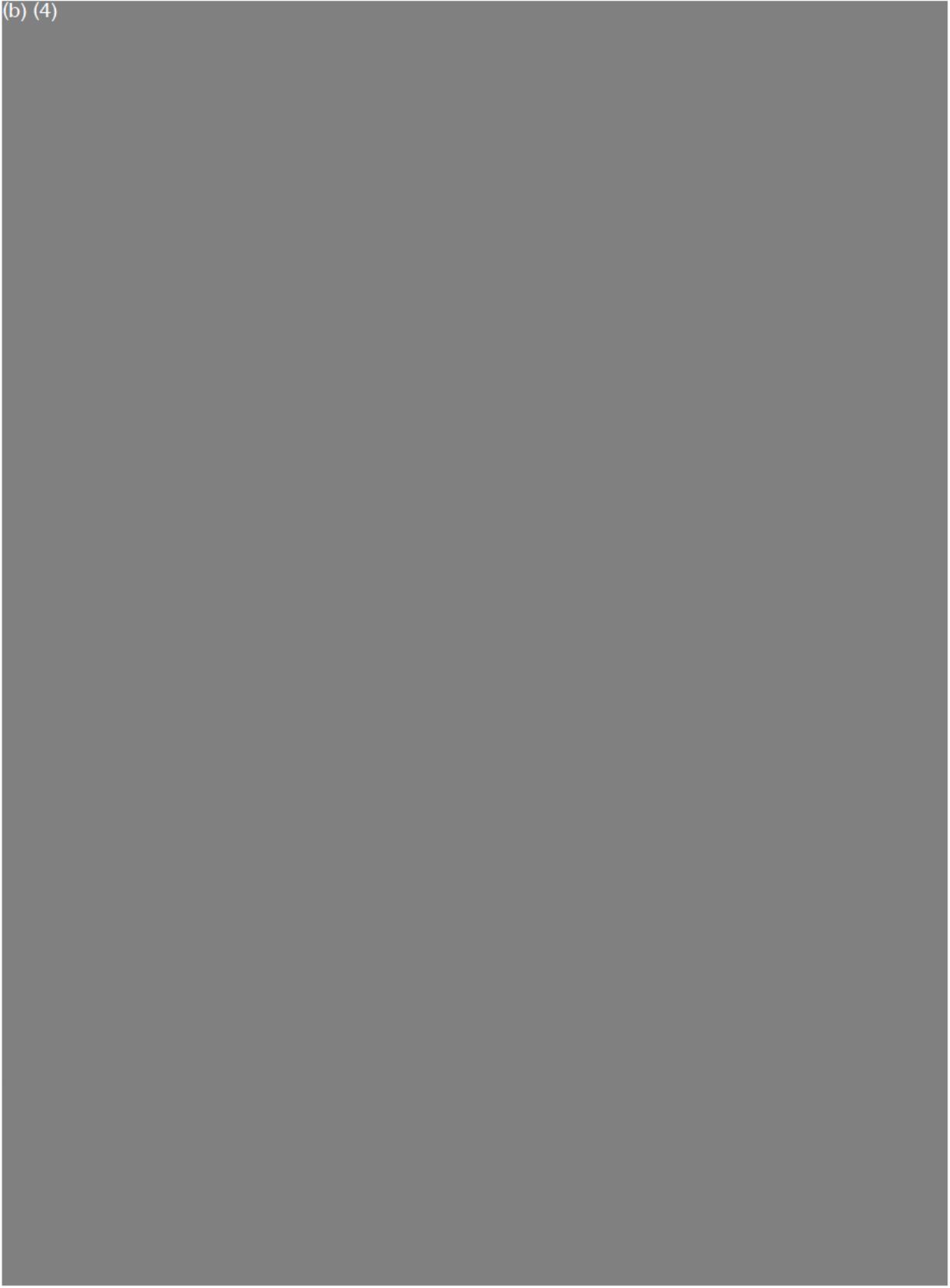


3 DEVICE DESCRIPTION/SPECIFICATIONS

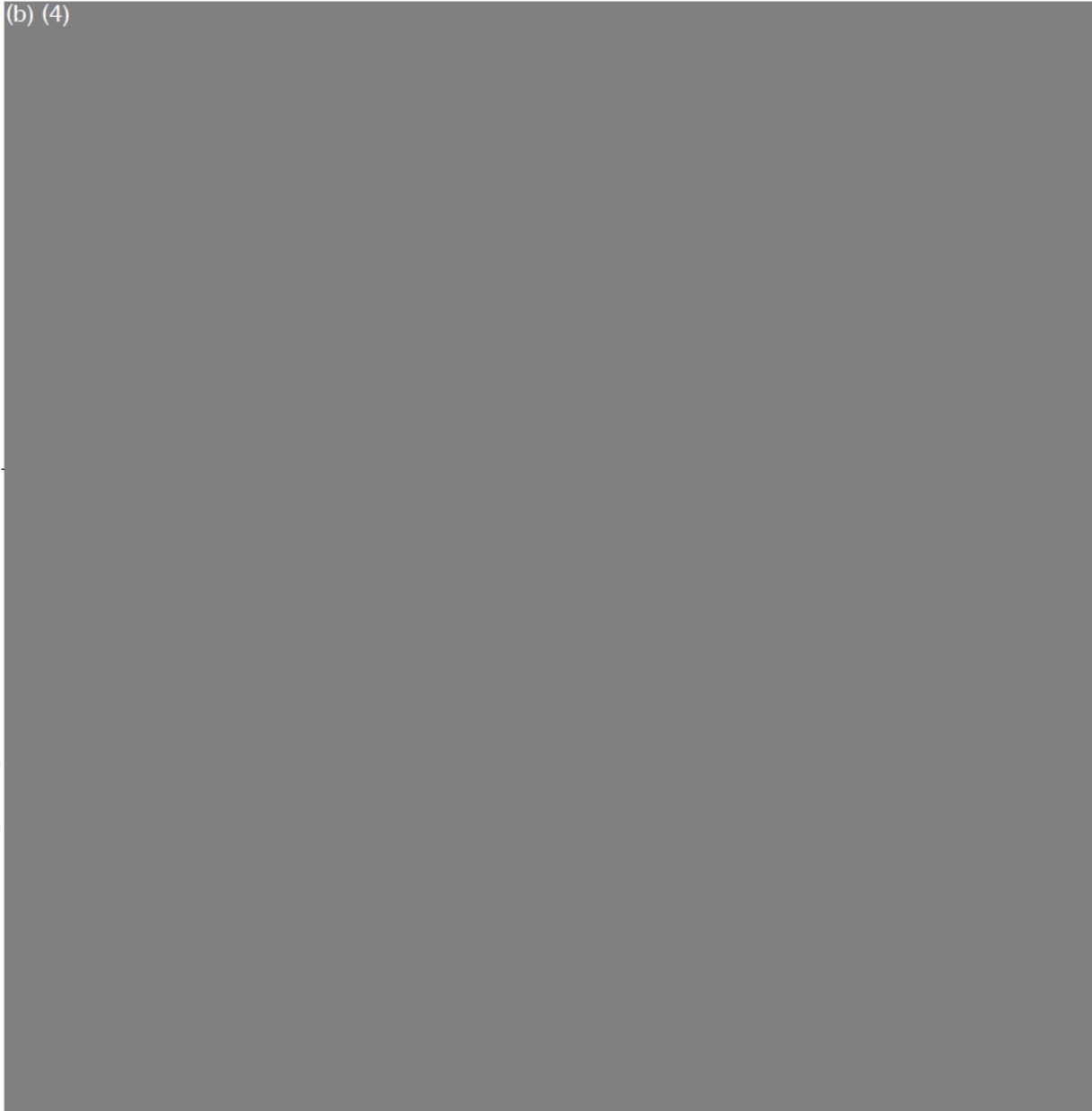
(b) (4)



(b) (4)



(b) (4)



4 PACKAGING INFORMATION

Each unit will be packaged in a molded tray sealed within a Tyvek-Poly pouch and properly labeled. This packaging system has a long history of use in Cook Incorporated processing. Packaging will include suggested instructions for use. After packaging, an accountability form will be completed for subsequent sterilization of the SPECTRUM® Ventricular Catheter.

5 STERILIZATION INFORMATION

The SPECTRUM[®] Ventricular Catheter will be supplied sterile, with sterilization to be performed at Cook Incorporated, 6300 North Matthews Drive, Ellettsville, Indiana (establishment registration number 1820334). Using an ethylene oxide (EtO) gas cycle, a 10^{-6} sterility assurance level will be obtained. The established method used to validate the sterilization cycle is consistent with the half-cycle method as described in ANSI/AAMI/ISO 11135:1994 *Medical Devices Validation and Routine Control of Ethylene Oxide Sterilization*. The sterilization cycle used for the device will be validated. Using the exhaustive extraction technique, the EtO sterilization residuals will be verified to be less than the maximum allowable limits as defined in ISO 10993-7: 1995, which are 20 mg for ethylene oxide and 12 mg for ethylene chlorohydrin.

6 METHOD OF OPERATION

(b) (4)



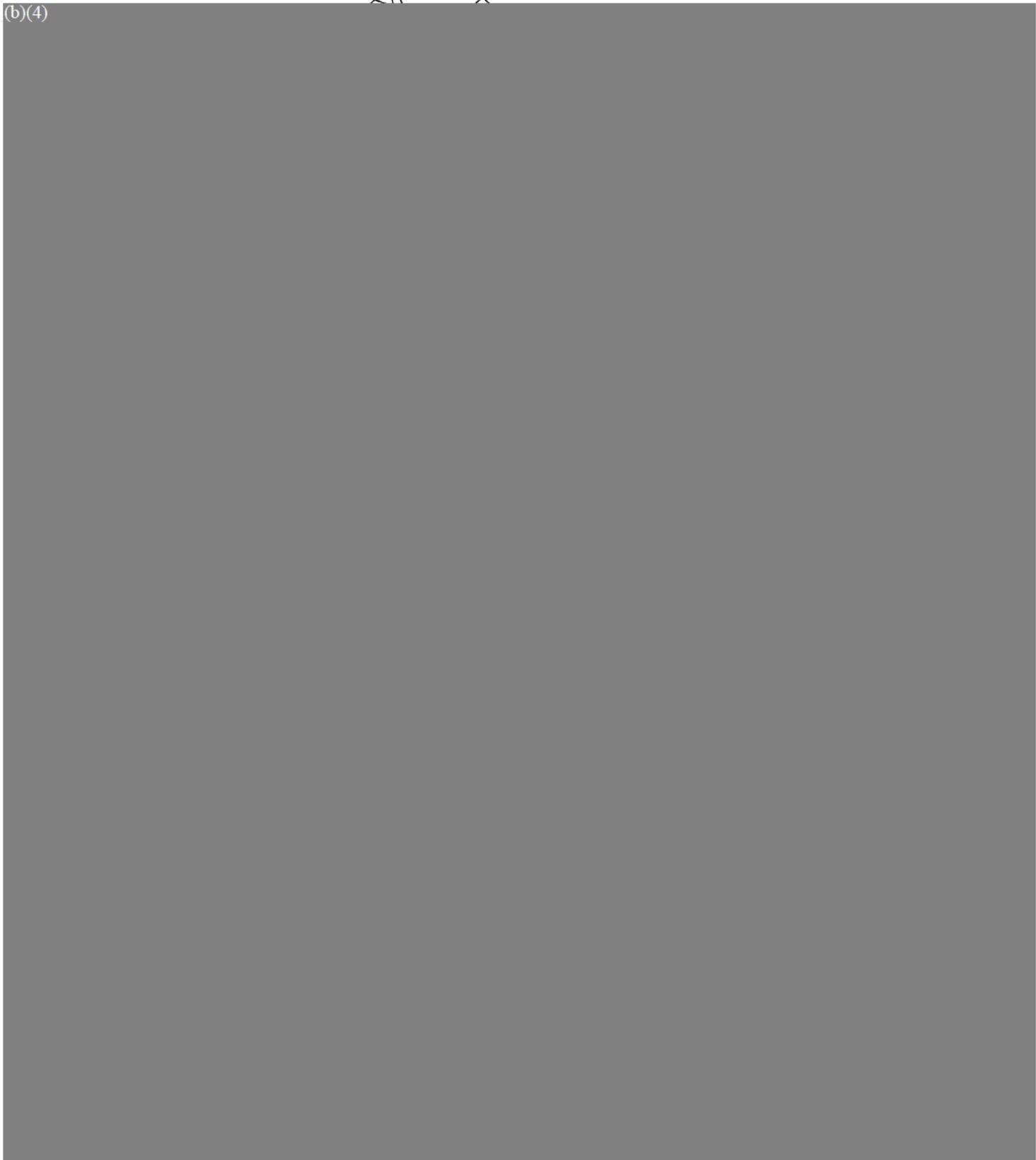
(b) (4)



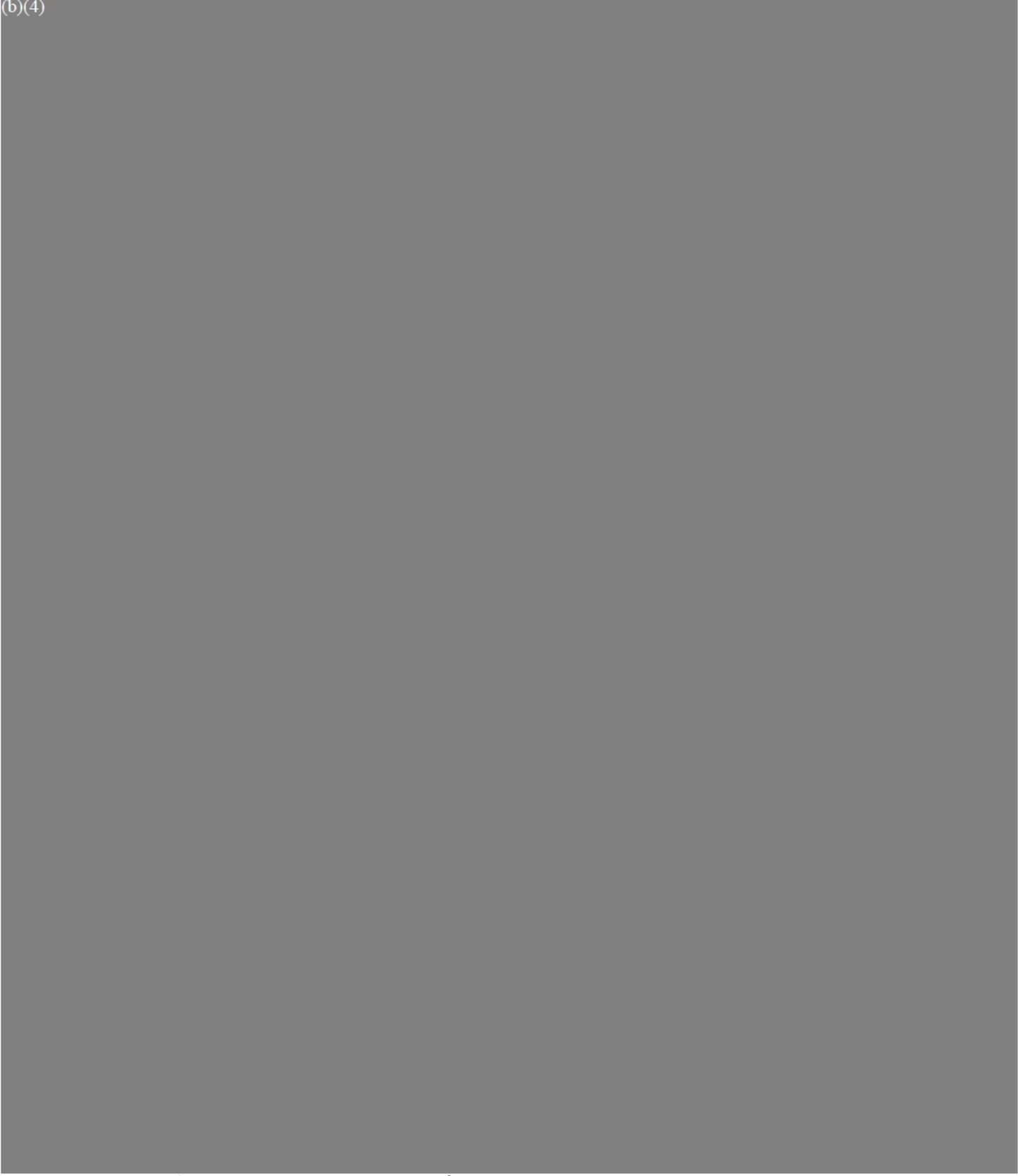
109

7 PERFORMANCE INFORMATION

(b)(4)



(b)(4)



111

(b)(4)



112

SPECTRUM® Ventricular Catheter
510(k) Premarket Notification

(b) (4)



(b) (4)



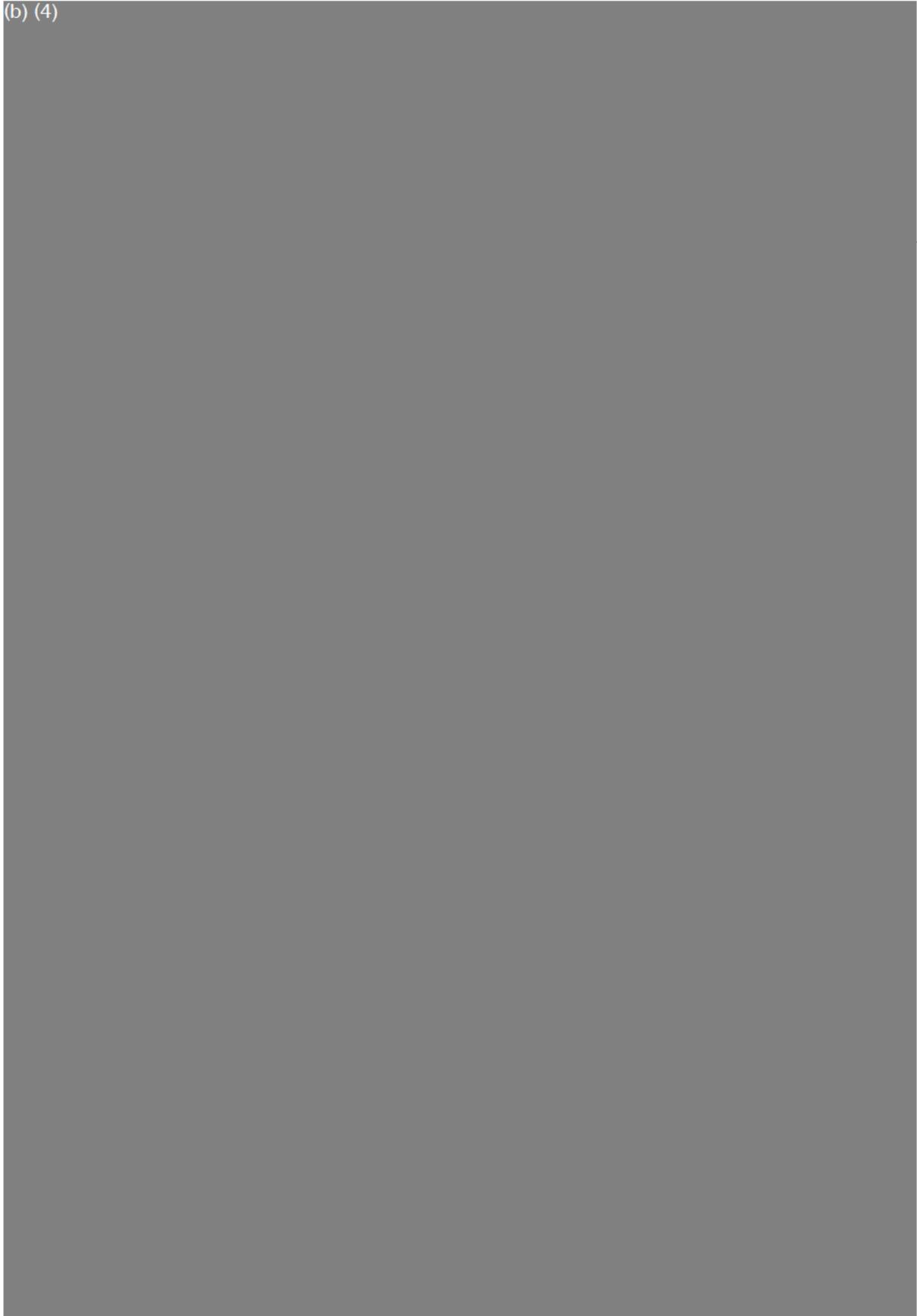
114

(b) (4)



115

(b) (4)



(b) (4)

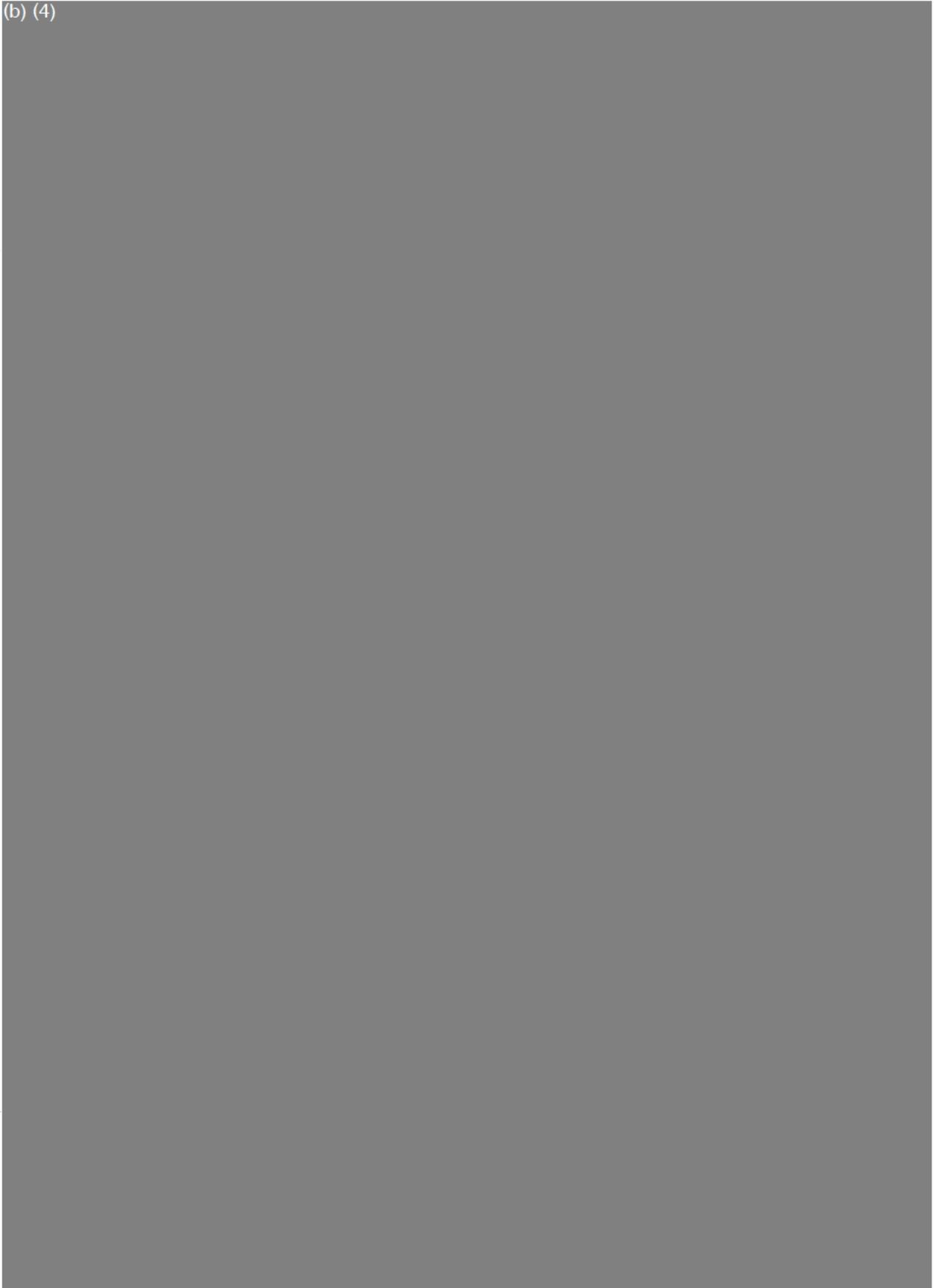


117

(b) (4)



(b) (4)



119

(b) (4)

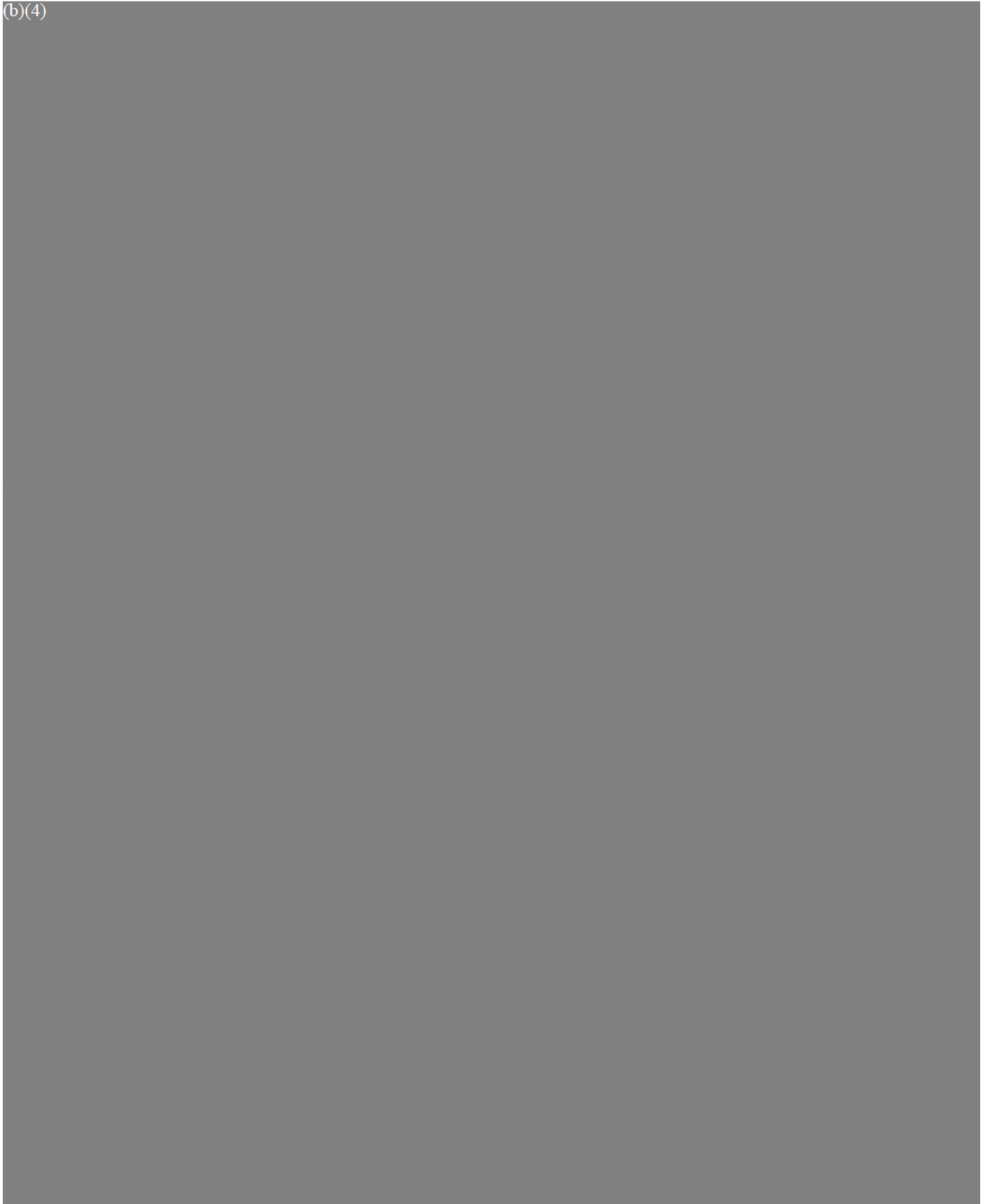


7.3 Clinical Evaluation of the SPECTRUM® Ventricular Catheter

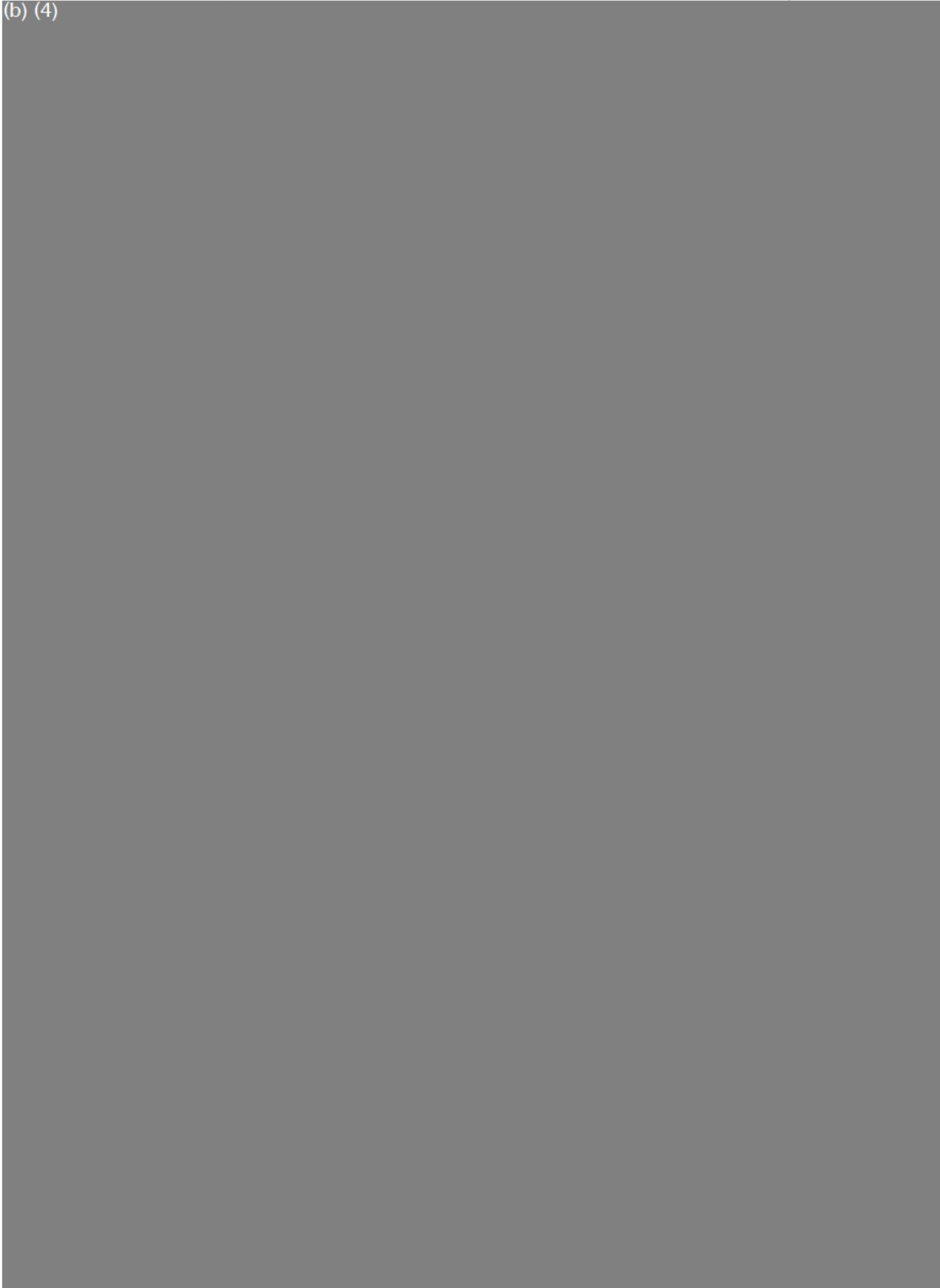
(b) (4)



(b)(4)



(b) (4)



122

(b)(4)



123

(b) (4)



124

(b)(4)



125

(b) (4)



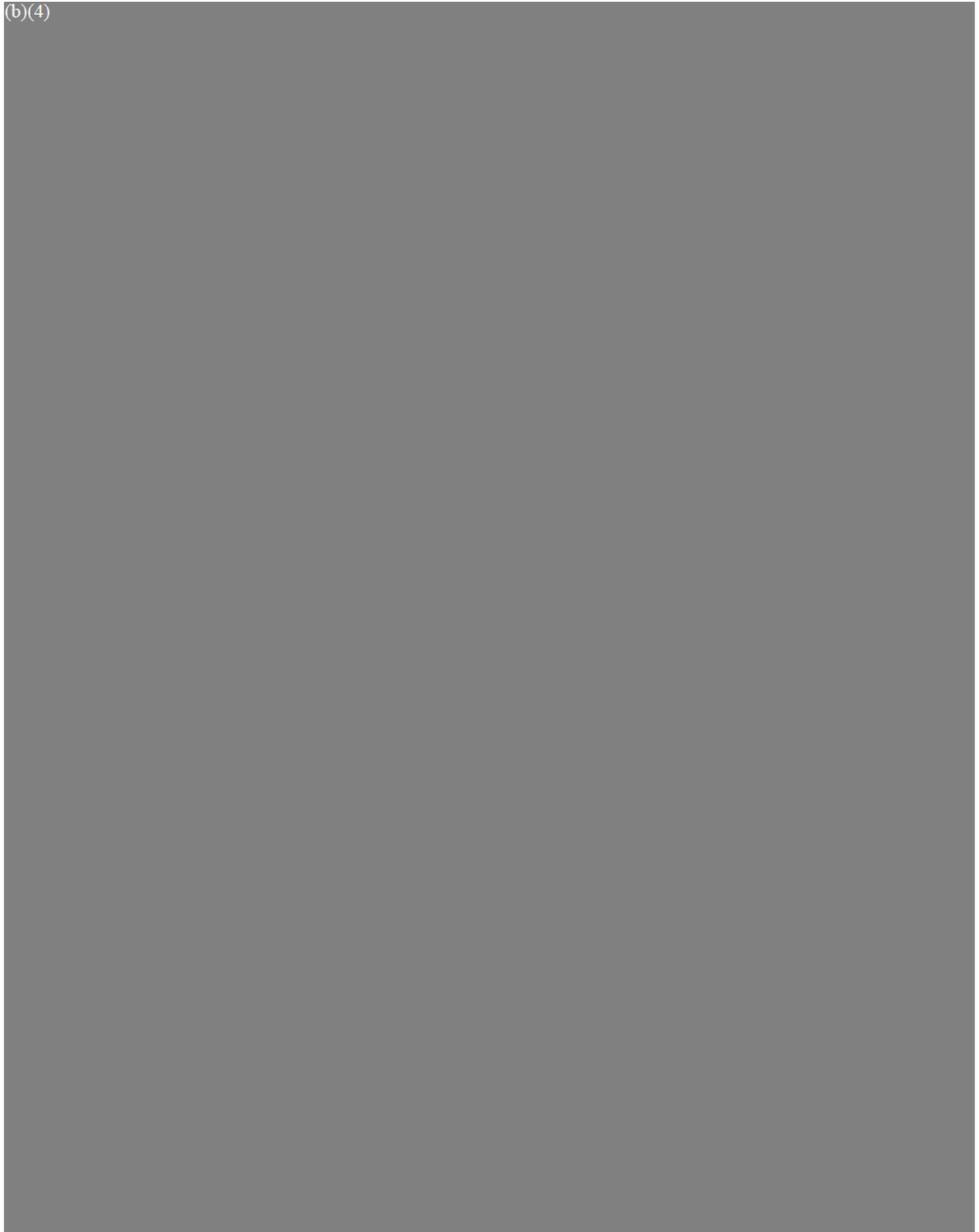
COMPANY
CONFIDENTIAL

(b) (4)

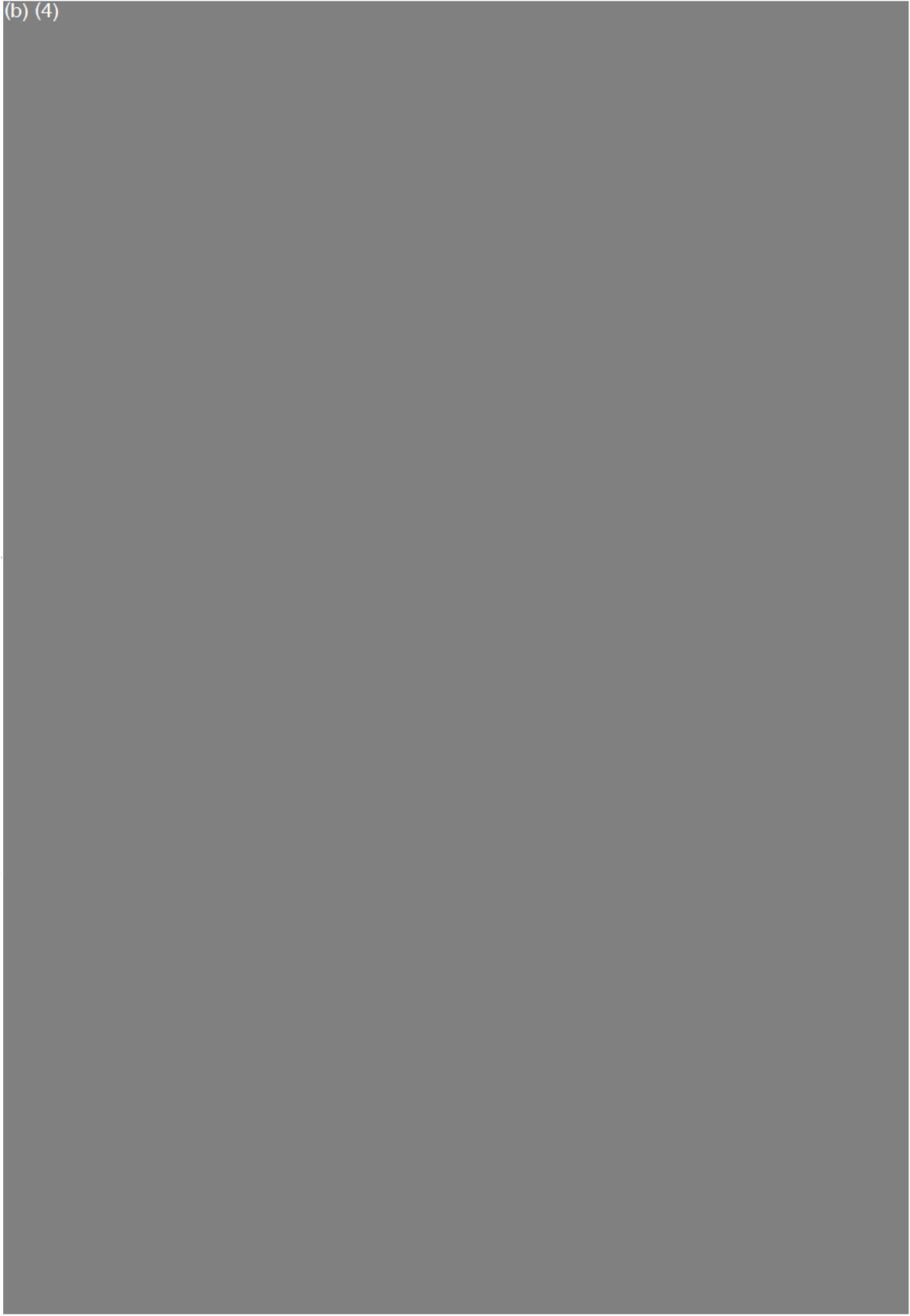


127

(b)(4)



(b) (4)



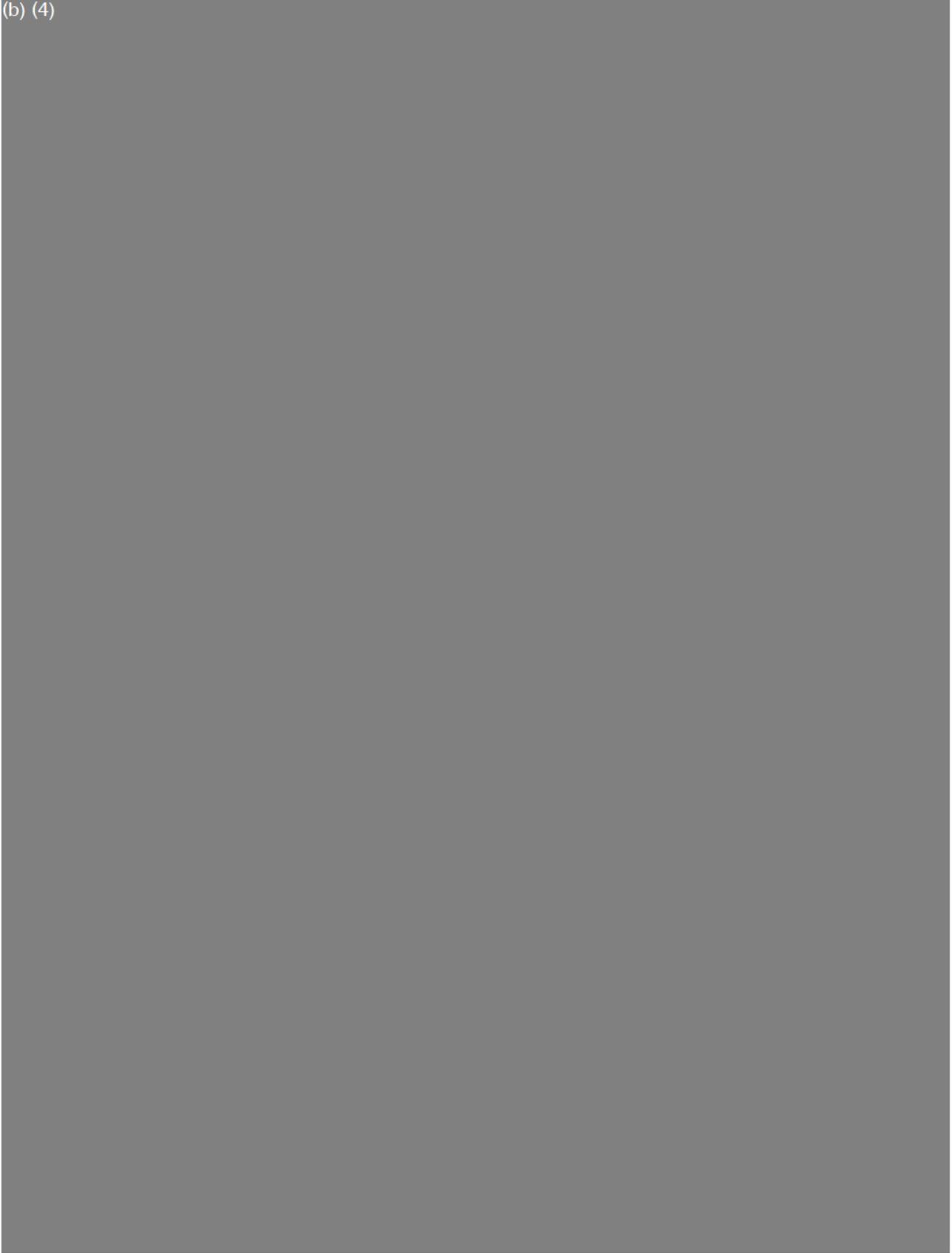
(b) (4)



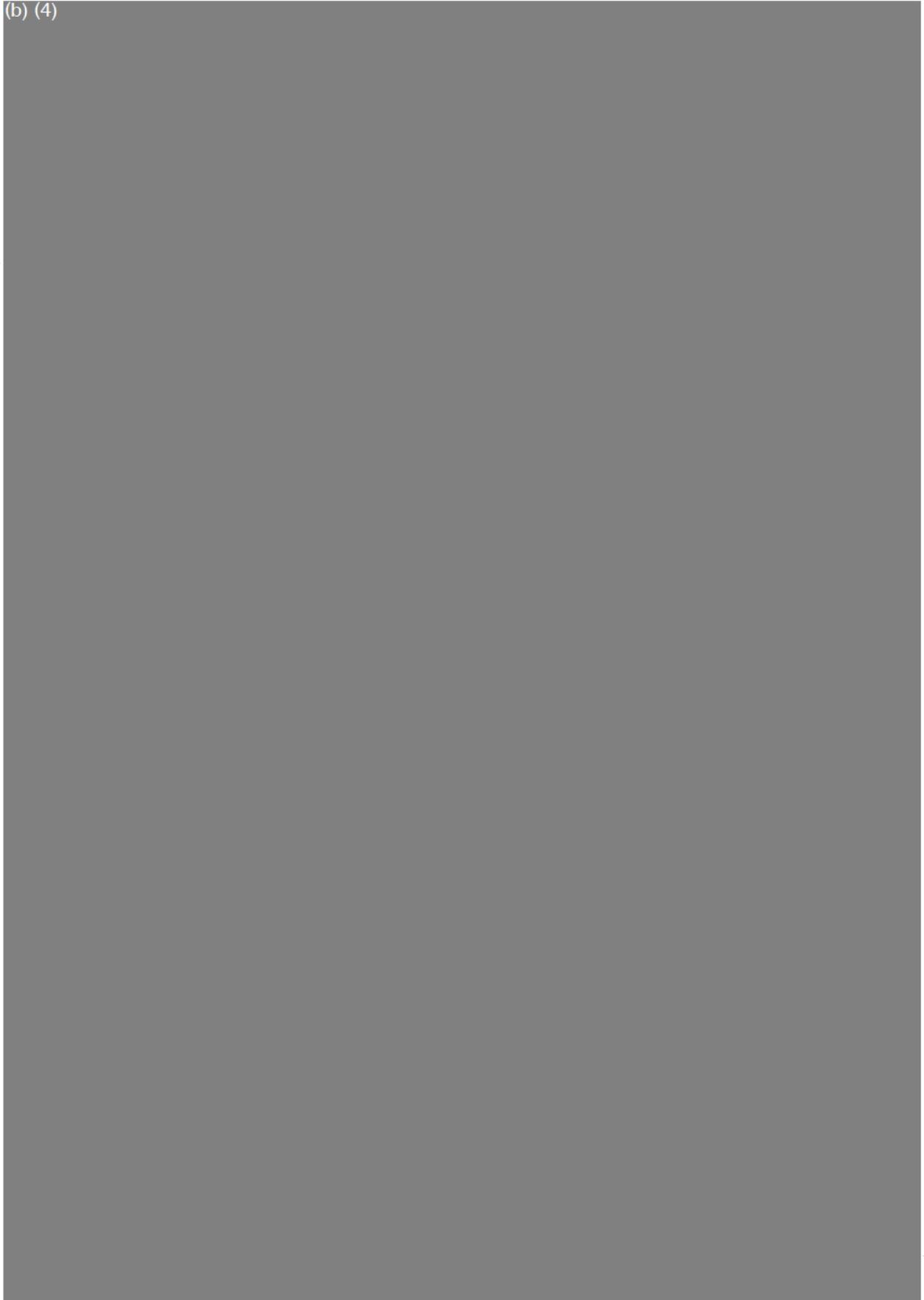
(b) (4)



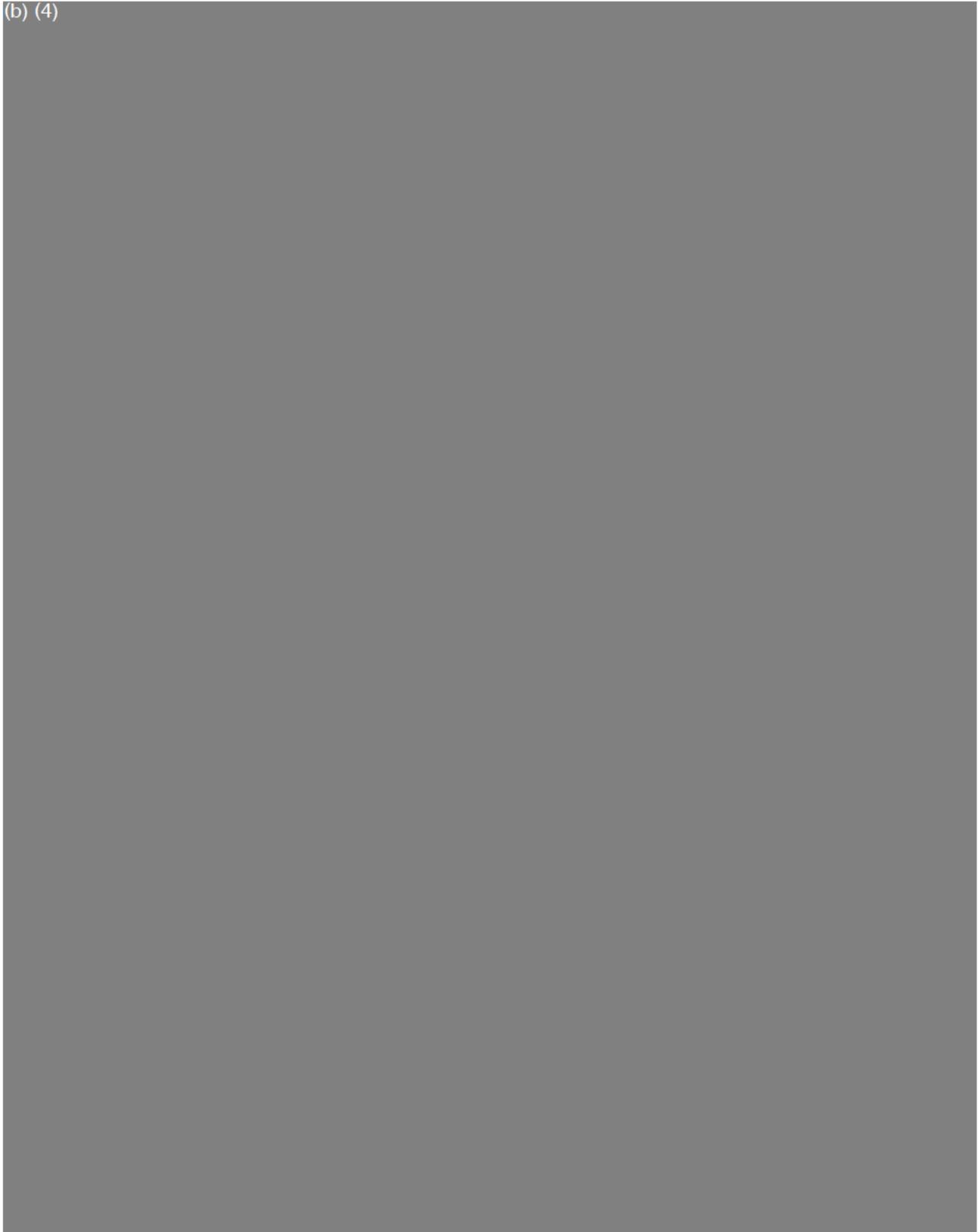
(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



137

(b) (4)



(b) (4)



(b) (4)



140

7.3.4 SUMMARY

In this prospective, randomized, multicenter clinical trial with treatment and control cohorts well matched, results indicate that the SPECTRUM® Ventricular Catheter can significantly reduce the rate of ventriculitis. Catheter colonization was also significantly lower in the treatment cohort, as was the rate of ventriculitis per 100 catheter days. No new issues were raised with respect to safety, and the complications reported were among those expected in this patient population.

COMPANY
CONFIDENTIAL

7.4 References

- [1] Sherertz RJ, Carruth WA, *et al.* Efficacy of antibiotic-coated catheters in preventing subcutaneous *S. aureus* infection in rabbits. *J Infect Dis* 1993;167:98-106.
- [2] Raad I, Darouiche R, Dupuis J, *et al.* Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. *Ann Intern Med* 1997;127(4):267-74.
- [3] Darouiche RO, Raad II, Heard SO, *et al.* A comparison of two antimicrobial-impregnated central venous catheters. *NEJM* 1999;340(1):1-8.
- [4] Darouiche RO, Hampel OZ, Boone TB and Raad II. Antimicrobial activity and durability of a novel antimicrobial-impregnated bladder catheter. *Int J Antimicrob Agents* 1997;8:243-7.
- [5] Darouiche RO, Smith JA, Hanna H, *et al.* Efficacy of antimicrobial-impregnated bladder catheters in reducing catheter-associated bacteriuria: a prospective, randomized, multicenter clinical trial. *Urology* 1999;54:976-81.
- [6] Marik PE, Abraham G, Careau P, *et al.* The *ex vivo* antimicrobial and colonization rate of two antimicrobial-bonded central venous catheters. *Crit Care Med* 1999;27:1128-31.
- [7] Mayhall CG, Archer NH, Lamb VA, *et al.* Ventriculostomy-related infections. *NEJM* 1984;310(9):553-9.
- [8] Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically: approved standard. 4th ed. Vol 17. No 2. Wayne, Pa.: National Committee for Clinical Laboratory Standards, 1997. (NCCLS document no. M7-A4.)
- [9] Raad I, Darouiche R, Hachem R, *et al.* The broad SPECTRUM® activity and efficacy of catheters coated with minocycline and rifampin. *J Infect Dis* 1996;173:418-24.
- [10] Raad I, Darouiche R, Hachem R, *et al.* Antibiotics and prevention of microbial colonization of catheters. *Antimicrob Agents Chemother* 1995;39(11):2397-400.

8 COMPARISON TO PREDICATE DEVICES

As shown in TABLE 14, the SPECTRUM® Ventricular Catheter is comparable to the following predicate devices in terms of intended use and technological characteristics: the Cook Ventricular Catheter (D.C. #K962097); the Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter (D.C. #K000251); and the Cook SPECTRUM® Catheter (ABRM Catheter, D.C. #K950118). The SPECTRUM® Ventricular Catheter is identical to the predicate Cook Ventricular Catheter except that it is impregnated with the antimicrobials minocycline and rifampin. The addition of minocycline and rifampin is also a feature of the predicate Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter and the predicate Cook SPECTRUM®/ABRM Central Venous Catheter. Please refer to the following table showing the comparable characteristics of these devices.

TABLE 14
SPECTRUM® VENTRICULAR CATHETER AND COMPARABLE PREDICATE DEVICES

CHARACTERISTIC	MANUFACTURER / DEVICE			
	Cook Incorporated SPECTRUM® Ventricular Catheter	Cook Incorporated Ventricular Catheter (D.C. #K962097)	Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter (DC #K000251)	Cook Incorporated SPECTRUM® Catheter (ABRM) Order #C-UTLM-701J-RSC-ABRM (DC #K950118)
Intended Use	For obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.	For obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.	For urinary tract drainage or urine collection.	For central venous access for venous pressure monitoring, blood sampling, and administration of drugs and fluids.
Materials	Silicone	Silicone	Silicone	Polyurethane
Size Length	9 Fr 33 cm	6-9 Fr 15-35 cm	20 Fr 37 cm	7 Fr; triple lumen 15-25 cm
Antimicrobial Component	Combination of minocycline and rifampin	None	Combination of minocycline and rifampin	Combination of minocycline and rifampin

144

9 510(K) SUMMARY

Submitted By:

April Lavender
Vice President Regulatory Affairs
Cook Incorporated
925 South Curry Pike
Bloomington, Indiana, 47402
(812) 339-2235

Device:

Trade Name: SPECTRUM® Ventricular Catheter
Common/Usual Name: Ventricular Catheter, External Drainage Catheter
Proposed Classification: Central Nervous System Fluid Shunt and Components
21 CFR Part 882.5550 (84JXG)
Class II

Intended Use:

The SPECTRUM® Ventricular Catheter is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume. The device will be supplied sterile and is intended for one-time use.

Predicate Devices:

The SPECTRUM® Ventricular Catheter is comparable in terms of intended use and technological characteristics to predicate Ventricular catheters, including Cook Incorporated's Ventricular Catheter. Like the Cook Urological and Cook OB/GYN™ SPECTRUM® Silicone Foley Catheter and the Cook SPECTRUM®/ABRM Catheter for intravascular use, the SPECTRUM® Ventricular Catheter has an antimicrobial component comprised of a combination of minocycline and rifampin.

Device Description:

The SPECTRUM® Ventricular Catheter is a 9 Fr catheter nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. The SPECTRUM® Ventricular Catheter is impregnated with an antimicrobial combination of minocycline and rifampin which may reduce the risk of ventriculitis during use. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 µg/cm), and the average amount of rifampin on the catheter is approximately 4 mg (116 µg/cm). Components supplied with the SPECTRUM® Ventricular Catheter include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

145

Substantial Equivalence:

The SPECTRUM® Ventricular Catheter is similar with respect to indications for use, materials and physical construction to predicate devices in terms of section 510(k) substantial equivalency, and has undergone testing to support substantial equivalence. The substantially equivalent determination under the Federal Food, Drug, and Cosmetic Act is not intended to have any bearing whatsoever on the resolution of patent infringement suits or other patent matters.

The device will be manufactured according to specified process controls, undergoing processing, sterilization and packaging procedures similar to predicate devices currently manufactured and marketed by Cook Incorporated.

Testing and Test Results

The SPECTRUM® Ventricular Catheter has undergone biocompatibility testing (Dermal Sensitization, Cytotoxicity, 7 Day Muscle Implantation with Histopathology, Intracutaneous Toxicity, Systemic Toxicity, Hemolysis, Genotoxicity, and a Two Week Brain Implantation Study), physical performance testing, HPLC analysis, zone of inhibition testing, susceptibility testing, and clinical evaluation. Results of this testing provide reasonable assurance of device performance for its intended use.

Clinical Study

To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of ventriculitis, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The average duration of catheter placement was 8.5 ± 5.8 days in the treatment group, and 8.2 ± 6.9 days in the control group. Results showed that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of ventriculitis than those receiving the control catheter (1.3% versus 9.4%, respectively).

EXHIBIT I

DRAFT LABELING

DRAFT LABELING

These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

SPECTRUM® VENTRICULAR DRAINAGE CATHETER SET

DESCRIPTION

The SPECTRUM® Ventricular Drainage Catheter Set allows external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain. The SPECTRUM® Ventricular Drainage Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of catheter colonization and ventriculitis during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of ventriculitis.

The SPECTRUM® Ventricular Drainage Catheter is available in a 9 Fr diameter and is nominally 33 cm in length. The catheter has a closed-end configuration with nominally 16 sideports, and has markings at 1 cm increments to aid in determining depth of placement. Based on HPLC analysis, the average amount of minocycline on the catheter is approximately 5 mg (159 $\mu\text{g}/\text{cm}$), and the average amount of rifampin on the catheter is approximately 4 mg (116 $\mu\text{g}/\text{cm}$). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The minocycline and rifampin antimicrobial agents contain yellow/orange pigments, therefore, some coloration of the catheter is normal. Components supplied with the SPECTRUM® Ventricular Catheter Set include a pre-loaded stainless steel stylet, a stainless steel tunneling trocar, and proximal fittings, which are included to facilitate placement and use of the Ventricular Catheter.

INDICATIONS FOR USE

The SPECTRUM® Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for short-term use to externally drain fluid for the purpose of relieving elevated intracranial pressure or fluid volume.

CONTRAINDICATIONS

This device is contraindicated in patients having allergy or history of allergy to tetracyclines or rifampin. **Note:** Because the SPECTRUM® Ventricular Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physician's Desk Reference*) should be considered when using this device, although there have been no reports of detected systemic levels of minocycline or rifampin in patients receiving a SPECTRUM® Catheter.

WARNINGS

- This device is not intended for permanent implantation.
- This device should not be used if dermatitis or scalp infection is present at the catheter insertion site.
- Care must be taken when using this device in patients receiving anticoagulants or those who are known to have a bleeding diathesis.
- Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headache, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may pre-dispose development of a subdural hematoma or hydroma, or collapse of the lateral ventricular walls leading to obstruction of the ventricular catheter.
- Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally raised or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.
- The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.
- Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. **Under no circumstances should the catheter be forcefully removed.** If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.
- Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTIONS

- Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be initiated after implantation.
- Inspect contents of this set for damage. If product is damaged, do not use.
- Refer to manufacturer's instructions when using accessory components other than Cook products.
- Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.
- Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions. **The catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.**

- Kinking of catheter tubing may result in restricted flow or damage to the catheter.
- Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.
- Use rubber shod forceps when handling the catheter to prevent tearing or cutting the catheter.

CLINICAL STUDY INFORMATION

•To evaluate efficacy of the Cook SPECTRUM® Ventricular Catheter in reducing the incidence of ventriculitis, a prospective, randomized, multicenter clinical trial was conducted in which patients were enrolled and randomly assigned to receive either a standard non-coated 9 Fr Cook Ventricular Catheter (control arm) or a 9 Fr Cook SPECTRUM® Ventricular Catheter (treatment arm). Of the 288 patients available for follow-up, 149 received the SPECTRUM® Ventricular Catheter and 139 patients received the control catheter. The patient characteristics (gender, age, ethnicity, indication for placement, receipt of systemic antibiotics, complications, duration of catheter placement, and reason for catheter removal) were comparable in the two groups. The average duration of catheter placement was 8.2 ± 6.9 days for patients in the control arm, and 8.5 ± 5.8 days for patients in the treatment arm. Results of the clinical study show that patients receiving the SPECTRUM® Ventricular Catheter had significantly lower rates of ventriculitis than those receiving the control catheter. The rate of ventriculitis was 9.4% (13 of 139 patients) in the control arm as compared to 1.3% (2 of 149 patients) in the treatment arm ($p=0.0022$, Chi-square). Organisms isolated from CSF cultures from the 13 patients having ventriculitis in the control group included: coagulase negative *Staphylococcus*, *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Corynebacterium*, *Klebsiella pneumonia*, coagulase positive *Staphylococcus* species, and diphtheroids. Organisms isolated from CSF cultures from patients having ventriculitis in the treatment group included *Enterobacter aerogenes*, *Enterococcus faecalis*, and *Staphylococcus aureus*. The proportions of patients free of ventriculitis as a function of the duration of placement of the catheter in each group were compared using a log-rank test on the Kaplan-Meier estimates; the conditional rates of ventriculitis per 100 catheter days were 2.6% for treatment devices as compared to 17% for control devices ($p=0.00095$ by log-rank test).

SUGGESTED INSTRUCTIONS FOR USE

1. Determine the site of insertion and aseptically prepare and drape.
2. Open the periosteum, skull, and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
3. Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
4. Carefully withdraw the stylet and check for free flow of fluid.
5. Verify proper positioning of catheter using CT or other imaging modality.

6. After verifying proper placement, position the barbed end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the tunneling device into the incision used for catheterization.
7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
8. After exiting the skin, pull catheter through the subcutaneous tunnel until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.
9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped or damaged. Slide snap-fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub of Luer lock adapter by sliding the snap-fit cap over the barbed portion of the adapter. **Avoid cutting or occluding tubing.**
10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie-down. Provide some slack in the catheter when securing the silicone winged tie-down to offer strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
11. Cap the catheter with the red sterile Luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

SPECTRUM® Ventricular Catheter
510(k) Premarket Notification

II-1

EXHIBIT II

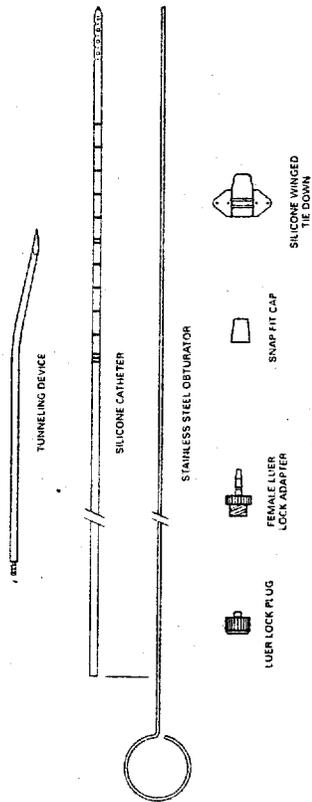
PRODUCT SHEETS FOR PREDICATE DEVICES

152

**SPECTRUM® Ventricular Catheter
510(k) Premarket Notification**

**ORDER NUMBER: HVDC-88-33
HVDC-110-33**

SET COMPONENTS



These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgement concerning patient care.

HAMILTON VENTRICULAR DRAINAGE CATHETER SET

The Hamilton Ventricular Drainage Catheter Set is intended for obtaining access to a ventricular cavity of the brain for fluid drainage and intracranial pressure monitoring.

INDICATIONS FOR USE

The Hamilton Ventricular Drainage Catheter Set is designed to allow external access and drainage of cerebrospinal fluid (CSF) from the ventricles of the brain.

WARNINGS

- This device is not intended for permanent implantation.
- This device should not be used if scalp infection is present.
- Care must be taken when using this device in patients receiving anticoagulants or are known to have a bleeding diathesis.
- Patients with ventricular catheters must remain under close observation during the postoperative period for signs and symptoms of increased intracranial pressure that suggest catheter malfunction or obstruction. Increasing intracranial pressure is characterized by headaches, vomiting, irritability, listlessness, drowsiness, nuchal rigidity, increased tension of the anterior fontanelle, congestion of scalp veins, and variable abnormal neurological findings. Over drainage of CSF may

- Refer to manufacturer's instructions when using accessory components other than COOK® products.
- Prior to procedure, in all but exceptional cases, prospective patients or their representatives should be informed of the possible complications associated with the use of this product.
- Exercise caution when placing and using the catheter to prevent contact with bare fingers, talc, towels, or any lint bearing surfaces that could contaminate the catheter surface and cause tissue reactions.
- Kinking of catheter tubing may result in restricted flow or damage to the catheter.
- Catheter should be secured with non-metallic sutures in such a manner as to avoid cutting or occluding the tubing. The use of stainless steel ligatures on silicone products is not recommended.
- Use rubber shoe forceps when handling the catheter to prevent tearing or cutting the catheter.

SUGGESTED INSTRUCTIONS FOR USE

1. Determine the site of insertion and aseptically prepare and drape.
2. Open the peritoneum, skull and dura by any technique consistent with the surgeon's experiences in placement of ventricular catheters.
3. Position the catheter into the ventricular space using the pre-loaded stylet within the catheter.
4. Carefully withdraw the stylet and check for free flow of fluid.
5. Verify proper positioning of catheter using CT or other imaging modality.
6. After verifying proper placement, position the beared end of the tunneling tool into the lumen of the proximal end of the catheter. Insert the trocar end of the tunneling device into the incision used for catheterization.

- Occasionally, fibrous adhesions will bind the catheter to the adjacent choroid plexus or brain tissue. Gentle rotation may free the catheter. Under no circumstances should the catheter be forcefully removed. If the catheter can not be removed without force, it is advisable to allow it to remain in place, rather than risk intraventricular hemorrhage.

PRECAUTIONS

- Aseptic technique is necessary in all phases of use with this product. Routine catheter care protocols should be indicated after implantation.
- Inspect content of this set for damage. If product is damaged, do not use.

- pre-dispose development of a subdural hematoma or hydrooma, or collapse of the lateral ventricular walls which could lead to obstruction of the ventricular catheter.
- Since intracranial pressure is controlled by the height of the drip chamber or collection bag relative to the patient, it is imperative that neither the drip chamber (collection bag) nor patient be accidentally tilted or lowered. The height of the drip chamber (collection bag) or patient should be changed only by qualified personnel or by physician order.
- The ventricular catheter may become obstructed by particulate matter such as blood clots, brain fragments, or other tissue particles, or by excessive reduction of ventricle size.

153

T-HVDC1198

ACKNOWLEDGEMENTS
 A. J. Hamilton, M.D., F.A.C.S., Associate Professor of
 Neurosurgery, The University of Arizona, Tucson, AZ.

HAMILTON VENTRICULAR DRAINAGE CATHETER SET

Suggested
 Instructions for Use

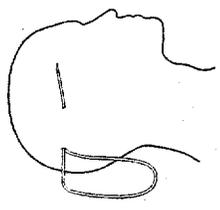


Figure 1

7. Push the tunneling device through the scalp taking care not to dislodge the intraventricular portion of the catheter. Push tunneling device and catheter subcutaneously until the desired exit site is realized. (Figure 1) The catheter can be held in place with a rubber shod hemostat or forceps while tunneling.
 8. After exiting the skin, pull catheter through until the catheter no longer protrudes from the incision site. Do this with great care to ensure the position of the catheter within the ventricle is not affected. Cut the catheter from the tunneling device.

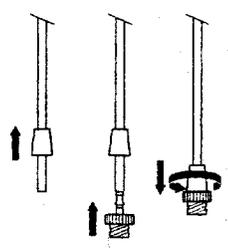


Figure 2

9. Trim the distal end of the catheter to size, cutting off the portion of the catheter that was crimped, or damaged. Slide snap fit cap (small end first) over the proximal end of catheter. Attach proximal end of the catheter to the barbed end of the female Luer lock connector. Secure catheter tapered hub over the barbed portion of the adapter. (Figure 2) **Avoid cutting or occluding tubing.**
 10. Suture the incision at the catheter exit site. Suture the catheter to the skin using the holes in the silicone winged tie down. Provide some slack in the catheter when securing the silicone winged tie down in order to allow strain relief to the catheter. The slack will compensate for patient movement. Cover the entire area with a sterile dressing.
 11. Cap the catheter with the red sterile luer plug or connect to a sterile drainage system for fluid collection. Follow directions carefully for connection and use of the drainage system utilized.
 12. Ensure the catheter remains capped or connected to a sterile drainage system at all times. All catheter or patient manipulations and fluid drainage system changes must be carried out utilizing strict sterile technique to reduce the risk of catheter related infections.

COOK INCORPORATED
 A COOK GROUP COMPANY
 12 Electronics Street
 Bloomington, IN 47402 U.S.A.
 Phone: 817.338.2238
 Toll Free: 800.457.1500
 Toll Free FAX: 800.554.9335

WILLIAM A. COOK AUSTRALIA PTY. LTD.
 12 Electronics Street
 Brisbane Technology Park
 Eight Mile Plains
 Queensland 4113 AUSTRALIA
 Phone: +61 7 38 41 11 88
 www.cookgroup.com

COOK (CANADA) INC.
 A COOK GROUP COMPANY
 12 Electronics Street
 Stouffville, Ontario
 L4A 7X6 CANADA
 Phone: 905.660.7110
 Toll Free: 800.660.6360

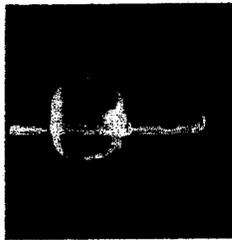
WILLIAM COOK EUROPE A/S
 A COOK GROUP COMPANY
 Sønderø Dk-4632
 Blevenskov, DENMARK
 Phone: +45 56 87 11 31

T-HVDC1198

© COPYRIGHT COOK INCORPORATED 1998

154

BLADDER ACCESS AND DRAINAGE



SPECTRUM[™] ANTIMICROBIAL SILICONE FOLEY CATHETERS

Used to provide drainage of urine from the bladder. The Spectrum[™] Silicone Foley Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of bacterial colonization of the catheter and catheter-related bacteriuria during use. The all-silicone construction provides a biocompatible latex-free alternative. Supplied sterile in peel-open packages. Intended for one-time use.



ORDER NUMBER	French Size	Length	Inflation Volume
CLOSED END			
FSC-200037-05-CE-ABRM	20.0	37 cm	5 ml
OPEN END			
FSC-200037-05-OE-ABRM	20.0	37 cm	5 ml

COOK[®]

www.cookurological.com

COOK UROLOGICAL INCORPORATED
 1100 West Morgan Street, P.O. Box 227, Spencer, Indiana 47460 U.S.A.
 Phone: 812 829-4891, Toll Free: 800 457-4448, Toll Free Fax: 800 837-4130

COOK IRELAND LTD.
 O'Halloran Road, National Technological Park
 Limerick, IRELAND, Phone: 353 61 334440, Fax: 353 61 334441

COOK (CANADA) INC.
 111 Sandiford Drive, Stouffville, Ontario L4A 7X5 CANADA
 Phone: 905 640-7110, Toll Free: 800 668-0300, Fax: 905 640-6804

© COPYRIGHT COOK UROLOGICAL INCORPORATED 2001

SSFC201

155

**Spectrum™
Silicone Foley Catheter**

COOK®

CONTRAINDICATIONS

• Allergy or history of allergy to tetracyclines or rifampin. **NOTE:** Because the Spectrum™ Silicone Foley Catheter is impregnated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), their associated contraindications, warnings and precautions (*Physicians' Desk Reference*) should be considered when using this device, although there have been no reports of detected urinary or systemic levels of minocycline and rifampin in patients receiving a Spectrum™ Catheter.

WARNING: Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.

PRECAUTION: The Spectrum™ Silicone Foley Catheter should not come into contact with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobials from the catheter and reduce the catheter's antimicrobial activity.

NOTE: The Spectrum™ Silicone Foley Catheter should not supercede aseptic technique as it relates to catheter placement and maintenance.

DISCUSSION OF ANTIMICROBIAL ACTIVITY

In vitro antimicrobial activity associated with the Spectrum™ Silicone Foley Catheter impregnated with minocycline and rifampin is demonstrated by zone of inhibition assays using indicator bacterial isolates (previously frozen isolates). In vitro antimicrobial activity was not determined with fresh clinical isolates (never frozen) isolated from urinary tract infections. The clinical significance of in vitro antimicrobial activity as measured by zone of inhibition assay is not established.

SPECTRUM™ SILICONE FOLEY CATHETER

DEVICE DESCRIPTION

The Spectrum™ Silicone Foley Catheter is impregnated with the antimicrobial agents minocycline and rifampin, which may reduce the risk of gram positive bacterial colonization of the catheter and catheter-related bacteriuria during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of urinary tract infections.

The Spectrum™ Silicone Foley Catheter is available in a 20 Fr diameter and 36.5 cm working length. Based on high performance liquid chromatography (HPLC) analysis, the average amount of minocycline on the catheter is 25.2 mg (690Fg/cm), and the average amount of rifampin on the catheter is 13.3 mg (363Fg/cm). These total amounts of minocycline and rifampin are lower than the daily systemic pharmacologic doses. The antimicrobial agents minocycline and rifampin contain yellow/orange pigments, therefore, some coloration of the catheter is normal.

The Spectrum™ Silicone Foley Catheter is designated by the suffix -ABRM in the reorder number (Example: FSC-200037-05-CE-ABRM).

INTENDED USE

The Spectrum™ Silicone Foley Catheter is a urological catheter indicated for use in urinary tract drainage or urine collection. Urinary tract access is generally accomplished by insertion of the catheter through the urethra and into the bladder, but may also be accomplished by suprapubic placement or by nephrostomy. The device will be supplied sterile and is intended for one-time use.

157

Urine cultures were obtained at approximately 3, 7 and 14 days after catheter insertion for evaluation of bacteriuria (defined as growth of organisms) in urine at a concentration of $\geq 10^5$ CFU/ml). Of the 124 patients available for follow-up, 56 received the Spectrum[™] Silicone Foley Catheter and 68 received the control catheter. The patient characteristics [age, duration of catheter placement, degree of immunosuppression, history of UTI, renal tract abnormalities, receipt of local antimicrobials, and catheter care violations] were comparable in the two groups. Kaplan-Meier analysis was used to compare the proportions of patients free of bacteriuria as a function of the duration of placement of the catheter in each group (those receiving the Spectrum[™] Foley and those receiving the control Foley). Results of the clinical study are summarized in the following tables.

RATE OF BACTERIURIA IN 124 PATIENTS		
DAY	SPECTRUM [™] FOLEY PATIENTS	NON-COATED FOLEY PATIENTS
3	0/56 (0%)	4/68 (5.9%)
7	8.5/56 (15.2%)	27/68 (39.7%)
14	31/53 (58.5%)	49/59 (83.1%)

CLINICAL TRIALS

The Spectrum[™] Silicone Foley Catheter was evaluated in two separate clinical studies. The first study was performed to evaluate the antimicrobial activity and durability,¹ and a second study was performed to evaluate efficacy in reducing bacteriuria.²

• To evaluate antimicrobial activity and durability, 30 Spectrum[™] Silicone Foley Catheters (18 Fr, 36.5 cm in length) were placed at different times in 12 spinal cord-injured patients who required insertion of a Foley catheter during hospitalization. The catheters were removed in six groups of five catheters each at days 3, 7, 10, 14, 17 or 21. Five 1 cm length segments (690µg/cm minocycline and 363µg/cm rifampin) from the five removed catheters at each interval underwent zone of inhibition (ZI) testing using agar diffusion/zone of inhibition assay³ against clinical isolates of ten urinary pathogens. Zones of inhibition and levels of antimicrobial agents of removed catheters were inversely related to the duration of catheter placement. Using HPLC analysis, blood and urine samples obtained from patients receiving the Spectrum[™] Silicone Foley Catheter (blood samples obtained one day after catheter insertion and upon catheter removal; urine samples obtained upon catheter removal) showed no detectable systemic or urinary levels of minocycline or rifampin (detectability limit of both antimicrobials 0.5 µg/ml). Results demonstrated that the Spectrum[™] Silicone Foley Catheter provided broad spectrum in vitro antimicrobial activity against the tested urinary pathogens, with the inhibitory activity lasting at least two weeks after insertion.

• To evaluate efficacy in reducing bacteriuria, a prospective, randomized, multicenter clinical trial of patients undergoing radical prostatectomy was conducted in which 141 patients were enrolled to receive intraoperatively either a 36.5 cm long 20 Fr Spectrum[™] Silicone Foley Catheter or 20 Fr standard non-coated silicone Foley catheter (control) to remain in place for 14 days.

<u>RATE OF BACTERIURIA BY ORGANISM TYPE AT DAY 14</u>		
ORGANISM	SPECTRUM™ FOLEY PATIENTS	NON-COATED FOLEY PATIENTS
Gram Positive	4/56 (7.1%)	26/68 (38.2%)
Gram Negative	26/56 (46.4%)	32/68 (47.1%)
Candiduria	2/56 (3.6%)	2/68 (2.9%)

NOTE: Bacteriuria in both groups of patients (those receiving the Spectrum™ Foley and those receiving the control Foley) was caused by a similar variety of organisms, with the *Enterococcus* species being the most common gram-positive bacterium and the *Enterobacter* species being the most common gram-negative bacterium.

<u>RATE OF SYMPTOMATIC UTI* BY DAY 14</u>	
SPECTRUM™ FOLEY PATIENTS	NON-COATED FOLEY PATIENTS
1/56 (1.8%)	6/68 (8.8%)

* bladder spasms, fever/chills, urethral discharge and/or bladder discomfort

<u>RATE OF BACTERIURIA IN 16 PATIENTS WHO RECEIVED ANTIBIOTICS POST-CATHETERIZATION</u>		
DAY	SPECTRUM™ FOLEY PATIENTS	NON-COATED FOLEY PATIENTS
7	1/7	3/9
14	1/7	6/9

<u>RATE OF SYMPTOMATIC UTI BY DAY 14 IN 16 PATIENTS WHO RECEIVED ANTIBIOTICS POST-CATHETERIZATION</u>	
SPECTRUM™ FOLEY PATIENTS	NON-COATED FOLEY PATIENTS
1/7	2/9

REFERENCES

- [1] Darouiche RO, Hampel OZ, Boone TB and Raad II. Antimicrobial activity and durability of a novel antimicrobial impregnated bladder catheter. *Int J Antimicrob Agents* 1997;8:243-7.
- [2] Darouiche RO, Smith JA, Hanna H, et al. Efficacy of antimicrobial-impregnated bladder catheters in reducing catheter-associated bacteriuria: a prospective, randomized, multicenter clinical trial. *Urology* 1999;54:976-81.

159

- [3] Darouiche RO, Safar H and Raad II. In vitro efficacy of antimicrobial-coated bladder catheters in inhibiting bacterial migration along catheter surface. *JID* 1997;176:1109-12.
- [4] Darouiche RO, Raad II, Heard SO, et al. A comparison of two antimicrobial-impregnated central venous catheters. *NEJM* 1999;340(1):1-8.
- [5] Raad I, Darouiche R, Dupuis J, et al. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. *Ann Intern Med* 1997;127(4):267-74.
- [6] Warren JW. Catheter-associated urinary tract infections. *Infect Dis Clin N Am* 1987;1:823-54.
- [7] Garibaldi RA, Burke JP, Britt MR, et al. Meatal colonization and catheter-associated bacteriuria. *N Engl J Med* 1980;303:316-8.
- [8] Daifuku R and Stamm WE. Association of rectal and urethral colonization with urinary tract infection in patients with indwelling catheters. *JAMA* 1984;252:2028-30.
- [9] Raad I, Darouiche R, Hachem R, et al. The broad spectrum activity and efficacy of catheters coated with minocycline and rifampin. *J Infect Dis* 1996;173:418-24.

COOK UROLOGICAL INCORPORATED

1100 West Morgan Street P.O. Box 227
Spencer, Indiana 47460 U.S.A.
Phone: 812 829-4891 Toll Free: 800 457-4448
Fax: 812 829-2022 Toll Free Fax: 800 837-4130

COOK OB/GYN®

1100 West Morgan Street P.O. Box 271
Spencer, Indiana 47460 U.S.A.
Phone: 812 829-6500 Toll Free: 800 541-5591
Fax: 812 829-2022 Toll Free Fax: 800 837-4130

© COPYRIGHT COOK UROLOGICAL INCORPORATED 2000

CE0123

BGS900

SILICONE FOLEY

Used to provide drainage of urine from the bladder. Intended for one-time use.

DESCRIPTION:

Silicone Foley balloon catheter

(Optional stainless steel wire guide 80 cm long with SlipCoat™ hydrophilic coating)

SUGGESTED INSTRUCTIONS FOR ACTIVATING SLIPCOAT™ HYDROPHILIC COATING ON WIRE GUIDE:

These instructions are provided in the event you are placing an open tip Silicone Foley with hydrophilic wire guide.

NOTE: SlipCoat™ wire guides are very slippery when wet. Always maintain control of the wire guide when manipulating it through any device.

1. Attach a syringe filled with sterile water or sterile saline solution to the Luer lock fitting of the wire guide holder.
2. Inject enough solution to wet the wire guide surface entirely. This will activate the SlipCoat™ hydrophilic coating.

NOTE: Always keep the surface of the wire guide wetted for optimal results.

3. Standard wire guide use may now be initiated.

NOTE: SlipCoat™ is not a permanent coating. If after extended use the SlipCoat™ wire guide does not perform smoothly, replace the wire guide with a new SlipCoat™ guide.

SUGGESTED INSTRUCTIONS FOR USING SILICONE FOLEY:

WARNINGS: For urological use only. Do not use petroleum based ointments or lubricants since they may damage silicone and burst balloons.

CAUTIONS: Visually inspect the product for any imperfections or surface deterioration prior to use. Use Luer syringe. Do not use needle. Should balloon rupture occur, care should be taken to ensure that all balloon fragments have been removed from the patient.

1. Pass the deflated Silicone Foley catheter through the urethra and into the bladder. The open ended 6.0 French catheter may be introduced over a well lubricated .021 inch (0.53 mm) in diameter wire guide to facilitate placement.

WARNING: Always inflate the balloon with a sterile liquid. Never inflate with air, carbon dioxide or any other gas.

2. Once position is confirmed (via aspiration of urine), connect a syringe containing sterile media to the Luer of the inflation lumen on the two pronged Y-fitting.

CAUTION: Do not overinflate the balloon.

3. Using the chart below, inflate the balloon with sterile media to the recommended inflation volume.

6.0 French Silicone Foley	1 ml
8.0 French Silicone Foley	3 ml
10.0 French Silicone Foley	3 ml
12.0 French Silicone Foley	5 ml
14.0 French Silicone Foley	5 ml
*16.0 French Silicone Foley	5 ml or 30 ml
*18.0 French Silicone Foley	5 ml or 30 ml
20.0 French Silicone Foley	30 ml
22.0 French Silicone Foley	30 ml
24.0 French Silicone Foley	30 ml

* These catheters are available in 5 ml or 30 ml inflation volumes. If you have a question as to the proper inflation volume for your catheter, consult the product label.

4. Connect the funnel drainage lumen of the two pronged Y-fitting to a drainage bag.

**SUGGESTED INSTRUCTIONS FOR REMOVING
SILICONE FOLEY:**

1. Disconnect drainage bag.
2. Using syringe aspiration, deflate the balloon.
3. Remove catheter from the urethra.

NOTE: In the event the retention balloon cannot be deflated, transect the shaft of the catheter, allow balloon to deflate, and remove.

COOK UROLOGICAL INCORPORATED
1100 West Morgan Street P.O. Box 227
Spencer, Indiana 47460 U.S.A.
Phone: 812 829-4891 Toll Free: 800 457-4448
Fax: 812 829-2022 Toll Free Fax: 800 837-4130

COOK OB/GYN®
1100 West Morgan Street P.O. Box 271
Spencer, Indiana 47460 U.S.A.
Phone: 812 829-6500 Toll Free: 800 541-5591
Fax: 812 829-2022 Toll Free Fax: 800 837-4130

CE0123

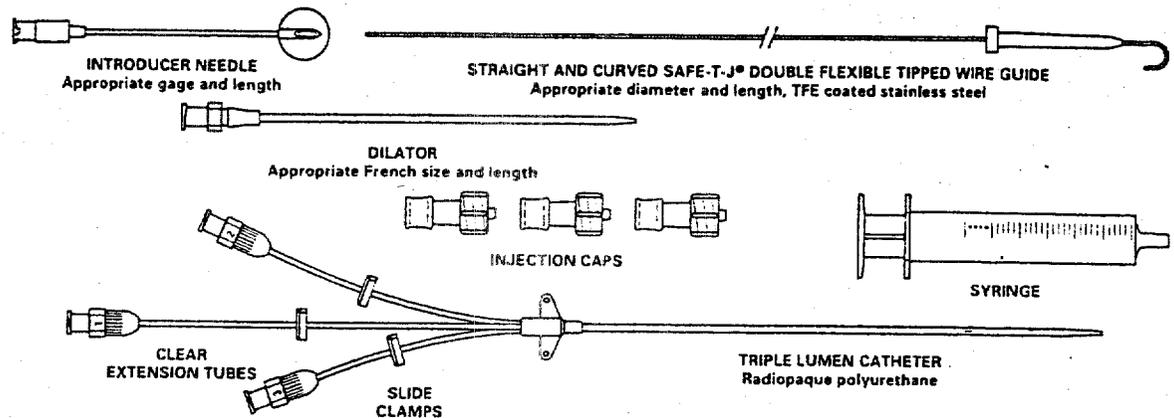
© COPYRIGHT COOK UROLOGICAL INCORPORATED 1994 SF900

162

BIO-GUARD SPECTRUM™ ANTIMICROBIAL BONDED TRIPLE LUMEN CENTRAL VENOUS CATHETER SETS AND TRAYS POLYURETHANE

Used for venous pressure monitoring, blood sampling and administration of drugs and fluids. The catheter incorporates three separate, noncommunicating vascular access lumens within a single catheter body. The triple lumen design reduces the necessity of utilizing multiple venipunctures or multiple stopcock configurations using single lumen catheters. Exit ports of individual lumens are separated by an appropriate distance in proportion to the catheter's French size and are oriented in a spiral configuration on the catheter body. This serves to separate fluids administered simultaneously. BIO-GUARD SPECTRUM™ catheters are bonded with the antimicrobials minocycline and rifampin, which may minimize the risk of bacterial colonization of the catheter and catheter-related bacteremia during use. Supplied sterile in peel-open packages. Intended for one-time use.

SET COMPONENTS



TRAY COMPONENTS

ALL TRAYS CONSIST OF ITEMS SHOWN ABOVE AND THE FOLLOWING ITEMS: 25 GAGE NEEDLE, 22 GAGE NEEDLE, LIDOCAINE, POVIDONE-IODINE SOLUTION, PREP SPONGES, FENESTRATED DRAPE, GAUZE SPONGES, DISPOSABLE SYRINGE, DISPOSABLE SCALPEL, SUTURE with NEEDLE, NEEDLE HOLDER, POVIDONE-IODINE OINTMENT, CSR WRAP and PREP TRAY.

U.S. Patent Numbers 4,442,133 and 4,740,382; Canadian Patent 1989, Patent Pending; Danish Patent Number 164474; Japanese Patent Number 1661553; European Patent Number 0191789; Australian Patent Number 578301

SET ORDER NUMBER	TRAY ORDER NUMBER	CATHETER			WIRE GUIDE	
		French Size	Equivalent Gage Size	Length ¹	Diameter	Tip
C-UTLM-501J-PED-ABRM	C-UTLMY-501J-PED-ABRM	5.0	16	5 cm	.025 inch (0.64 mm)	straight and 2 mm "J"
C-UTLM-501J-ABRM	C-UTLMY-501J-ABRM	5.0	16	8 cm	.025 inch (0.64 mm)	straight and 2 mm "J"
C-UTLM-501J-RSC-ABRM	C-UTLMY-501J-RSC-ABRM	5.0	16	12 cm	.025 inch (0.64 mm)	straight and 2 mm "J"
C-UTLM-501J-LSC-ABRM	C-UTLMY-501J-LSC-ABRM	5.0	16	15 cm	.025 inch (0.64 mm)	straight and 2 mm "J"
C-UTLM-701J-ABRM	C-UTLMY-701J-ABRM	7.0	13	15 cm	.035 inch (0.89 mm)	straight and 3 mm "J"
C-UTLM-701J-RSC-ABRM	C-UTLMY-701J-RSC-ABRM	7.0	13	20 cm	.035 inch (0.89 mm)	straight and 3 mm "J"
C-UTLM-701J-LSC-ABRM	C-UTLMY-701J-LSC-ABRM	7.0	13	25 cm	.035 inch (0.89 mm)	straight and 3 mm "J"

19T 18T
Fits Needle Gage

¹Length of catheter should be determined according to the anatomy of the patient and the entry site of the catheter. To guarantee extrapericardial location, catheter tip should not be advanced beyond innominate vein or initial segment of superior vena cava.

163

BIO-GUARD SPECTRUM™

BIO GUARD SPECTRUM™ catheters are bonded with the antimicrobial agents minocycline and rifampin, which may minimize the risk of bacterial colonization of the catheter and catheter-related bacteremia, during use. The activity of these antimicrobial agents is localized at the catheter surface and is not intended for treatment of systemic infections. The BIO-GUARD SPECTRUM™ antimicrobial bonded catheter is designated by the suffix -ABRM, in the recorder number (Example: C-UTLTMV-70TJ-RSC-ABRM).

Because the BIO GUARD SPECTRUM™ Catheter is coated with a combination of the antimicrobial agents minocycline (a derivative of tetracycline) and rifampin (a derivative of rifamycin B), the contraindications, warnings and precautions regarding use of these antimicrobials apply and should be adhered to for use of this device, although systemic levels of minocycline and rifampin in patients receiving this device are unlikely to be detected.

CONTRAINDICATIONS

- Allergy or history of allergy to tetracyclines or rifampin.
- WARNING:** Development of a hypersensitivity reaction should be followed by removal of the catheter and appropriate treatment at the discretion of the attending physician.
- CAUTION:** The BIO-GUARD SPECTRUM™ Catheter should not come into contact

with ethyl alcohol, isopropyl alcohol, or other alcohols, acetone or other non-polar solvents. These solvents may remove the antimicrobial from the catheter and reduce the catheter's antimicrobial efficacy.

Substantial antimicrobial activity associated with the BIO-GUARD SPECTRUM™ Catheter has been demonstrated in the following ways:

- During zone of inhibition testing, significant antimicrobial activity (defined as producing a zone greater than 10 mm in diameter) was demonstrated against the following organisms (five strains each) based on 10 catheter samples tested for each organism:
 - Staphylococcus epidermidis*
 - Staphylococcus aureus*
 - Acinetobacter species*
 - Xanthomonas (Stenotrophomonas) maltophilia*
 - Enterobacter aerogenes*
 - Escherichia coli*
 - Enterococcus faecalis*
 - Corynebacterium species*

- During zone of inhibition testing after suspension in serum at 37°C, significant antimicrobial activity was demonstrated for at least 15 days against *Staphylococcus epidermidis*, the most common organism implicated in catheter-related infection.
- Substantial decrease in the rate of bacterial colonization of the catheter was demonstrated in animal studies using *Staphylococcus aureus*.

• A prospective, randomized, clinical trial was conducted in which 288 patients were enrolled to receive either the BIO-GUARD SPECTRUM™ Catheter or a control catheter (standard coated, multi-lumen, central venous access catheter) with 117 patients available for follow-up in each study arm. The patient characteristics (age, sex, underlying disease, degree of immunosuppression, therapeutic intervention, site of insertion, duration of catheterization and reason for catheter removal) were comparable in the two groups. Results from the clinical study showed a statistically significant decrease in the incidence of bacterial colonization of the BIO-GUARD SPECTRUM™ Catheter (9% as compared to 30% for the control catheter, $p < 0.001$), and a statistically significant decrease in the incidence of catheter-related bacteremia in patients receiving the BIO-GUARD SPECTRUM™ Catheter (0% as compared to 6% for the control catheter, $p = 0.014$). Additionally, scanning electron microscopy studies on a representative sample of 40 catheters removed from patients (20 BIO-GUARD SPECTRUM™ and 20 uncoated catheters) demonstrated significant decrease in the rate of ultrastructural colonization of the BIO-GUARD SPECTRUM™ Catheters. The antimicrobial durability of the BIO-GUARD SPECTRUM™ Catheter against *Staphylococcus epidermidis* tested for at least 2 weeks after catheter insertion in patients (zone of inhibition ≥ 15 mm). Moreover, there were no detectable changes in antibiotic susceptibilities of bacteria cultured from the BIO-GUARD SPECTRUM™ Catheter and from adjacent skin.

**BIO-GUARD SPECTRUM™
Antimicrobial Catheter Surface**

The antimicrobial coating on the BIO-GUARD SPECTRUM™ Catheter is comprised of minocycline and rifampin. The principal site of action of the antimicrobial coating is on the surface of the catheter. The antimicrobial agents minocycline and rifampin contain yellow/orange pigments. Some coloration of the catheter is normal. Using high performance liquid chromatography (HPLC) analysis, blood samples obtained from 15 patients at 2, 6 hours, 1 day, 2 days and 3 days after insertion of the BIO-GUARD SPECTRUM™ Catheter showed no detectable systemic levels of minocycline or rifampin (detectability limit of both antimicrobials 0.5 µg/ml). Based on HPLC analysis the amounts of minocycline and rifampin bound to the 7 French, 20 cm BIO GUARD SPECTRUM™ Catheter are 139.3 µg/cm and 13.9 µg/cm, respectively. For catheters ranging in length from 5-25 cm, the total amount of minocycline bound to the BIO-GUARD SPECTRUM™ Catheter ranges from 7 to 3.5 mg, and the total amount of rifampin bound to the BIO-GUARD SPECTRUM™ Catheter ranges from .07 to 0.35 mg. These total amounts of minocycline and rifampin are much lower than the corresponding systemic pharmacologic doses, and are not expected to produce systemic blood levels. The chemical compositions of the antimicrobial agents are as follows:

Continued

164

EXHIBIT III

BIOCOMPATIBILITY TESTING

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016

Records processed under FOIA Request # 2016-1105; Released by CDRH on 09-09-2016