



U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER: (cwf)
FOLDER: K892364 - 110 pages
COMPANY: CALGON VESTAL DIV. (CALGVEST)
PRODUCT: DRESSING, WOUND, DRUG (FRO)
SUMMARY: Product: KALTOSTAT(TM) WOUND DRESSING

DATE REQUESTED: Feb 24, 2016

DATE PRINTED: Feb 24, 2016

Note: Printed





JUN 23 1989

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

Mr. Richard C. Jente
Manager, Regulatory and
Trade Affairs
Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
P. O. Box 147
St. Louis, Missouri 63166

Re: K892364
Kaltostat Wound Dressing
K892868
Kaltostat Wound Packing

Regulatory Class: None
Dated: June 14, 1989
Received: June 19, 1989

Dear Mr. Jente:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market your device subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act) and the following limitations:

1. This device may not be labeled for use on third degree burns or for use on full thickness skin wounds of any nature without specific Food and Drug Administration (FDA) approval for such labeling.
2. This device may not be labeled as having any accelerating effect on the rate of wound healing or epithelization without evidence of said effect being reviewed and approved by FDA.
3. This device may not be labeled as a long-term or permanent, no change dressing, or as an artificial or synthetic skin without specific FDA approval for such labeling.
4. This device may not be labeled as a treatment or a cure for vascular stasis ulcers without specific FDA approval for such labeling.

BEST COPY AVAILABLE

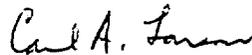
Page 2 - Mr. Jente

The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Performance Standards) or class III (Premarket Approval) 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 895. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under the Radiation Control for Health and Safety Act of 1968, or other Federal Laws or Regulations.

This letter immediately will allow you to begin marketing your device as described. An FDA finding of substantial equivalence of your device to a pre-amendments device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in any way represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-8040. Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6597.

Sincerely yours,



Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE





Memorandum

Date 6/23/89

From REVIEWER(S) - NAME(S) EM Maclard

Subject 510(k) NOTIFICATION K892364 / B

To THE RECORD

It is my recommendation that the subject 510(k) Notification:

- (A) Is substantially equivalent to marketed devices.
- (B) Requires premarket approval. NOT substantially equivalent to marketed devices.
- (C) Requires more data.
- (D) Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Additional Comments:

*see attached memo
6/23/89*

The submitter requests under 21 CFR §807.95:

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

Predicate Product Code w/Panel and class:

79 FRO

Additional Product Code(s) w/Panel (optional):

REVIEW: Kenneth A. Palmer 6/23/89
(BRANCH CHIEF) (DATE)

FINAL REVIEW: Kenneth A. Palmer 6/23/89
for (DIVISION DIRECTOR) (DATE)

BEST COPY AVAILABLE

[Handwritten mark]

6/23/89

RMU

Subject: Review of K892364
Kaltostat Wound Dressing
Calgon Vestal Laboratories

K892868
Kaltostat Wound Packing
Calgon Vestal Laboratories

The sponsor has submitted the requested label changes, i.e., he has included the requested contraindication statement for use of the device(s) as surgical sponge, and he has also deleted references to foreign body responses. With these changes effected, the device can now be considered substantially equivalent to other products currently being marketed, such as Sorbsan wound dressing.

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, MD 20910

JUNE 20, 1989

CALGON VESTAL LABORATORIES
ATTN: RICHARD C. JENTE
P.O. BOX 147
ST. LOUIS, MO 63166

D.C. Number : K892364
Received : 04-06-89
90th Day : 09-17-89
Product : KALTOSTAT(TM) WOUND
DRESSING

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. You are required to wait ninety (90) days after the received date shown above or until receipt of a "substantially equivalent" letter before placing the product into commercial distribution. We intend to complete our review expeditiously and within ninety days. Occasionally, however, a submitter will not receive a final decision or a request for additional information until after ninety days has elapsed. Be aware that FDA is able to continue the review of a submission beyond the ninety day period and might conclude that the device is not substantially equivalent. A "not substantially equivalent" device may not be in commercial distribution without an approved premarket approval application or reclassification of the device. We, therefore, recommend that you not market this device before FDA has made a final decision. Thus, if you have not received a decision within ninety days, it would be prudent to check with FDA to determine the status of your submission.

All correspondence concerning your submission MUST be sent to the Document Mail Center at the above address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification application. Telefax material will not be accepted nor considered as part of your official premarket notification application, unless specifically requested of you by an FDA official.

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at (301) 443-6597 or their toll-free number (800) 638-2041, or contact me at (301) 427-8162.

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE



K892364/B

DIVISION OF CALGON CORPORATION • SUBSIDIARY OF MERCK & CO., INC. • P.O. BOX 147 • ST. LOUIS, MO 63166 • (314) 535-1810

VIA COURIER

June 14, 1989

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Springs, MD 20910

Re: Section 510(k) D.C. #K892364
Kaltostat Wound Dressing

To Whom It May Concern:

This letter will confirm a conversation with Ms. Fran Moreland on June 14 which has resulted in certain amendments to this Section 510(k).

Specifically, we have revised the "Instructions for Use," pages 18, 19 and 20 of our submission of May 30, 1989 to:

- 1) Add an additional statement to the "Contraindications" (page 18) indicating this device is not for use as a surgical sponge.
- 2) Delete the phrase referring to foreign body reactions from paragraph 3(e) (page 19) of "Dressing Change and Removal."
- 3) Delete the paragraph referring to foreign body reactions paragraph 4 (page 20) from "Precautions and Observations."

We believe this is fully responsive to the matters brought to our attention. If you have further concerns, please contact me at (314) 535-1810, Ext. 562.

Sincerely,

R. C. Jente, Manager
Regulatory and Trade Affairs

RCJ/bar

BEST COPY AVAILABLE

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

DRAFT

INSTRUCTIONS FOR USE

KALTOSTAT WOUND DRESSING
Calcium-Sodium Alginate Fiber

DESCRIPTION

Kaltostat Wound Dressing is a soft, white, sterile non-woven dressing of calcium-sodium alginate fiber. The alginate fibers can absorb wound exudate or saline and convert to a firm gel/fiber mat. This gel forms a moist, warm environment at the wound interface. The gel allows trauma-free removal with little or no damage to newly formed tissue. Depending on the wound, the dressing may be left in place up to seven days.

INDICATIONS

Kaltostat Wound Dressing is an external wound dressing designed to absorb exudate and protect the wound from contamination.

Kaltostat Wound Dressing is indicated as an external wound dressing for use in the local wound management of external wounds such as pressure sores, venous stasis ulcers, arterial ulcers, diabetic ulcers, donor sites, abrasions, lacerations and superficial burns, post-surgical incisions, and other external wounds inflicted by trauma.

CONTRAINDICATIONS

This dressing is not indicated for wounds involving muscle, tendon, or bone, or for third degree burns. This device is contraindicated for use as a surgical sponge.

APPLICATION OF KALTOSTAT WOUND DRESSING

1. Wound Site Preparation and Cleansing

Prior to application of the Kaltostat Wound Dressing, the wound should be debrided of excessive necrotic tissue and eschar and irrigated with an appropriate non-toxic cleansing solution.

BEST COPY AVAILABLE

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Dressing Preparation and Application

- a. Kaltostat Wound Dressing should be trimmed to the exact size of the wound.
- b. For heavily exudating wounds, Kaltostat Wound Dressing should be applied dry onto the wound. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.
- c. For lightly exudating wounds, the Kaltostat Wound Dressing should be placed on the wound and moistened with saline. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.

3. Dressing Change and Removal

- a. On heavily exudating wounds, change the Kaltostat Wound Dressing when strike-through of the secondary dressing occurs or whenever good nursing practice dictates the dressing should be changed.
- b. Removal should be trouble free on heavily exudating wounds as Kaltostat Wound Dressing will gel at the wound/dressing interface and easily lift away.
- c. Removal from lightly exudating wounds may be assisted by saturating the dressing with saline.
- d. Cleanse the wound site prior to application of a new dressing.
- e. As with any dressing, Kaltostat Wound Dressing should be removed from the wound and the wound cleansed at appropriate intervals. Alginate fibers and gels inadvertently left in the wound will simply be absorbed by the body.

PRECAUTIONS AND OBSERVATIONS

1. Infection: All wounds can be expected to contain some microorganisms. However, if true clinical infection (fever, tenderness or redness in the area of the wound) should develop, appropriate steps, as defined by the attending physician, should be taken to address that infection. Regular evaluation and cleansing of infected wounds should be a common practice. Since Kaltostat Wound Dressing is not an occlusive dressing, Kaltostat Wound Dressing may be continued in use provided it is changed on a regular basis (at least daily while infection is present).

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Underlying Causes: Some wounds, such as leg ulcers and pressure sores, can be "non-healing" unless steps are taken to correct the underlying pathology. Kaltostat Wound Dressing is designed for local wound management and can be part of the overall management program for these types of wounds.
3. Dessication: Kaltostat Wound Dressing is designed for moist wound healing. If a Kaltostat Wound Dressing which has initially formed a gel is allowed to dry out, removal from the wound can be difficult. This dessication is generally not a problem with exudating wounds. On non-exudating wounds, Kaltostat Wound Dressing should only be applied with saline. Reapplication of saline may be necessary to maintain the gel. If the gel dries out, saturate the dried gel with saline to rehydrate it; this process may take several hours to soften the dried gel.

Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
St. Louis, Missouri 63110

Lit No. _____

-20-

BEST COPY AVAILABLE



DIVISION OF CALGON CORPORATION • SUBSIDIARY OF MERCK & CO., INC. • P.O. BOX 147 • ST. LOUIS, MO 63166 • (314) 535-1810

VIA COURIER

June 14, 1989

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Springs, MD 20910

Re: Section 510(k) D.C. #K892364
Kaltostat Wound Dressing

To Whom It May Concern:

This letter will confirm a conversation with Ms. Fran Moreland on June 14 which has resulted in certain amendments to this Section 510(k).

Specifically, we have revised the "Instructions for Use," pages 18, 19 and 20 of our submission of May 30, 1989 to:

- 1) Add an additional statement to the "Contraindications" (page 18) indicating this device is not for use as a surgical sponge.
- 2) Delete the phrase referring to foreign body reactions from paragraph 3(e) (page 19) of "Dressing Change and Removal."
- 3) Delete the paragraph referring to foreign body reactions paragraph 4 (page 20) from "Precautions and Observations."

We believe this is fully responsive to the matters brought to our attention. If you have further concerns, please contact me at (314) 535-1810, Ext. 562.

Sincerely,

R. C. Jente, Manager
Regulatory and Trade Affairs

RCJ/bar

BEST COPY AVAILABLE

11

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

DRAFT

INSTRUCTIONS FOR USE

KALTOSTAT WOUND DRESSING
Calcium-Sodium Alginate Fiber

DESCRIPTION

Kaltostat Wound Dressing is a soft, white, sterile non-woven dressing of calcium-sodium alginate fiber. The alginate fibers can absorb wound exudate or saline and convert to a firm gel/fiber mat. This gel forms a moist, warm environment at the wound interface. The gel allows trauma-free removal with little or no damage to newly formed tissue. Depending on the wound, the dressing may be left in place up to seven days.

INDICATIONS

Kaltostat Wound Dressing is an external wound dressing designed to absorb exudate and protect the wound from contamination.

Kaltostat Wound Dressing is indicated as an external wound dressing for use in the local wound management of external wounds such as pressure sores, venous stasis ulcers, arterial ulcers, diabetic ulcers, donor sites, abrasions, lacerations and superficial burns, post-surgical incisions, and other external wounds inflicted by trauma.

CONTRAINDICATIONS

This dressing is not indicated for wounds involving muscle, tendon, or bone, or for third degree burns. This device is contraindicated for use as a surgical sponge.

APPLICATION OF KALTOSTAT WOUND DRESSING

1. Wound Site Preparation and Cleansing

Prior to application of the Kaltostat Wound Dressing, the wound should be debrided of excessive necrotic tissue and eschar and irrigated with an appropriate non-toxic cleansing solution.

BEST COPY AVAILABLE

12

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Dressing Preparation and Application

- a. Kaltostat Wound Dressing should be trimmed to the exact size of the wound.
- b. For heavily exudating wounds, Kaltostat Wound Dressing should be applied dry onto the wound. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.
- c. For lightly exudating wounds, the Kaltostat Wound Dressing should be placed on the wound and moistened with saline. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.

3. Dressing Change and Removal

- a. On heavily exudating wounds, change the Kaltostat Wound Dressing when strike-through of the secondary dressing occurs or whenever good nursing practice dictates the dressing should be changed.
- b. Removal should be trouble free on heavily exudating wounds as Kaltostat Wound Dressing will gel at the wound/dressing interface and easily lift away.
- c. Removal from lightly exudating wounds may be assisted by saturating the dressing with saline.
- d. Cleanse the wound site prior to application of a new dressing.
- e. As with any dressing, Kaltostat Wound Dressing should be removed from the wound and the wound cleansed at appropriate intervals. Alginate fibers and gels inadvertently left in the wound will simply be absorbed by the body.

PRECAUTIONS AND OBSERVATIONS

1. Infection: All wounds can be expected to contain some microorganisms. However, if true clinical infection (fever, tenderness or redness in the area of the wound) should develop, appropriate steps, as defined by the attending physician, should be taken to address that infection. Regular evaluation and cleansing of infected wounds should be a common practice. Since Kaltostat Wound Dressing is not an occlusive dressing, Kaltostat Wound Dressing may be continued in use provided it is changed on a regular basis (at least daily while infection is present).

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Underlying Causes: Some wounds, such as leg ulcers and pressure sores, can be "non-healing" unless steps are taken to correct the underlying pathology. Kaltostat Wound Dressing is designed for local wound management and can be part of the overall management program for these types of wounds.
3. Dessication: Kaltostat Wound Dressing is designed for moist wound healing. If a Kaltostat Wound Dressing which has initially formed a gel is allowed to dry out, removal from the wound can be difficult. This dessication is generally not a problem with exudating wounds. On non-exudating wounds, Kaltostat Wound Dressing should only be applied with saline. Reapplication of saline may be necessary to maintain the gel. If the gel dries out, saturate the dried gel with saline to rehydrate it; this process may take several hours to soften the dried gel.

Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
St. Louis, Missouri 63110

Lit No. _____

-20-

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, MD 20910

JUNE 15, 1989

CALGON VESTAL LABORATORIES
ATTN: RICHARD C. JENTE
P.O. BOX 147
ST. LOUIS, MO 63166

D.C. Number: K892364
Product : KALTOSTAT(TM) WOUND
DRESSING

-- 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. This information and all correspondence concerning your submission MUST be sent to the Document Mail Center at the above address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification application. Telefax material will not be accepted nor considered as part of your official premarket notification application, unless specifically requested of you by an FDA official.

When your additional information is received by the Office of Device Evaluation Document Mail Center (address above), the 90-day period will begin again.

If after 30 days the requested information is not received, we will stop reviewing your submission and proceed to withdraw 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 the 90-day time period will begin again.

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at (301) 443-6597 or their toll-free number (800) 638-2041, or contact me at (301) 427-8162.

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE

DO NOT REMOVE THIS ROUTE SLIP!!!!

K-89-2364

6/15/89

FROM: CALGON VESTAL LABORATORIES ATTN: RICHARD C. JENTE P.O. BOX 147 ST. LOUIS, MO 63166		LETTER DATE 04/03/89	LOGIN DATE 04/06/89	DUE DATE 09/03/89
SHORT NAME: CALGVESTLABO		ESTABLISHMENT NO: 1940768		CONTROL # K892364
TO: ODE/DMC		CONT. CONF.: ? STATUS : H REV PANEL : SU PAN/PROD CODE(S): SU/ / /		
SUBJECT: KALTOSTAT(TM) WOUND DRESSING				
DECISION: DECISION DATE: / /	RQST INFO	DATE: 05/16/89 DATE: 06/15/89 DATE: / / DATE: / / DATE: / / DATE: / /	INFO DUE	DATE: 06/15/89 DATE: 07/15/89 DATE: / / DATE: / / DATE: / / DATE: / /

SUPPLEMENT: 01

LTR DATE: 890530

LOGIN DATE: 890605

BEST COPY AVAILABLE

16



Memorandum

To: _____
 From: REVIEWER(S) - NAME(S) 6/14/89 [Signature]
 Subject: 510(k) NOTIFICATION K892364/A
 To: THE RECORD

It is my recommendation that the subject 510(k) Notification:

- (A) Is substantially equivalent to marketed devices.
- (B) Requires premarket approval. NOT substantially equivalent to marketed devices.
- (C) Requires more data.
- (D) Is an incomplete submission. (See Submission Sheet).

Additional Comments:

see attached memo [Signature]

The submitter requests:

Class Code w/Panel:

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

79KRE

REVIEW:

(BRANCH CHIEF) (DATE)

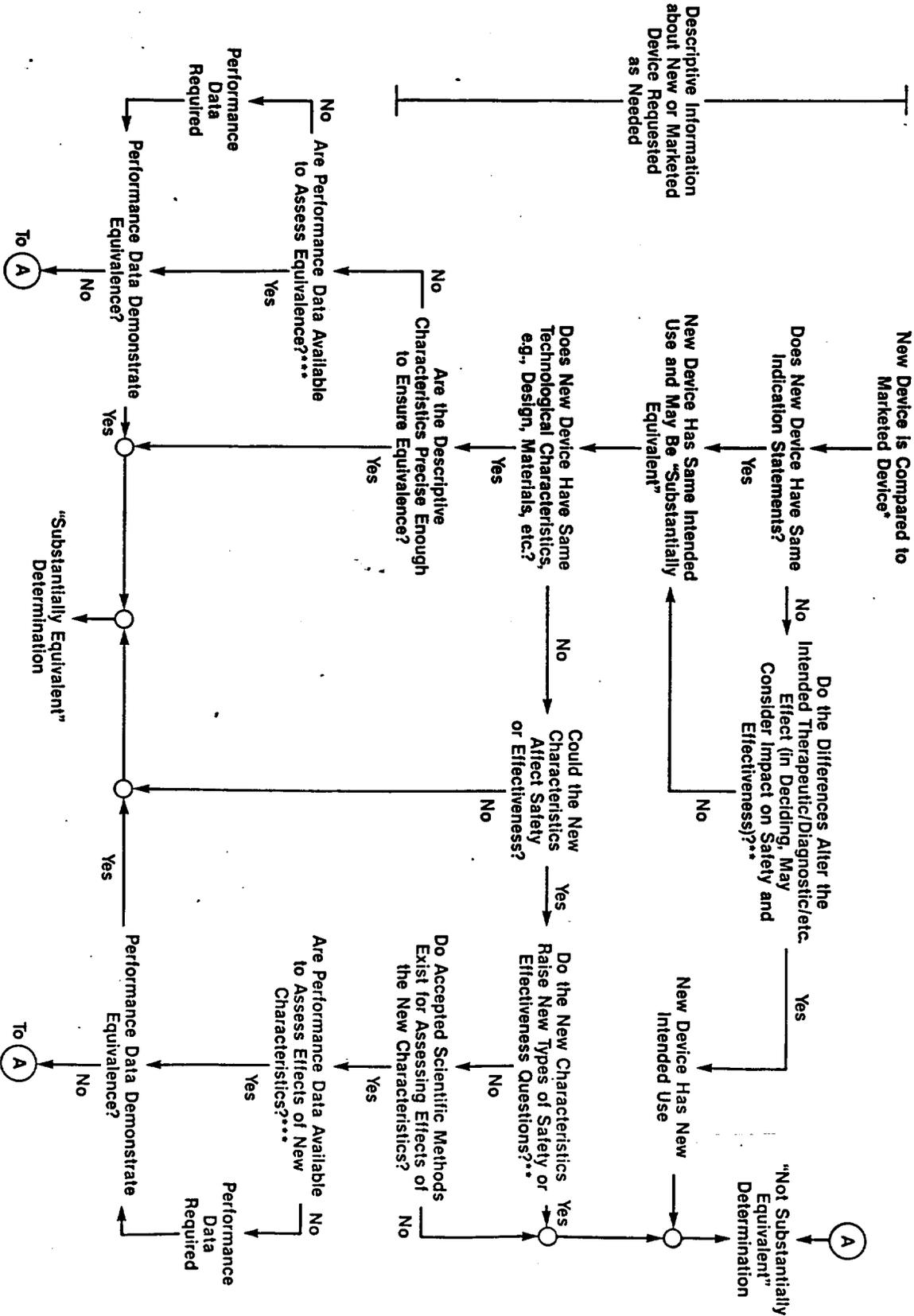
FINAL REVIEW:

(DIVISION DIRECTOR) (DATE)

BEST COPY AVAILABLE

X
17

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



* 510(k) Submissions Compare New Devices to Marketed Devices. FDA Requests Additional Information if the Relationship Between Marketed and "Predicate" (Pre-Amendments or Reclassified Post-Amendments) Devices is Unclear.

** This Decision is Normally Based on Descriptive Information Alone, But Limited Testing Information is Sometimes Required.
*** Data May Be in the 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

BEST COPY AVAILABLE

18

6/13/89

rum

Subject: Review of K892364
Kaltostat Wound Dressing
Calgon Vestal Laboratories

K892868
Kaltostat Wound Packing
Calgon Vestal Laboratories

Again, because these submissions are very similar, they will be reviewed in a combined manner. The sponsor has responded to our telephone request for additional information and he has submitted the following:

1. Revised labeling indicating that this device does not function as a hemostatic agent with regard to its function as a wound dressing agent to control bleeding.
2. biocompatibility data from the following procedures (individual data included for all tests submitted)
 - a. cytotoxicity (negative)
 - b. acute systemic toxicity-saline only**, (negative)
 - c. intracutaneous(this test procedure was not requested nor required-negative)
 - d. primary skin (negative)
 - e. guinea pig sensitization: N.B. this test procedure was performed with

(b)(4)

Additional points:

The sponsor has claimed substantial equivalence to the gauze J&J sponges as well as to duoderm hydroactive dressings for the wound dressing device and substantial equivalence to J&J gauze sponges, Bard Absorption dressing and duoderm for the wound packing device. A better comparative device would have been the Sorbsan device, but this product is not currently on the market here in this country and perhaps this is the reason that the device was not claimed.

(b)(4)

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
8757 Georgia Avenue
Silver Spring, MD 20910

JUNE 5, 1989

CALGON VESTAL LABORATORIES
ATTN: RICHARD C. JENTE
P.O. BOX 147
ST. LOUIS, MO 63166

D.C. Number : K892364
Received : 06-05-89
Product : KALTOSTAT(TM) WOUND
DRESSING

The additional information you have submitted has been received.

-- We will notify you when the processing of your submission has been completed or if any additional information is required. You are required to wait ninety (90) days after the received date shown above or until receipt of a "substantially equivalent" letter before placing the product into commercial distribution. I suggest that you contact us if you have not been notified in writing at the end of this ninety (90) day period before you begin marketing you device. Written questions concerning the status of your submission should be sent to:

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at their toll-free number (800) 638-2041 or me at (301) 427-8162

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE



K892364/A

DIVISION OF CALGON CORPORATION • SUBSIDIARY OF MERCK & CO., INC. • P.O. BOX 147 • ST. LOUIS, MO 63166 • (314) 535-1810

May 30, 1989

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

Re: Section 510(k) D.C. #K892364 - Kaltostat Wound Dressing

To Whom It May Concern:

Conversations with Ms. Fran Moreland on 5/15/89 and 5/16/89 prompted us to amend several pages of this 510(k). In specific, Ms. Moreland's comments centered around three areas: (1) the "controls bleeding" indication, (2) supporting toxicity data on the finished product, and (3) sterility methods. Below are the responses for each of these items.

1. We have revised the "Instructions for Use" (package insert) to remove any references to control of bleeding by the product. The revised package insert is attached.
2. The toxicity testing has been done as follows.

a) Cytotoxicity - (b)(4)

[Redacted]

b) Acute Systemic Toxicity - (b)(4)

[Redacted]

c) Intracutaneous Toxicity - (b)(4)

[Redacted]

BEST COPY AVAILABLE

21

Food and Drug Administration
Silver Spring, Maryland
Page Two

d) Primary Skin Irritation - (b)(4)
[Redacted]

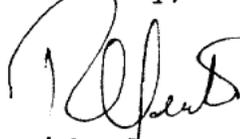
e) Magnusson Kligman Sensitization - (b)(4)
[Redacted]

Copies of all these test results are attached.

3. Kaltostat Wound Dressing is sterilized by gamma irradiation with a minimum dose of 2.5 Mrad. The sterility assurance level (SAL) is 10^{-6} . The method of release of Kaltostat Wound Dressing is biological.

We believe this information satisfies all the concerns brought out by the FDA in response to this 510(k). If you have further questions, please contact me at (314) 535-1810, Ext. 562.

Sincerely,



Richard C. Jente
Manager, Regulatory and
Trade Affairs

RCJ/st/dresf&d

BEST COPY AVAILABLE

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

DRAFT

INSTRUCTIONS FOR USE

KALTOSTAT WOUND DRESSING
Calcium-Sodium Alginate Fiber

DESCRIPTION

Kaltostat Wound Dressing is a soft, white, sterile non-woven dressing of calcium-sodium alginate fiber. The alginate fibers can absorb wound exudate or saline and convert to a firm gel/fiber mat. This gel forms a moist, warm environment at the wound interface. The gel allows trauma-free removal with little or no damage to newly formed tissue. Depending on the wound, the dressing may be left in place up to seven days.

INDICATIONS

Kaltostat Wound Dressing is an external wound dressing designed to absorb exudate and protect the wound from contamination.

Kaltostat Wound Dressing is indicated as an external wound dressing for use in the local wound management of external wounds such as pressure sores, venous stasis ulcers, arterial ulcers, diabetic ulcers, donor sites, abrasions, lacerations and superficial burns, post-surgical incisions, and other external wounds inflicted by trauma.

CONTRAINDICATIONS

This dressing is not indicated for wounds involving muscle, tendon, or bone, or for third degree burns.

APPLICATION OF KALTOSTAT WOUND DRESSING

1. Wound Site Preparation and Cleansing

Prior to application of the Kaltostat Wound Dressing, the wound should be debrided of excessive necrotic tissue and eschar and irrigated with an appropriate non-toxic cleansing solution.

BEST COPY AVAILABLE

23

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Dressing Preparation and Application

- a. Kaltostat Wound Dressing should be trimmed to the exact size of the wound.
- b. For heavily exudating wounds, Kaltostat Wound Dressing should be applied dry onto the wound. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.
- c. For lightly exudating wounds, the Kaltostat Wound Dressing should be placed on the wound and moistened with saline. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.

3. Dressing Change and Removal

- a. On heavily exudating wounds, change the Kaltostat Wound Dressing when strike-through of the secondary dressing occurs or whenever good nursing practice dictates the dressing should be changed.
- b. Removal should be trouble free on heavily exudating wounds as Kaltostat Wound Dressing will gel at the wound/dressing interface and easily lift away.
- c. Removal from lightly exudating wounds may be assisted by saturating the dressing with saline.
- d. Cleanse the wound site prior to application of a new dressing.
- e. As with any dressing, Kaltostat Wound Dressing should be removed from the wound and the wound cleansed at appropriate intervals. Alginate fibers and gels inadvertently left in the wound will simply be absorbed by the body and will not produce a foreign body reaction.

PRECAUTIONS AND OBSERVATIONS

1. Infection: All wounds can be expected to contain some microorganisms. However, if true clinical infection (fever, tenderness or redness in the area of the wound) should develop, appropriate steps, as defined by the attending physician, should be taken to address that infection. Regular evaluation and cleansing of infected wounds should be a common practice. Since Kaltostat Wound Dressing is not an occlusive dressing, Kaltostat Wound Dressing may be continued in use provided it is changed on a regular basis (at least daily while infection is present).

510(k) - Kaltostat Wound Dressing DC #K892364 Amended

2. Underlying Causes: Some wounds, such as leg ulcers and pressure sores, can be "non-healing" unless steps are taken to correct the underlying pathology. Kaltostat Wound Dressing is designed for local wound management and can be part of the overall management program for these types of wounds.
3. Dessication: Kaltostat Wound Dressing is designed for moist wound healing. If a Kaltostat Wound Dressing which has initially formed a gel is allowed to dry out, removal from the wound can be difficult. This dessication is generally not a problem with exudating wounds. On non-exudating wounds, Kaltostat Wound Dressing should only be applied with saline. Reapplication of saline may be necessary to maintain the gel. If the gel dries out, saturate the dried gel with saline to rehydrate it; this process may take several hours to soften the dried gel.
4. Foreign Body Reactions: As with any dressing, Kaltostat Wound Dressing should be changed at appropriate intervals. Occasional alginate fiber and gel inadvertently left in the wound will simply be absorbed by the body and will not produce a foreign body reaction.

Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
St. Louis, Missouri 63110

Lit No. _____

-20-

BEST COPY AVAILABLE

25

(b)(4)



PRIMARY SKIN IRRITATION TEST
IN THE RABBIT OF
KALTOSTAT WOUND DRESSING -

(b)(4) Testing



SPONSOR

Calgon Vestal Labs R & D
Division of Calgon Corporation
5035 Manchester
St. Louis, MO 63110

TEST FACILITY (b)(4)

(b)(4) Testing



Attn: Rita A. Brenden, Ph.D.

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
8757 Georgia Avenue
Silver Spring, MD 20910

MAY 16, 1989

CALGON VESTAL LABORATORIES
ATTN: RICHARD C. JENTE
P.O. BOX 147
ST. LOUIS, MO 63166

Ref : K892364
Product : KALTOSTAT(TM) WOUND
DRESSING

-- 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. This information should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

When your additional information is received by the Office of Device Evaluation the 90-day period will begin again.

If after 30 days the requested information is not received, we will stop reviewing your submission. 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 the 90-day time period will begin again.

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at their toll-free number (800) 638-2041 or me at (301) 427-8162.

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE

67

DO NOT REMOVE THIS ROUTE SLIP!!!!

K-89-2364

5/16/89

FROM: CALGON VESTAL LABORATORIES ATTN: RICHARD C. JENTE P.O. BOX 147 ST. LOUIS, MO 63166		LETTER DATE 04/03/89	LOGIN DATE 04/06/89	DUE DATE 07/05/89	
		TYPE OF DOCUMENT: 510 (k)		CONTROL # K892364	
SHORT NAME: CALGVESTLABO		ESTABLISHMENT NO: 1940768			
TO: ODE/DMC		CONT. CONF.: ? STATUS : H REV PANEL : SU PAN/PROD CODE(S): SU/ / /			
SUBJECT: KALTOSTAT(TM) WOUND DRESSING					
DECISION: DECISION DATE: / /		RQST INFO DATE: 05/16/89 DATE: / / DATE: / / DATE: / / DATE: / / DATE: / /			INFO DUE DATE: 06/15/89 DATE: / / DATE: / / DATE: / / DATE: / / DATE: / /

68



Memorandum

Date 5/15/89
 From REVIEWER(S) - NAME(S) RM Moller
 Subject 510(k) NOTIFICATION K892364
 To THE RECORD

It is my recommendation that the subject 510(k) Notification:

- (A) Is substantially equivalent to marketed devices.
- (B) Requires premarket approval. NOT substantially equivalent to marketed devices.
- (C) Requires more data.
- (D) Is an incomplete submission. (See Submission Sheet).

Additional Comments:

see attached memo

*5/15/89
RM*

The submitter requests:

Class Code w/Panel:

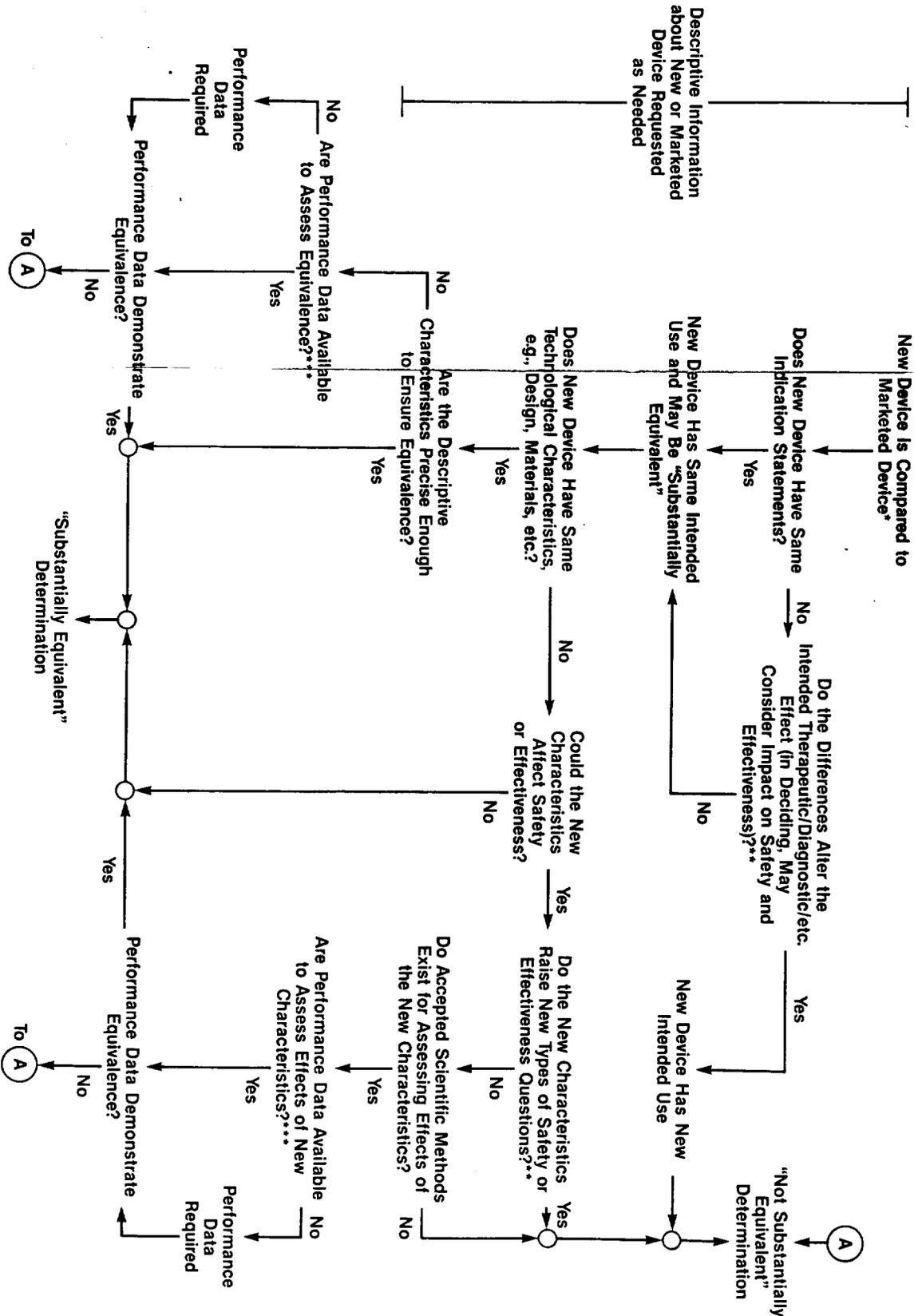
- No Confidentiality
 - Confidentiality for 90 days
 - Continued Confidentiality exceeding 90 days
- 79 FRO

REVIEW: _____ (BRANCH CHIEF) (DATE)

FINAL REVIEW: _____ (DIVISION DIRECTOR) (DATE)

*X
09*

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



* 510(k) Submissions Compare New Devices to Marketed Devices. FDA Requests Additional Information if the Relationship Between Marketed and "Predicate" (Pre-Amendments or Reclassified Post-Amendments) Devices is Unclear.

** This Decision is Normally Based on Descriptive Information Alone, But Limited Testing Information is Sometimes Required.
 *** Data May Be in the 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

BEST COPY AVAILABLE

5/10/89

rem/5/18/89

Subject: **Review of K892364**
Kaltostat Wound Dressing
Calgon Vestal Laboratories
and
K892868
Kaltostat Wound Packing
Calgon Vestal Laboratories

The sponsor has submitted two 510(k)s that are composed of the same material but with slightly different indications for use, i.e., as a wound dressing and also as a packing agent. Because the biomaterial issues as well as the sterility and biocompatibility and to a degree the labeling issues will be quite similar, the devices will be reviewed together.

(b)(4) Study - Testing

To be mentioned is the fact that the class of alginate compounds are generally recognized as hemostatic agents.

Both devices carry the following statement(s): "...is indicated as an external wound dressing/packing agent for use in the local wound management of external wounds, etc. It is designed to control bleeding, absorb exudate and protect the wound from contamination." This wording is lifted directly from the device definitions and there are no problems with this portion of the labeling. Nor are there any difficulties with the additional labeling that has been included in Appendix II, that refers to the proper application techniques, usages, i.e the contraindications for full thickness wounds, etc.. However, Item 5 of this section contains a statement that the device will control bleeding because it SERVES AS A MATRIX FOR COAGULATION AND BECAUSE CALCIUM ALGINATE IS WELL KNOWN TO INITIATE THE BLOOD CLOTTING CASCADE. The sponsor further cautions against the use of this product on bleeding from an arterial source and also for use on internal wounds. The issue here is whether or not we wish to take this submission any further. If they are going to make the hemostatic claim, then this is not a 510(k)able device. But if they are willing to delete this portion of their labeling, then they could go the 510(k) route.

We really need to make a cut on this because the information that has been

submitted for the biocompatibility issues is not satisfactory (they claim that this is a food additive and therefore no additional testing should be required) and more testing will be required. Also, additional sterility information must be submitted. Do we want to check on the pyrogenicity issue also???? Or is this a mute question? *no - see Johnson data - ETO going to be x, so why waste the rabbits.*

Comments please.

5/15/89

RE: conversation with KAP/KJC

This submission can be handled as a regular 510(k) if the manufacturer agrees to modify the labeling by deleting all references to hemostatic activity. In addition, if the sponsor agrees to this caveat, then the biocompatibility data can be negotiated by having them submit by reference, information concerning the toxicity of the device. They should be able to supply the following on the end product:

1. primary skin;
2. Magnusson/Kligman sensitization assay;
3. sterility information as follows:
 - a. SAL
 - b. method of release
 - c. type of sterilization (if ETO, residue levels, etc., if applicable)

Also, need to ask why the name Kaltostat and also need to reinforce the fact that they MUST SUBMITT the modified labeling as part of their official record.

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
8757 Georgia Avenue
Silver Spring, MD 20910

APRIL 19, 1989

CALGON VESTAL LABORATORIES
ATTN: RICHARD C. JENTE
P.O. BOX 147
ST. LOUIS, MO 63166

D.C. Number : K892364
Received : 04-06-89
Product : KALTOSTAT(TM) WOUND
DRESSING

-- The Premarket Notification you have submitted as required under Section 510(k) of the Federal Food, Drug and Cosmetic Act for the above referenced device has been received and assigned a unique document control number (D.C. Number above). Please cite this D.C. Number in any future correspondence that relates to this submission.

We will notify you when the processing of this submission has been completed or if any additional information is required. You are required to wait ninety (90) days after the received date shown above or until receipt of a "substantially equivalent" letter before placing the product into commercial distribution. I suggest that you contact us if you have not been notified in writing at the end of this ninety (90) day period before you begin marketing your device. Written questions concerning the status of your submission should be sent to:

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at their toll-free number (800) 638-2041 or me at (301) 427-8162.

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health

BEST COPY AVAILABLE



15892364

RECEIVED

DIVISION OF CALGON CORPORATION • SUBSIDIARY OF MERCK & CO., INC. • P.O. BOX 147 • ST. LOUIS, MO 63166 • (314) 535-1810

1989 APR -6 AM 10:35

CENTER

April 3, 1989

Food and Drug Administration
Bureau of Medical Devices (HFK-20)
8757 Georgia Avenue
Silver Spring, Maryland 20910

Re: Section 510(k) Premarket Notification - Kaltostat Wound Dressing

To Whom It May Concern:

Enclosed please find in duplicate a Premarket Notification for Kaltostat Wound Dressing submitted pursuant to Section 510(k) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR Part 807. Calgon Vestal Laboratories, Division of Calgon Corporation, proposes to introduce into interstate commerce for commercial distribution in not less than 90 days a device known as Kaltostat Wound Dressing. This device is substantially equivalent to other devices currently in commercial distribution which have been previously determined by FDA to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Calgon Vestal Laboratories requests that FDA hold as confidential information our intent to market Kaltostat Wound Dressing. We request that this confidentiality be observed until such time that we provide a written certification that our intent to market this device has been publicly disclosed or that the product has been introduced into the commercial market. Further, we request that any manufacturing or formulation information contained in this Notification be considered trade secret and, thus, confidential commercial information.

Should you have any questions with regard to this Notification, please do not hesitate to contact me. We look forward to favorable consideration of this 510(k) Notification at your earliest convenience.

Sincerely,

Richard C. Jerte
Manager, Regulatory & Trade Affairs

RCJ/st

Enclosures

BEST COPY AVAILABLE

74

PREMARKET NOTIFICATION SUBMISSION - 510(k)

FOR

KALTOSTAT™ WOUND DRESSING

Submission Date: April 3, 1989

Submitted By:

**Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
5035 Manchester Avenue
St. Louis, Missouri 63110
(314) 535-1810**

Contact Person:

Richard C. Jente

RECEIVED
1989 APR - 6 AM 10: 35
CENTER

75

PREMARKET NOTIFICATION - 510(k)

KALTOSTAT WOUND DRESSING

TABLE OF CONTENTS

	<u>PAGE No.</u>
A. DEVICE NAME	3
B. ESTABLISHMENT REGISTRATION NUMBER	4
C. DEVICE CLASSIFICATION	5
D. PERFORMANCE STANDARDS	6
E. PRODUCT DESCRIPTION, INTENDED USES AND LABELING	7
F. COMPARISON TO MARKETED PRODUCTS14
G. SAFETY EVALUATION16
APPENDIX 1: PROPOSED LABELING AND INSTRUCTIONS FOR USE17
APPENDIX 2: PRODUCT LABELING AND PROMOTIONAL MATERIALS FOR COMPARABLE PRODUCTS21
APPENDIX 3: BIBRA TOXICITY PROFILE OF ALGINIC ACID AND ITS COMMON SALTS28

510(k) - Kaltostat Wound Dressing

**A. THE DEVICE NAME, INCLUDING BOTH THE TRADE OR
PROPRIETARY NAME AND THE COMMON OR USUAL NAME
OR CLASSIFICATION NAME OF THE DEVICE.**

Device Proprietary Name: Kaltostat Wound Dressing

Device Common, Usual or Classification Name: Wound Dressing For
External Use

BEST COPY AVAILABLE

510(k) - Kaltostat Wound Dressing

**B. THE ESTABLISHMENT REGISTRATION NUMBER, IF APPLICABLE, OF
THE OWNER OR OPERATOR SUBMITTING THE PREMARKET NOTIFICATION
SUBMISSION.**

Establishment Registration Number: 1940768

Establishment Name and Address: Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
5035 Manchester Avenue
St. Louis, Missouri 63110

510(k) - Kaltostat Wound Dressing

- C. **THE CLASS IN WHICH THE DEVICE HAS BEEN PUT UNDER SECTION 513 OF THE ACT AND, IF KNOWN, ITS APPROPRIATE PANEL; OR, IF THE OWNER OR OPERATOR DETERMINES THAT THE DEVICE HAS NOT BEEN CLASSIFIED UNDER SUCH SECTION, A STATEMENT OF THAT DETERMINATION AND THE BASIS FOR THE PERSON'S DETERMINATION THAT THE DEVICE IS NOT SO CLASSIFIED.**

Devices to which Kaltostat Wound Dressing are substantially equivalent are identified as either medical adhesive tapes and adhesive bandages or wound dressings for external use. The final order classifying medical adhesive tapes and adhesive bandages as Class I (general control) medical devices was published in the Federal Register on October 21, 1980, and codified in 21 CFR 880.5240. The panel responsible for such devices is the General Hospital and Personal Use Devices Panel.

The proposed rule recommending that "nonabsorbable gauze, surgical sponge and wound dressings for external use" be classified as Class I (general control) medical devices was published in the Federal Register on January 19, 1982. These devices are described there as "devices made of an open mesh fabric of cotton or synthetic materials that are intended to control bleeding, absorb body fluids, or protect wounds from contamination". The panel responsible for these devices is the General and Plastic Surgery Devices Panel.

510(k) - Kaltostat Wound Dressing

D. ACTION TAKEN BY THE PERSON REQUIRED TO REGISTER TO COMPLY WITH THE REQUIREMENTS OF THE ACT UNDER SECTION 514 FOR PERFORMANCE STANDARDS.

As a Class I medical device, there are no performance standards for this device.

510(k) - Kaltostat Wound Dressing

- E. PROPOSED LABELS, LABELING, AND ADVERTISEMENTS SUFFICIENT TO DESCRIBE THE DEVICE, ITS INTENDED USE, AND THE DIRECTIONS FOR ITS USE. WHERE APPLICABLE, PHOTOGRAPHS OR ENGINEERING DRAWINGS SHOULD BE SUPPLIED.

PRODUCT DESCRIPTION

APPEARANCE:

Kaltostat Wound Dressing is a synthetic, nonwoven fibrous dressing produced from a naturally occurring polymer, alginic acid, which is derived from seaweed. The dressing is white to off-white in color, odorless, and resembles cotton in its physical appearance. The packaged product is sterilized by gamma irradiation with a minimum dose of 2.5 MRad. No coloring, flavoring or perfume compounds are present.

CHEMISTRY:

(b)(4)

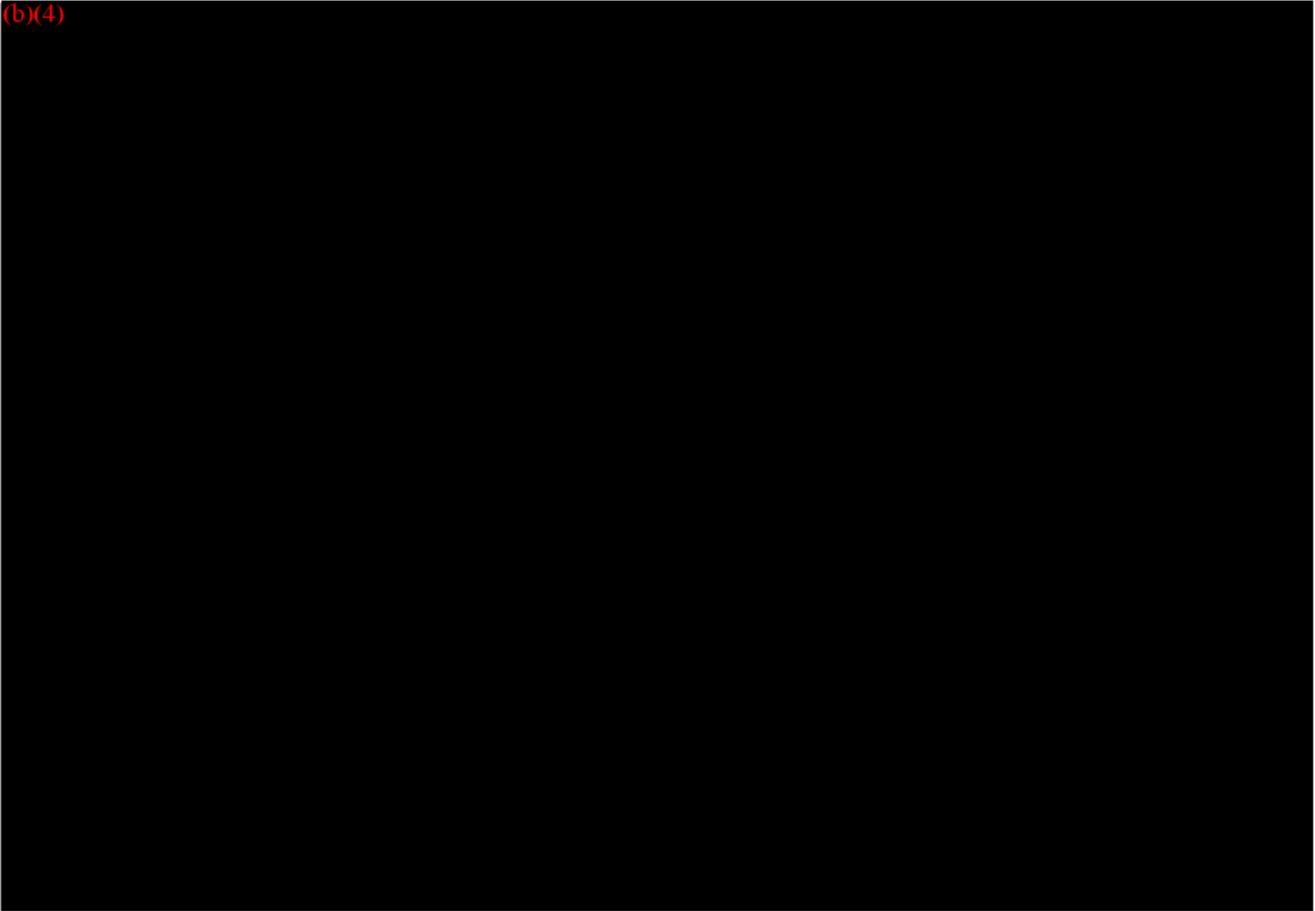
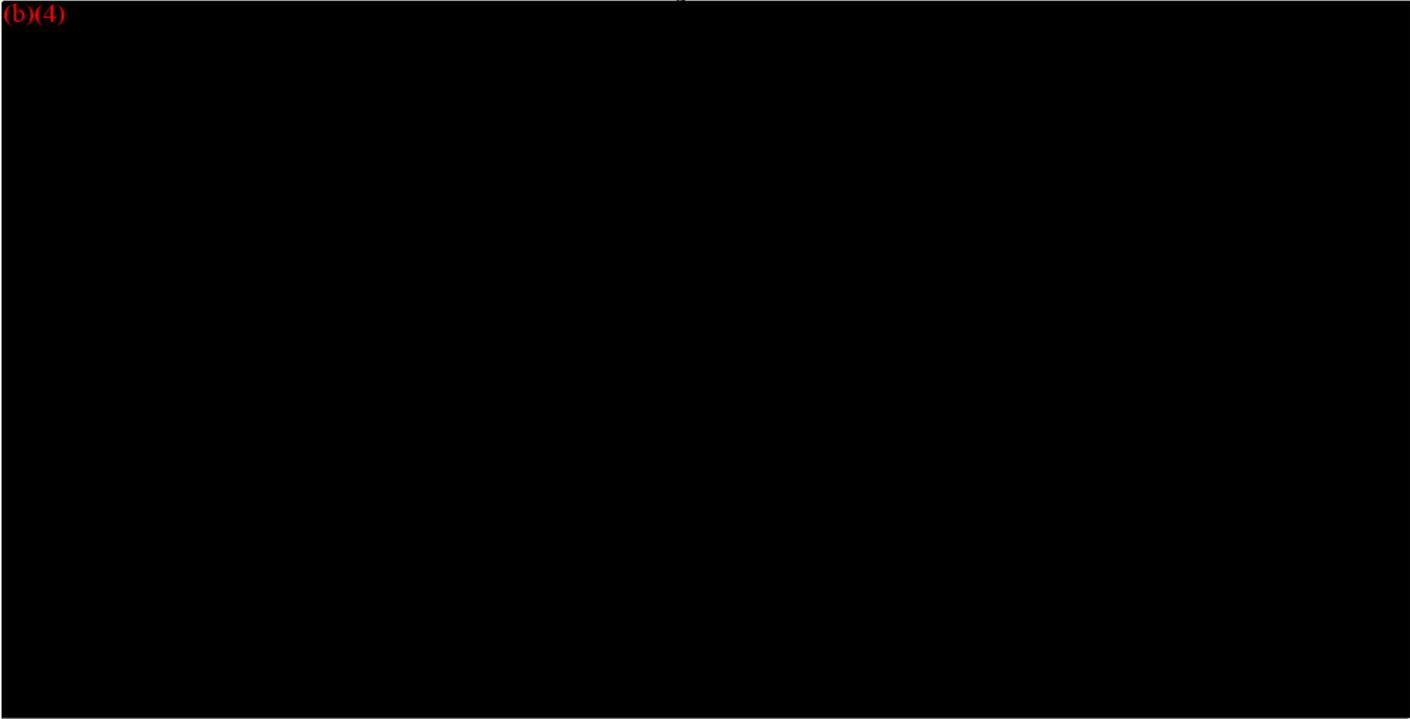


Figure 2 - Structure of a poly-L-guluronic acid segment.

510(k) - Kaltostat Wound Dressing

(b)(4)



(b)(4)



Figure 4 - Bonding between mannuronic acid moieties.

BEST COPY AVAILABLE



510(k) - Kaltostat Wound Dressing

(b)(4)

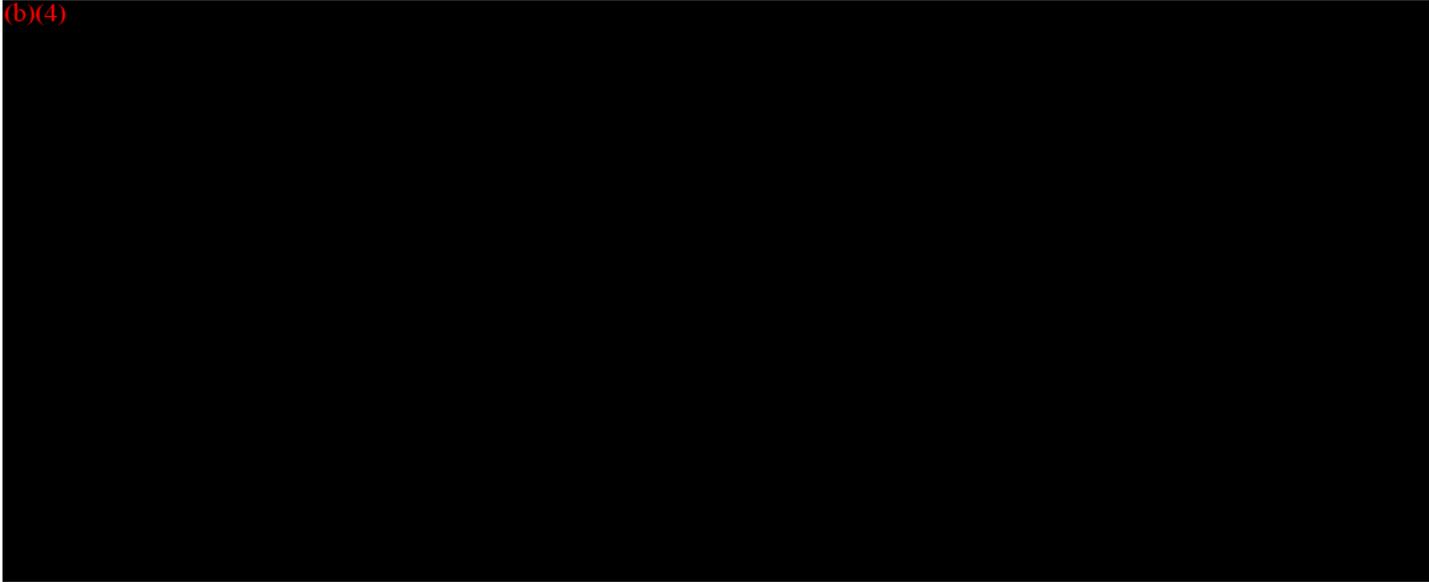


Figure 5 - Shape of polyguluronic acid.

(b)(4)



Figure 6 - Bonding between guluronic acid moities.

83

510(k) - Kaltostat Wound Dressing

Kaltostat is composed of (b)(4)

[REDACTED]

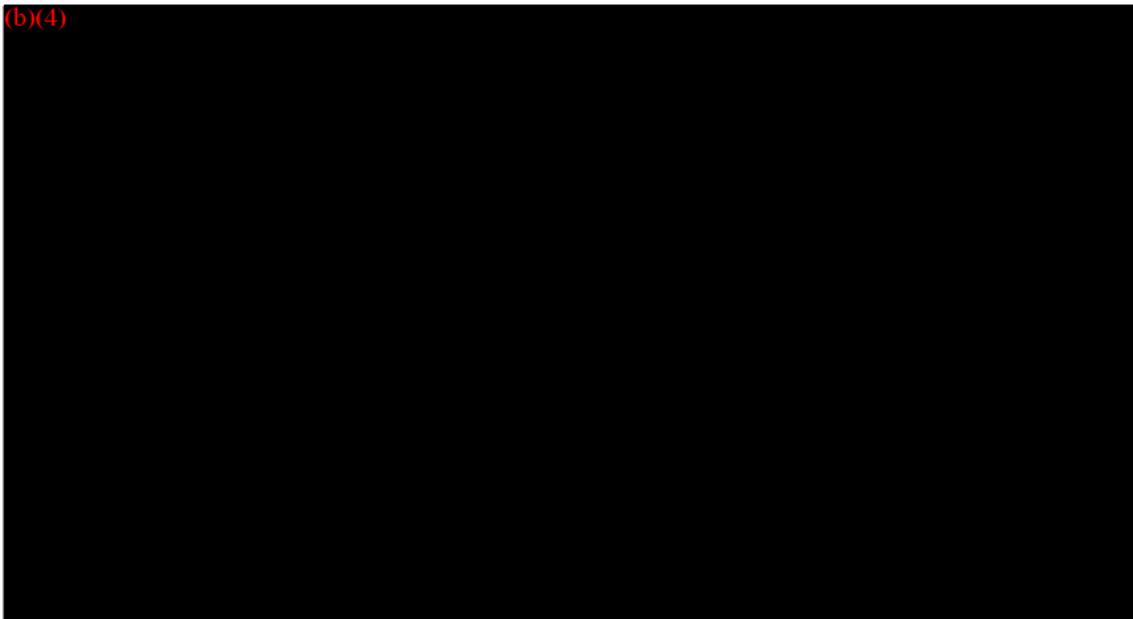


Figure 7 - Schematic representation of Kaltostat fiber structure.

One of the most important and useful properties of (b)(4) ability to (b)(4)

The reason for this insolubility is that the metal combines

(b)(4)

BEST COPY AVAILABLE

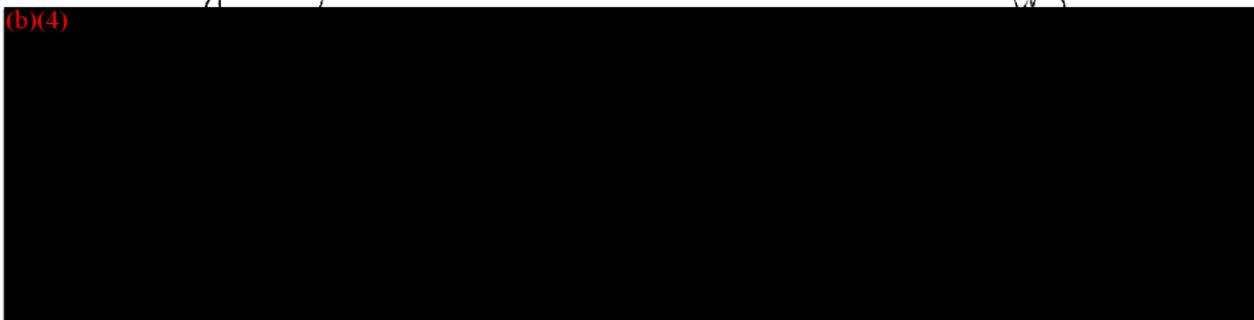
84

510(k) - Kaltostat Wound Dressing

MANUFACTURING PROCESS:

*mann / skin
0.45
50/20
10/100*

(b)(4)



FUNCTION:

Kaltostat Wound Dressing fibers interact with wound exudate to form a strong ion-active gel/fiber mat. This natural gel/mat coats the wound surface and keeps it moist and at a comfortable temperature. The combination provides the best possible environment for effective healing and easy, pain-free removal.

A summary of the suitability of Kaltostat Wound Dressing fibers to act as a wound dressing resides in the following:

1. The fiber strength allows a soft, conformable sterilizable dressing to be mass produced.
2. The alginic acid structure, with a (b) ratio of guluronic acid: mannuronic acid confers a high gel strength which allows a pain free dressing removal.
3. The ratio of sodium: (b)(4) makes for rapid gelling on the wound after absorbance of exudate or saline.
4. The high absorbency of alginic acid fibers ensures that Kaltostat can cope with heavily exudating wounds and thereby reduce the frequency of dressing change.
5. Alginates have no toxic properties for external use that have been described to date.
6. Extra flushing with a sodium containing solution (b)(4) will remove all gel residues and ungelled fibers from the wound, ensuring dressing removal with no damage to underlying new epithelium or granulation tissue.
7. Because alginates are biodegraded by the body, small amounts of fibers or gel inadvertently left in the wound will not cause foreign body reactions.

85

510(k) - Kaltostat Wound Dressing

INDICATIONS FOR USE:

Kaltostat Wound Dressing is indicated as an external wound dressing for use in the local wound management of external wounds such as pressure sores, venous stasis ulcers, arterial ulcers, diabetic ulcers, donor sites, abrasions, lacerations and superficial burns, post-surgical incisions, and other external wounds inflicted by trauma. It is designed to control bleeding, absorb exudate, and protect the wound from contamination.

PROPOSED LABELING:

Draft copies of the proposed package label and the instructions for use for Kaltostat Wound Dressing are included in Appendix 1.

510(k) - Kaltostat Wound Dressing

- F. A STATEMENT INDICATING THE DEVICE IS SIMILAR TO AND/OR DIFFERENT FROM OTHER PRODUCTS OF COMPARABLE TYPE IN COMMERCIAL DISTRIBUTION, ACCOMPANIED BY DATA TO SUPPORT THE STATEMENT. THIS INFORMATION MAY INCLUDE AN IDENTIFICATION OF SIMILAR PRODUCTS, MATERIALS, DESIGN CONSIDERATIONS, ENERGY EXPECTED TO BE USED OR DELIVERED BY THE DEVICE, AND A DESCRIPTION OF THE OPERATIONAL PRINCIPLES OF THE DEVICE.

The intended clinical uses of Kaltostat Wound Dressing are comparable to both gauze sponges, manufactured by Johnson & Johnson, and Duoderm Hydroactive Dressing, manufactured by ConvaTec. It has been previously determined by FDA that both of these products were either into interstate commerce prior to May 28, 1976 or are substantially equivalent to other products that had been introduced into interstate commerce prior to May 28, 1976. Both of these products are currently commercially marketed in the United States. Kaltostat Wound Dressing is described by the proposed classification rule of January 19, 1982 (FR 47:12, pp 2810+) as "nonabsorbable gauze, surgical sponge and wound dressings for external use" (Section 878.4080, Docket No. 78N-2666)

A comparison of these three products is given in Table 1. Labeling and promotional materials for the predicate products are given in Appendix 2.

510(k) - Kaltostat Wound Dressing

TABLE 1

COMPARISON OF KALTOSTAT, COTTON GAUZE, AND
DUODERM WOUND DRESSINGS

Product Trade Name:	Kaltostat Wound Dressing	Gauze Sponges	Duoderm Hydroactive Dressing
Supplier:	Calgon Vestal Laboratories	Johnson & Johnson	ConvaTec
Materials of Construction:	Calcium-sodium alginate	Cellulose	Carboxymethyl cellulose pectin
Form:	Non-woven fibers	Woven fibers	Gel with film backing
Adhesive:	NO	NO	YES
Absorptive:	YES	YES	YES
Interactive:	YES	NO	YES
Occlusive:	NO	NO	YES
Conformable:	YES	YES	SOMEWHAT
Controls Bleeding:	YES	YES	NO
Sterile	YES	YES	YES
Maintains Controlled Wound Environment:	YES	YES	YES
Indicated Uses as Wound Dressing:			
Controls Bleeding	YES	NO *	NO
Protects Wounds	YES	NO *	YES
Absorbs Body Fluids	YES	NO *	YES

* NOTE: Indicated uses for Johnson & Johnson gauze sponges based on label; based on proposed FDA description of "non-absorbable gauze, surgical sponge, and wound dressings for external use" (Federal Register, January 19, 1982, p. 2827), these gauze sponges would fit these indicated uses.

510(k) - Kaltostat Wound Dressing

G. Summary of Safety

Algin and alginate salts (b) (4) have been evaluated extensively for use as food additives, and all are listed as GRAS as "direct human food ingredients with limitations" by the FDA (1). This limitation involves percentage limitations in foods depending on estimated relative consumption of those foods.

While not directly applicable to the use as wound dressings, this fact serves as a general indication of the overall low toxicity profile of algin and its salts. For comparison, a (b)(4)

For human skin application, alginates have found to be non-irritants(2). Further testing for skin sensitization on humans have found that alginates are unlikely to be skin sensitizers (3).

The attached (Appendix 3) toxicity profile from the British Industrial Biological Research Association on alginic acid and its common salts summarizes and gives a current bibliography on these products. There is nothing in this report that would indicate that Kaltostat Wound Dressing, when used as an external wound dressing, would pose an increased hazard as compared to the predicate products.

Alginates have been used as wound dressings in the United Kingdom for several years with no reported unusual adverse events.

1. Federal Register 47, no. 132, pp 29946-29952, July 9, 1982.
2. Fisher A.A. Contact Dermatitis, 3rd ed. Lea & Febiger, Philadelphia p 903 (1986).
3. Marks R. and A.D. Pearse, Cutest Systems Limited, Unpublished Report (1985).

510(k) - Kaltostat Wound Dressing

APPENDIX 1

PROPOSED LABELING AND INSTRUCTIONS

FOR USE

-16-

BEST COPY AVAILABLE

90

510(k) - Kaltostat Wound Dressing

DRAFT

UNIT PACKAGE LABEL

KALTOSTAT WOUND DRESSING
Calcium-Sodium Alginate Fiber

Size: _____ cm x _____ cm

Contents: One single use dressing.

Contents sterile unless individual package is opened
or damaged.

Expiration: Store in cool, dry place

Batch:

Marketed by: Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
St. Louis, Missouri 63110

510(k) - Kaltostat Wound Dressing

DRAFT

INSTRUCTIONS FOR USE

KALTOSTAT WOUND DRESSING
Calcium-Sodium Alginate Fiber

DESCRIPTION

Kaltostat Wound Dressing is a soft, white, sterile non-woven dressing of calcium-sodium alginate fiber. The alginate fibers can absorb wound exudate or saline and convert to a firm gel/fiber mat. This gel forms a moist, warm environment at the wound interface. The gel allows trauma-free removal with little or no damage to newly formed tissue. Depending on the wound, the dressing may be left in place up to seven days.

INDICATIONS

Kaltostat Wound Dressing is an external wound dressing designed to control bleeding, absorb exudate and protect the wound from contamination.

Kaltostat Wound Dressing is indicated as an external wound dressing for use in the local wound management of external wounds such as pressure sores, venous stasis ulcers, arterial ulcers, diabetic ulcers, donor sites, abrasions, lacerations and superficial burns, post-surgical incisions, and other external wounds inflicted by trauma.

CONTRAINDICATIONS

This dressing is not indicated for wounds involving muscle, tendon, or bone, nor for third degree burns.

APPLICATION OF KALTOSTAT WOUND DRESSING

1. Wound Site Preparation and Cleansing

Prior to application of the Kaltostat Wound Dressing, the wound should be debrided of excessive necrotic tissue and eschar and irrigated with an appropriate non-toxic cleansing solution.

BEST COPY AVAILABLE

92

510(k) - Kaltostat Wound Dressing

2. Dressing Preparation and Application

- a. Kaltostat Wound Dressing should be trimmed to the exact size of the wound.
- b. For heavily exudating wounds, Kaltostat Wound Dressing should be applied dry onto the wound. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.
- c. For lightly exudating wounds, the Kaltostat Wound Dressing should be placed on the wound and moistened with saline. An appropriate secondary dressing should be used to secure Kaltostat Wound Dressing in place.

3. Dressing Change and Removal

- a. On heavily exudating wounds, change the Kaltostat Wound Dressing when strike-through of the secondary dressing occurs or whenever good nursing practice dictates the dressing should be changed.
- b. Removal should be trouble free on heavily exudating wounds as Kaltostat Wound Dressing will gel at the wound/dressing interface and easily lift away.
- c. Removal from lightly exudating wounds may be assisted by saturating the dressing with saline.
- d. Cleanse the wound site prior to application of a new dressing.
- e. As with any dressing, Kaltostat Wound Dressing should be removed from the wound and the wound cleansed at appropriate intervals. Alginate fibers and gels inadvertently left in the wound will simply be absorbed by the body and will not produce a foreign body reaction.

PRECAUTIONS AND OBSERVATIONS

1. Infection: All wounds can be expected to contain some microorganisms. However, if true clinical infection (fever, tenderness or redness in the area of the wound) should develop, appropriate steps, as defined by the attending physician, should be taken to address that infection. Regular evaluation and cleansing of infected wounds should be a common practice. Since Kaltostat Wound Dressing is not an occlusive dressing, Kaltostat Wound Dressing may be continued in use provided it is changed on a regular basis (at least daily while infection is present).

510(k) - Kaltostat Wound Dressing

2. Underlying Causes: Some wounds, such as leg ulcers and pressure sores, can be "non-healing" unless steps are taken to correct the underlying pathology. Kaltostat Wound Dressing is designed for local wound management, and can be part of the overall management program for these types of wounds.
3. Dessication: Kaltostat Wound Dressing is designed for moist wound healing. If a Kaltostat Wound Dressing which has initially formed a gel is allowed to dry out, removal from the wound can be difficult. This dessication is generally not a problem with exudating wounds. On non-exudating wounds, Kaltostat Wound Dressing should only be applied with saline. Reapplication of saline may be necessary to maintain the gel. If the gel dries out, saturate the dried gel with saline to re-hydrate it; this process may take several hours to soften the dried gel.
4. Foreign Body Reactions: As with any dressing, Kaltostat Wound Dressing should be changed at appropriate intervals. Occasional alginate fiber and gel inadvertently left in the wound will simply be absorbed by the body and will not produce a foreign body reaction.
5. Control of Bleeding: When used as a dressing on bleeding wounds, Kaltostat Wound Dressing will help control bleeding both because it serves as a matrix for coagulation and because calcium alginate is well known to initiate the blood clotting cascade. While Kaltostat Wound Dressing will help control minor bleeding on external wounds, such as surgical debridement or donor sites, it is not indicated on arterial bleeding, nor is it indicated for use on internal wounds.

CJC →

Calgon Vestal Laboratories
Division of Calgon Corporation
Subsidiary of Merck & Co., Inc.
St. Louis, Missouri 63110

Lit No. _____

BEST COPY AVAILABLE

94

510(k) - Kaltostat Wound Dressing

APPENDIX 2

LABELING AND PROMOTIONAL MATERIALS
FOR COMPARABLE PRODUCTS

-21-

BEST COPY AVAILABLE

CONTROL 8232732 EXP DATE DEC 01 93

DUODERM[®]
 SQUIBB
 C752D

Hydroactive[™]
 Dressing

Convatec[®]
 guaranteed unless
 damaged prior to use

Sterility of enclosed dressing is guaranteed unless the blister package is torn or damaged prior to use

DUODERM[®]
 SQUIBB
 C752D

Hydroactive[™]
 Dressing

Convatec[®]
 guaranteed unless
 damaged prior to use

Sterility of enclosed dressing is guaranteed unless the blister package is torn or damaged prior to use

DUODERM[®]
 SQUIBB
 C752D

Hydroactive[™]
 Dressing

Convatec[®]
 guaranteed unless
 damaged prior to use

Sterility of enclosed dressing is guaranteed unless the blister package is torn or damaged prior to use

96

PRODUCT DESCRIPTION

DuoDERM dressings interact with the available moisture on the skin creating a bond that helps them remain securely in place. Over the wound site, DuoDERM dressings interact with wound exudate producing a soft moist gel at the wound interface. This gel enables removal of the dressing with little or no damage to newly formed tissues. These dressings possess most of the features of the ideal dressing and are designed to remain in place up to seven days.

DuoDERM dressings help isolate the wound against further bacterial contamination. In the incontinent patient, they prevent wound contamination from urine or feces.

DuoDERM granules are similar in composition to the hydroactive particles in the dressing and will gradually form a gel in the presence of moisture.

PRODUCT INFORMATION

Rapid Healing -

Studies conducted on a well-controlled wound model in swine have shown that the wound environment created by the DuoDERM dressing speeds the healing process. Superficial wounds healed 39% and 19% faster when compared respectively with wet to dry dressings and semi-permeable adhesive polyurethane dressings.

2

Dermal Ulcer Management -

Clinical studies have demonstrated the advantages of DuoDERM as a routine dressing for the local management of dermal ulcers such as leg ulcers and pressure sores. Unlike most wounds, dermal ulcers are generally "nonhealing" conditions in which tissue damage is progressive if steps are not taken to correct the underlying pathology and/or improve the wound environment.

Pressure Sore Management - Excellent clinical results have been reported using DuoDERM dressings on pressure sores. Of 94 overt pressure sores, 60% healed with an average treatment time of 32 days. A further 15% showed marked improvement. The dressings were easy to apply and reduced the nursing time spent on routine dressing changes.

Pressure Sore Prevention - Results of controlled studies in the management of bilateral pressure areas indicate that DuoDERM dressings help prevent further tissue deterioration. They reduce friction between the skin and bed sheets. In the incontinent patient they protect the fragile area from contamination with feces or urine.

3

Leg Ulcer Management - Excellent clinical results have been reported using DuoDERM dressings. In 152 leg ulcers which were referred to dermatology clinics, 62% healed and 15% showed marked improvement using DuoDERM dressings. Sixty-nine percent of these ulcers had deteriorated or had shown no change using other dressings and conventional treatments. In addition to any promotion of healing, DuoDERM dressings are easy to apply, are hypoallergenic, reduce pain, and increase patient comfort. DuoDERM dressings are flexible, will adhere to ankles, heels or toes, and can be left in place while bathing or showering. They can also be used under a compression bandage in stasis ulcer management.

Burns - Second Degree -

The effectiveness of DuoDERM dressings in the management of burns has been established. In addition to being effective, these dressings are easy to use and protect the wound surface.

Occlusive Dressing Technique -

When the occlusive dressing technique is indicated such as in recalcitrant dermatological conditions, DuoDERM may be used as the occlusive dressing.

4

INDICATIONS

Dermal Ulcers - IMPORTANT

1. Initial use of these products on dermal ulcers should be under the direction of a health professional.
2. DuoDERM dressings only provide local management of the wound site and nutritional support should not be neglected.
3. Lack of adequate rest in patients with vascular (arterial or venous) insufficiency can increase the amount of local edema and hinder potential healing.

Pressure Sore Management

Pressure Sore Prevention

Leg Ulcer Management

NOTE: DuoDERM Granules are indicated only for the local management of exuding dermal ulcers in association with DuoDERM Dressings. Used in this manner, the granules may reduce the frequency of dressing changes.

5

Superficial Wounds

Minor Abrasions

Donor Sites

Burns - Second Degree

Occlusive Dressing Technique

CONTRAINDICATIONS

Pressure Sores and Leg Ulcers

involving muscle, tendon or bone
resulting from infection, such as tuberculosis, syphilis and deep fungal infections.

Ulcers in patients with active vasculitis, such as periarteritis nodosa, systemic lupus erythematosus and cryoglobulinemia.

Third Degree Burns

PRECAUTIONS AND OBSERVATIONS

Appearance: This liquefied material that remains in the wound when the dressing is removed may have the appearance of pus. This is normal and should be washed away (see instructions for Use Section) before evaluating the wound

6

7

Odor: Wounds, particularly those that are large or necrotic, are often accompanied by a disagreeable odor. DuoDERM dressings are impermeable and will normally help prevent odor escape. The odor that accumulates in this way is, according to some investigators, characteristic and may be pronounced when the dressing is removed or when leakage occurs. The odor will normally disappear when the wound has been cleansed and the dressing discarded.

Wound Deterioration: When using any occlusive dressing in the presence of necrotic material, it is to be expected that the wound may increase in size and depth during the initial phase of management as the necrotic debris is cleaned away. This apparent deterioration is normally accompanied by a gradual improvement in the appearance of the wound bed.

Deeper tissue damage has sometimes already occurred under an apparent superficial pressure area. The initial deterioration that commonly occurs in these cases when using an occlusive dressing may be dramatic but is not in itself a contraindication for further use of DuoDERM.

Infection: The reported incidence of infection when using "occlusive" dressings does not seem higher than with other conventional dressing techniques. However, it is advised that bacterial culture of the wound site be undertaken if any of the

following circumstances develop: uncharacteristic odor or change in the color of the exudate, fever or cellulitis (tenderness and erythema in the area of the wound). If a clinical infection should develop, discontinue DuoDERM management and institute appropriate treatment. DuoDERM management may be restarted when the infection has been eradicated.

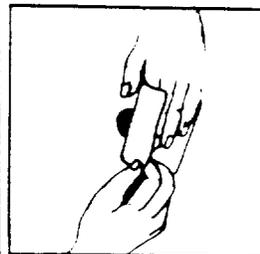
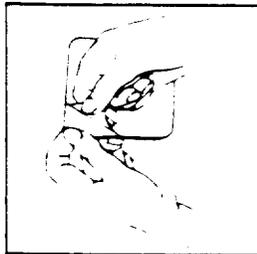
Granulation: Excessive granulation tissue may develop in some wounds when using "occlusive" dressings.

INSTRUCTIONS FOR USE - DERMAL ULCERS

Preparing and Cleansing the Wound Site

Carefully clean the wound site with 3% hydrogen peroxide or other effective cleansing agent. Irrigate with saline and dry the surrounding skin carefully being sure it is clean and free of any greasy substance. Application and use of DuoDERM dressings help facilitate the liquefaction and removal of eschar. Eschar that is particularly thick or fused to the wound margins should be removed.

8



Preparing the Dressing

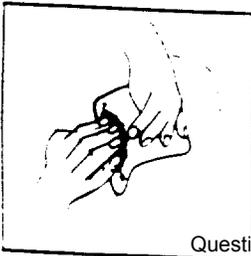
DuoDERM dressings are sterile and should be handled appropriately.

Choose a DuoDERM dressing that will extend at least 1/2" beyond the wound margin where it can be attached to healthy skin. Remove the silicone release paper from the dressing minimizing finger contact with the adhesive surface.

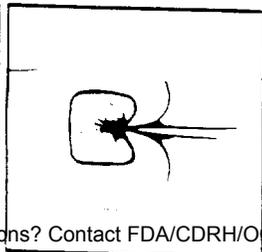
Applying the Dressing

Apply in a rolling motion. Do not stretch unnecessarily.

9



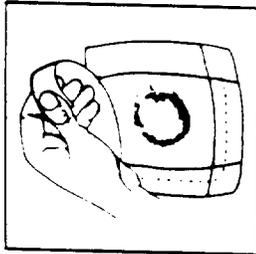
Smooth gently but firmly into place paying particular attention to the wound margins. Do not hurry this procedure as initial adhesion improves as the dressing becomes warm.



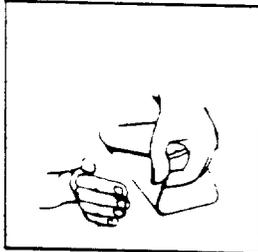
When applying to a sacral ulcer, press well down into the anal fold.

10

Questions? Contact FDA/CDRH/OCE/D



Taping the edges using 1" wide hypoallergenic tape will reduce the risk of peeling especially during showering or bathing



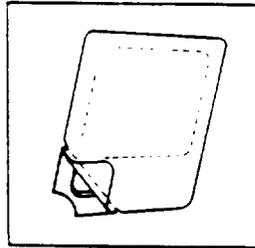
Removing the Dressing
Press down on the skin as shown and carefully lift an edge of the dressing. Continue slowly around the wound margins until all edges are free from the skin surface. Lift carefully from the wound. Repeat cleansing procedure to remove any remaining material from the wound surface. When a new dressing is applied, it is unnecessary

11

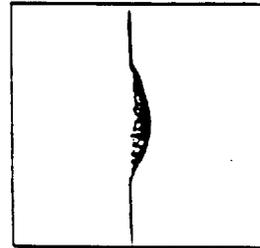
To remove all residual dressing material from the surrounding skin the dressing may be left undisturbed for up to 7 days as long as it is comfortable, is not leaking and there are no clinical signs of infection. It is to be expected that large and necrotic wounds, or sacral ulcers, particularly in continent patients, will require more frequent dressing changes. It is recommended to continue the use of DuoDERM dressings for one to two weeks after apparent healing.

Using DuoDERM Hydroactive Granulés

In the presence of excess exudate the ability of DuoDERM dressings to remain in place with less frequent leakage may be improved by the application of DuoDERM granulés directly into the wound site. Used in this way together with the dressings, DuoDERM Hydroactive Granulés may reduce the frequency of dressing changes.



Peel back the corner of the backing paper on the blister



Dry the skin surrounding the wound to prevent the adhesion of excess granules. Fill the wound with granules to a level not higher than the surrounding skin. Do not overfill. Apply the dressing

12

13

INSTRUCTIONS FOR USE - DONOR SITES, SECOND DEGREE BURNS AND MINOR ABRASIONS

It is advisable to shave the skin surrounding the wound prior to initiating treatment. The wound and surrounding skin should be cleansed with sterile saline. Any ointments, creams or other oily substances previously applied should be removed. Select a DuoDERM dressing that extends at least 1/4" beyond the wound margins.

Sterile dressing technique should be observed and employed. After carefully drying the surrounding skin, apply the dressing in a rolling motion. Do not stretch unnecessarily.

NOTE: Taping the edges using 1" wide hypoallergenic tape will reduce the risk of it peeling.

The dressing may be left undisturbed for up to seven days provided it is comfortable, is not leaking and there are no clinical signs of infection.

NOTES

- a. The dressing should be changed if leakage of exudate occurs.
- b. Postoperatively, DuoDERM dressings may have to be changed once or twice daily. Similarly, frequent dressing changes may be required for the initial management of burns. The frequency of dressing changes reduces dramatically once re-epithelialization occurs.

Dressing Removal - Press down on the skin and carefully lift an edge of the dressing. Continue slowly around the wound margins until all edges are free from the skin surface. Lift the dressing carefully from the wound. Repeat the cleansing procedure and apply a new dressing.

NOTES:

- a. When a new dressing is applied, it is unnecessary to remove all residual dressing material from the surrounding skin.
- b. Frequent dressing changes during the latter stages of healing should be avoided in order to minimize potential re-injury of the wound. If a dressing change is required and the wound is non-exuding, the application of small amounts of sterile saline during the removal procedure may help prevent re-injury.
- c. It is recommended to continue the use of DuoDERM dressings one to two weeks after apparent healing.

INSTRUCTIONS FOR USE - OCCLUSIVE DRESSING TECHNIQUE

DuoDERM dressings adhere well to dry clean skin. They will not stick to an oily or greasy surface. When used as an occlusive dressing, adhesion will not occur where the dressing's adhesive surface makes contact with ointments, creams, lotions, et cetera.

HOW SUPPLIED:

DuoDERM® Hydroactive™ Dressings Sterile	Order No.
4 8 x 4": Box of 5 individually blister packed	187610
6 8 x 8": Box of 3 individually wrapped	187640
8 8 x 8": Box of 3 individually blister packed	187620
8 8 x 12": Box of 3 individually wrapped	187630
DuoDERM® Hydroactive™ Granules Sterile	
4 grams per packet, box of 5 blister packets	187710

REFERENCES

1. Turner, TD: Products and their development in wound management. Symposium on Wound Healing, Plastic Surgical and Dermatologic Aspects, 1979
2. Mertz, P: University of Pittsburgh School of Medicine, Department of Dermatology 1982. Publication pending.
3. Alvarez, OM, Mertz, PM, Eaglstein, WH: The Effect of Occlusive Dressings on Collagen Synthesis and Re-epithelialization in Superficial Wounds. Journal of Surgical Research 35, 142-148 (1983)
4. Information on file, ConvaTec.
5. Information on file, ConvaTec.
6. van Rijswijk, L. et al: Clinical Evaluation of a Hydrocolloid Dressing in Leg Ulcer Management. Cutis, in press
7. Information on file, ConvaTec.
8. Information on file, ConvaTec.
9. McGowan, CA: Management of Pressure Sores using DuoDERM® Hydroactive™ Dressings. Michigan Veteran's Facility, Grand Rapids, Michigan, 1982. Paper given at Symposium - Nursing Research, Department of Nursing Service, Stanford University Hospital, November 18-20, 1982. Reprint available - ConvaTec files.
10. Tudhope, M.: Management of Pressure Ulcers Using a Moisture-Reactive Occlusive Dressing. Results on 23 Patients. Journal of Enterostomal Therapy 1984, in press.



Johnson & Johnson
PRODUCTS INC.
NEW BRUNSWICK, NEW JERSEY 08903
© J.J.P.I. 61 MADE IN U.S.A.
STERILITY OF CONTENTS GUARANTEED UNLESS
INDIVIDUAL PACKAGE IS DAMAGED OR OPENED 80

510(k) - Kaltostat Wound Dressing

APPENDIX 3

BIBRA TOXICITY PROFILE OF
ALGINIC ACID AND ITS COMMON SALTS

102

TOXICITY PROFILE



Copyright © 1988 The British Industrial Biological Research Association

ALGINIC ACID AND ITS COMMON SALTS

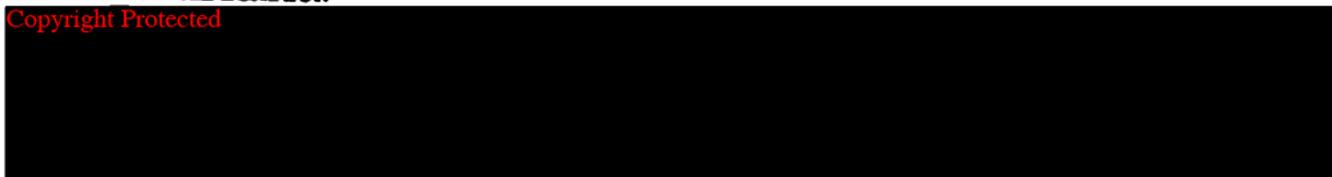
SUMMARY

Copyright Protected



IDENTIFICATION

Copyright Protected



BEST COPY AVAILABLE

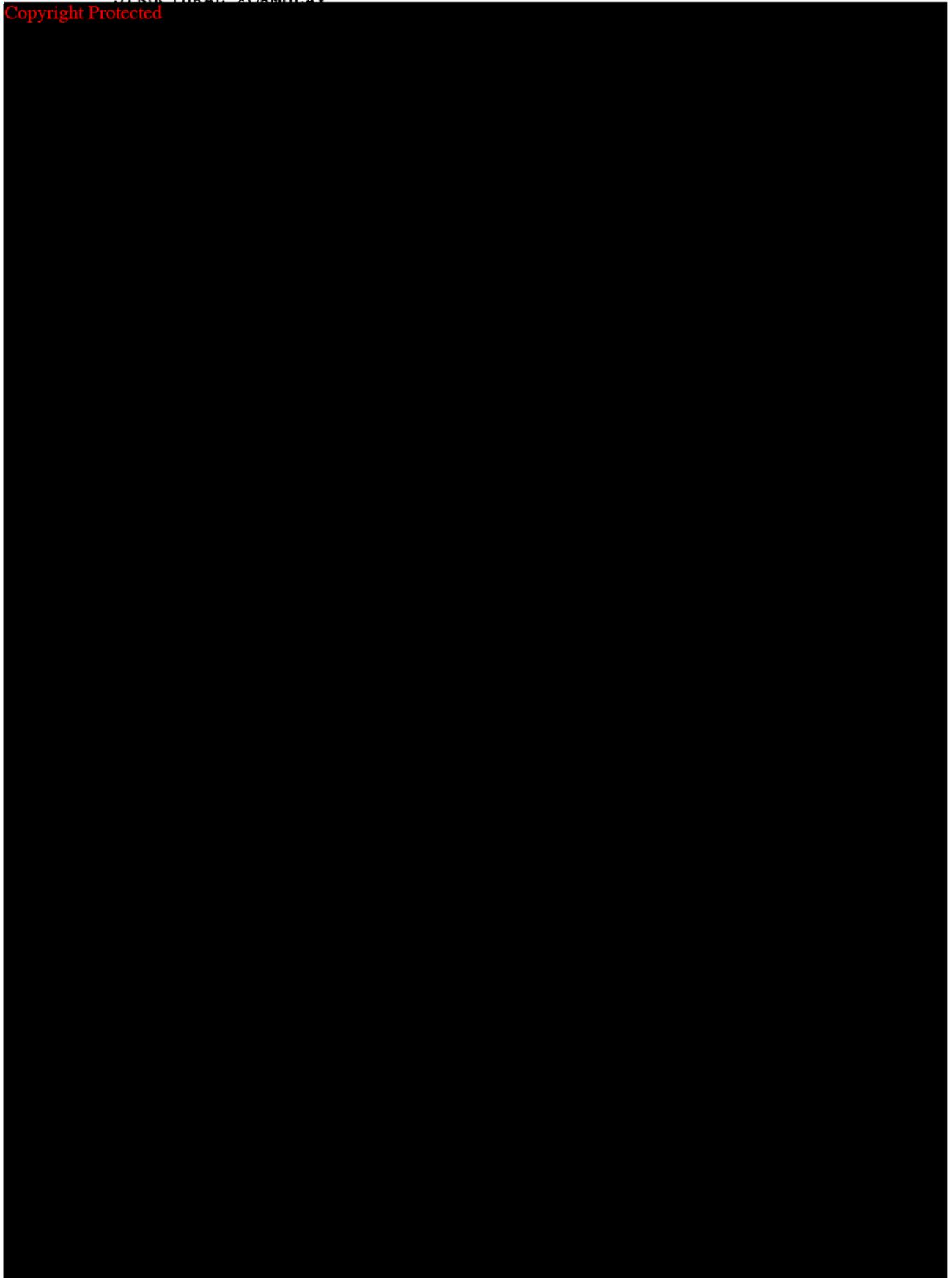
BIBRA COPYRIGHT BIBRA

Further information may be obtained from the BIBRA Information Section
Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOI STATUS@fda.hhs.gov or 301-796-6115
Woodmansterne Road, Carshalton, Surrey SM5 4DS, Great Britain
Telephone: 01-643 4411 Telex: 25438 Fax: 01-661 7029



STRUCTURAL FORMULA

Copyright Protected

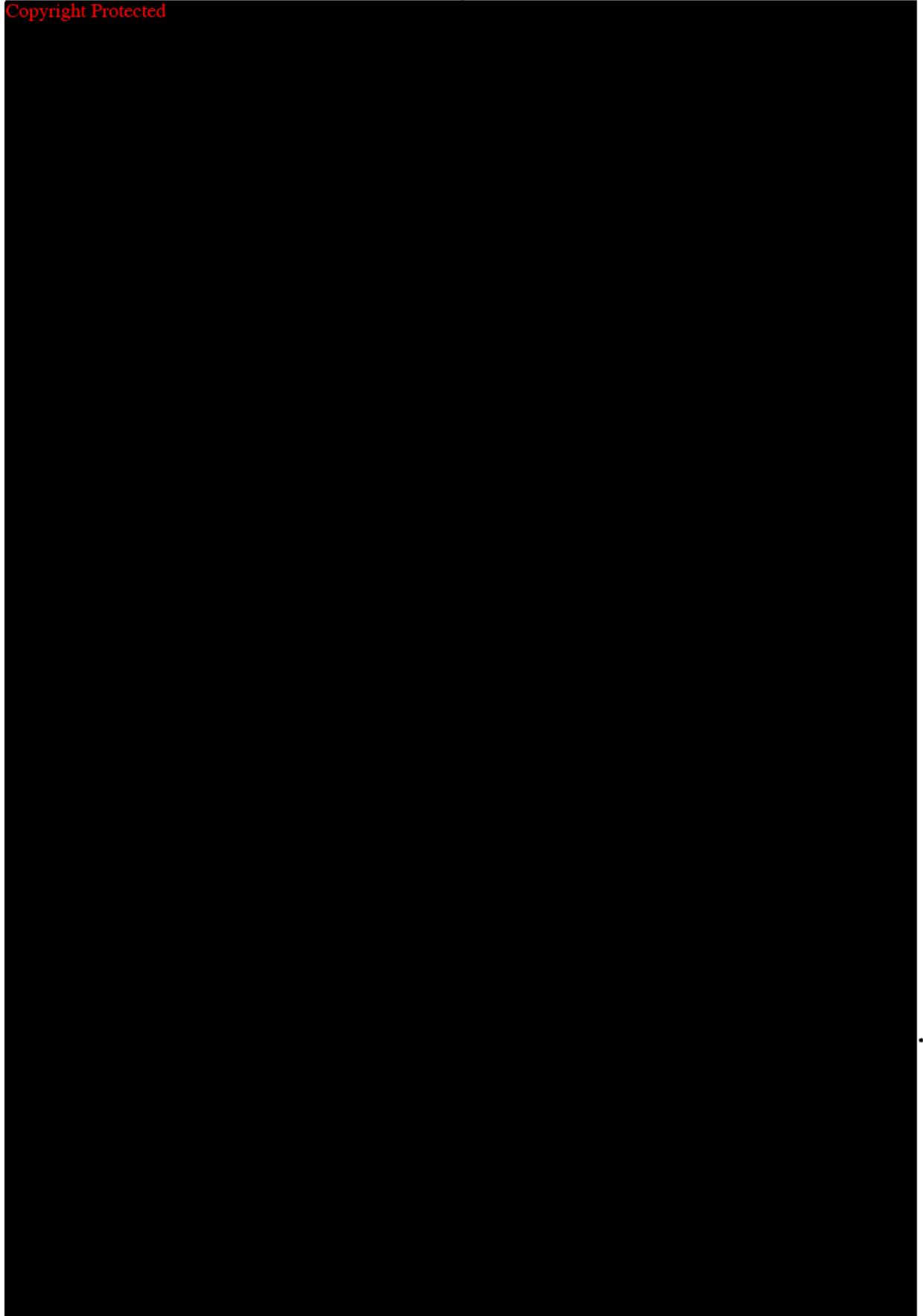


Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

104



Copyright Protected



BEST COPY AVAILABLE

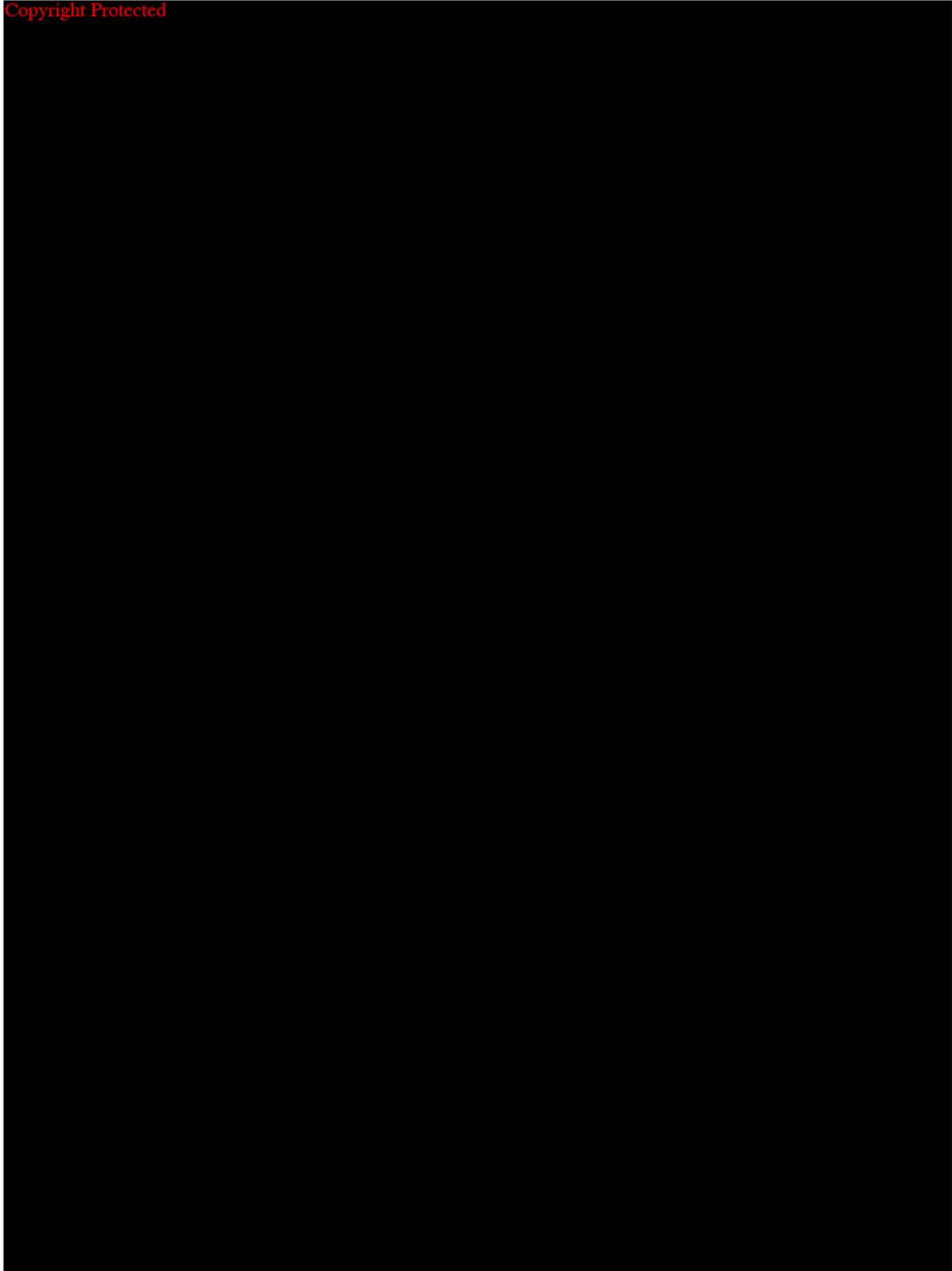
Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOIS@FDA.HHS.gov or 301-796-8118

BIBRA COPYRIGHT BIBRA

106



Copyright Protected

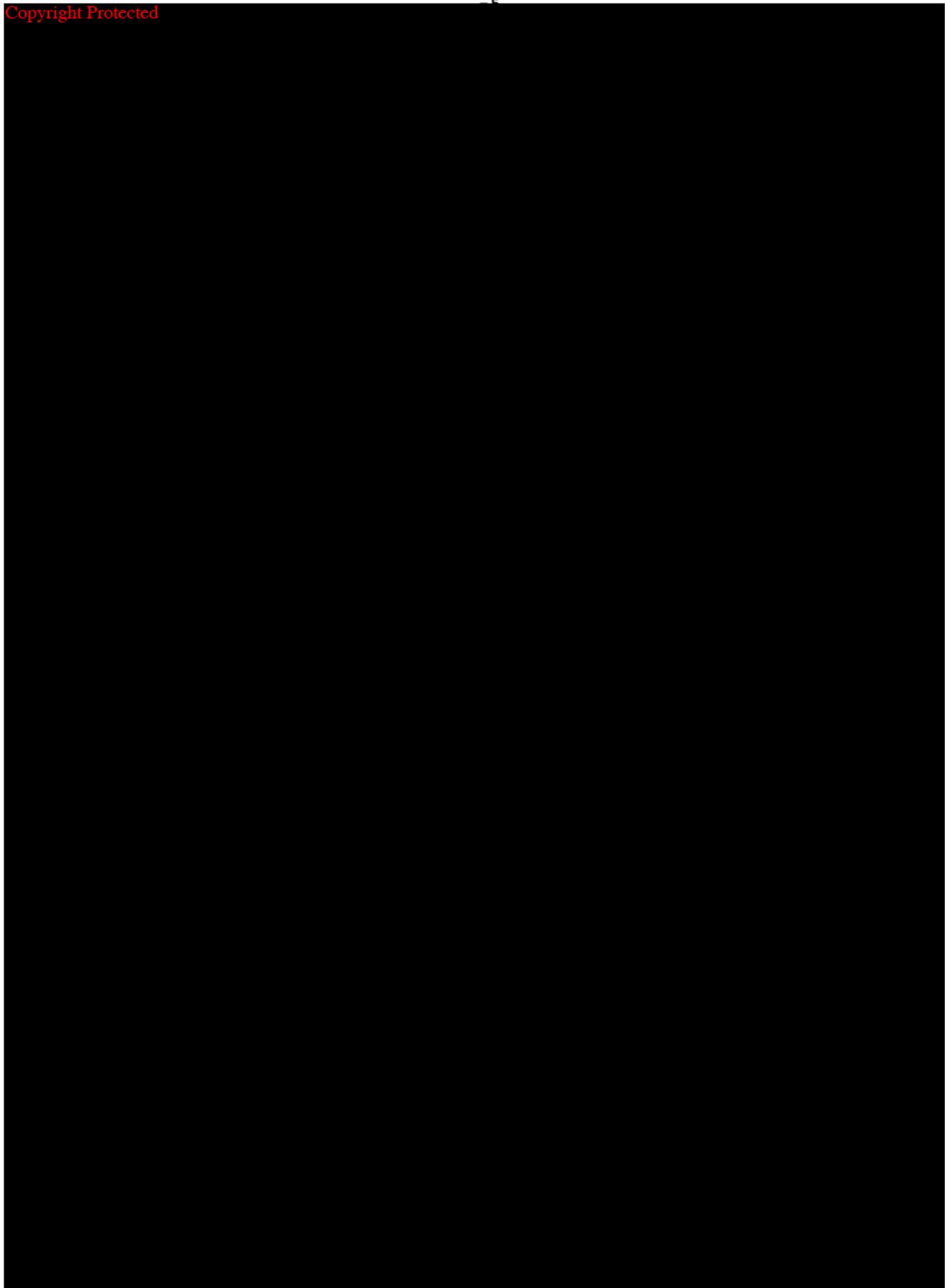


BEST COPY AVAILABLE

A handwritten signature or set of initials is located in the bottom right corner of the page.



Copyright Protected



Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

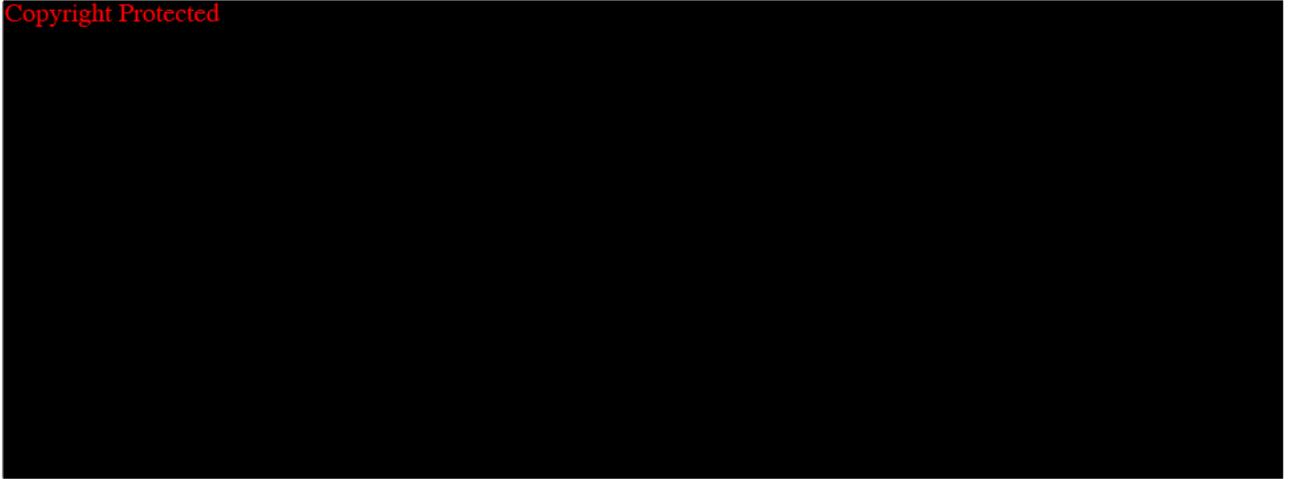
BEST COPY AVAILABLE

BIBRA COPYRIGHT BIBRA

107



Copyright Protected



OTHER TOXICITY CONSIDERATIONS

Copyright Protected



Copyright Protected

REFERENCES

- Camarasa J.M.G. (1982). *Contact Dermatitis* 8, 347.
- Carr T.E.F. et al. (1968). *Int. J. Radiat. Biol.* 14, 225.
- Carr T.E.F. et al. (1969). *Nature, Lond.* 224, 1115.
- Daigo K. et al. (1981). *Yakugaku Zasshi* 101, 458.
- Epstein S.S. et al. (1970). *Toxic. appl. Pharmac.* 16, 321.
- Epstein S.S. et al. (1972). *Toxic. appl. Pharmac.* 23, 288.
- FASEB (1973). *Evaluation of the Health Aspects of Alginates as Food Ingredients.* Federation of American Societies for Experimental Biology. PB-265 503, pp. 15.
- Feldman H.S. et al. (1952). *Proc. Soc. exp. Biol. Med.* 79, 439.
- Feron V.J. et al. (1967). *Central Institute for Nutrition and Food Research, Zeist. TNO Report no. R.2456*, pp. 11.
- Fisher A.A. (1986). *Contact Dermatitis.* Third edition. Lea & Febiger, Philadelphia, p. 903.
- Gill R.J. & Duncan G.G. (1952). *Am. J. med. Sci.* 224, 569.
- Grant W.M. (1974). *Toxicology of the Eye.* 2nd Edition. Charles C. Thomas Publishers, Springfield, Illinois.
- Guillot J.P. et al. (1982). *Int. J. cosmet. Sci.* 4, 53.
- Guillot J.P. et al. (1983). *Int. J. cosmet. Sci.* 5, 255.
- Harrison G.E. (1968) p. 333 in: *Diagnosis and Treatment of Deposited Radionuclides.* Ed. H.A. Kornberg & W.D. Norwood. Excerpta Medica Foundation.
- Harrison G.E. et al. (1969). *Nature, Lond.* 224, 1115.
- Harrison J. et al. (1966). *Can. med. Ass. J.* 95, 532.
- Hodgkinson A. et al. (1967). *Can. med. Ass. J.* 97, 1139.
- Ikegami S. et al. (1983). *Nippon Eiyo Shokuryo Gakkaishi* 36, 163.
- JECFA (1974). *Joint WHO/FAO Expert Committee on Food Additives.* WHO Fd Add. Ser. No. 5, p. 381.
- Johnston C.D. (1972). Unpublished report (cited in FASEB, 1973).
- Kollwitz A.-A. & Jankowski M. (1968). *Urologe* 7, 50.
- McHardy G. (1978). *Sth med. J.* 71, Suppl. 1, p. 16.
- Merck (1983). *The Merck Index*, 10th Edition. Merck & Co. Inc., Rahway, New Jersey.
- Millis J. & Reed F.B. (1947). *Biochem. J.* 41, 273.
- Morgan C.F. et al. [undated]. Unpublished report (cited in JECFA, 1974).
- Mori S. (1967). *Acta Soc. Ophthal. Jap.* 71, 22 (cited in Grant, 1974).
- Morita S. (1983). *Seikatsu Eisei* 27(1), 22 (Chem. Abstr. 98, 138661w).
- Nilson H.W. & Wagner J.A. (1951). *Proc. Soc. exp. Biol. Med.* 76, 630.
- Rose H.E. & Quarterman J. (1987). *Envir. Res.* 42, 166.
- Silva A.J. et al. (1970). *Hlth Phys.* 19, 245.
- Slat B. et al. (1971). *Hlth Phys.* 21, 811.
- Stara J.F. & Waldron-Edward D. (1968). p. 340 in: *Diagnosis and Treatment of Deposited Radionuclides.* Ed. H.A. Kornberg & W.D. Norwood. Excerpta Medica Foundation.
- Sutton A. (1967). *Nature, Lond.* 216, 1005.
- Sutton A. et al. (1971). *Int. J. Radiat. Biol.* 19, 79.
- Thienes C.H. et al. (1957). *Archs int. Pharmacodyn. Ther.* 111, 167.
- Til H.P. et al. (1986). *Fd Chem. Toxic.* 24, 825.
- Viola S. et al. (1970). *Nutr. Rep. Int.* 1, 367.
- Watt J. & Marcus R. (1971). *Proc. Nutr. Soc.* 30, 81A.



Woodard Research Corp. (1959). Unpublished report (cited in JECFA, 1974).
Woodard Research Corp. (1972). Unpublished report (cited in JECFA, 1974).
Zinsser H.H. (1962). Rein Foie 4, 41.

CR/BMS/December 1987(g)/P.168/T.426

BEST COPY AVAILABLE

BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA COPYRIGHT BIBRA

This profile is an assessment of toxic potential, not of safety-in-use. Evaluating possible risks associated with a chemical's use requires consideration of various factors (such as exposure levels) in addition to toxic potential.
Questions? Contact FDA/CDRHT/OCEDID at CDRHTPOSTATUS@aa.hhs.gov or 800-833-7343.
Although every care is taken in providing information and advice, The British Industrial Biological Research Association accepts no responsibility or liability for any consequences arising from such information and advice.

110