

K100695

1063

COLLAMATRIX Co. Ltd.

510(k) summary
Summary information

JAN 03 2013

1. **Date Prepared**

March 3, 2010

2. **Submitter name and address**

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. **Contact person**

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. **Device names**

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. **Device classification**

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

6. **Device description**

CollaDental Barrier is a nonfriable, resorbable membrane made of purified type I collagen derived from pig skin using standardized controlled manufacturing process. The collagen is obtained from veterinary certified pigs and purified to avoid its antigenicity. The manufacturing process complies with the standards for virus inactivation. The CollaDental

1F, No. 50-1, Keyan Road, Jhunan Science Park, Miaoli Country, 350, Taiwan
Tel: +886 2 7711 3299 Fax: +886 2 7711 3599

Page 1 of 3

K100695
2 of 3

COLLAMATRIX Co. Ltd.

~~Barrier has been tested for purity using standard purity testing procedures, sterilized by~~
gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

CollaDental Barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

8. Statement of Substantial equivalence

CollaDental Barrier is a device similar to predicate devices that are previously approved by the agency. CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices, BioMend Extend absorbable collagen membrane (K992216) and BIO-GIDE® (K042197), each of which has been determined by FDA to be substantially equivalent to preamendment devices. CollaDental Barrier has the following similarities to the predicate devices in terms of indication for use, technological characteristics, material use and the process for sterilization. In summary, CollaDental Barrier is substantially equivalent to the predicate devices under the 510(k) regulations.

9. Biocompatibility

CollaDental Barrier has been demonstrated to be safe. To support the biocompatibility of this product, safety tests were conducted in accordance with ISO 10993 Part 1 Biological Evaluation of Medical Devices.

All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

K 100695
3073

COLLAMATRIX Co. Ltd.

10. Conclusion

CollaDental Barrier is essentially equivalent in indication for use, technological characteristics and material to the commercially available predicate device, and therefore meets the requirements as defined in 21 CFR § 807.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

January 3, 2013

Mr. Dennis J.N. Seah
Collamatrix, Incorporated
26F No. 105, Section 2 Dunhua
South Road, DA-AN Distric
Taipei, China 106

Re: K100695

Trade/Device Name: CollaDental Barrier
Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: II
Product Code: NPL
Dated: January 5, 2011
Received: December 14, 2012

Dear Mr. Seah:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to 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.

Page 2 – Mr. Seah

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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to <http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucml15809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Susan Runner DDS, MA

2013.01.03

08:32:49

-05'00'

Anthony D. Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Respiratory, Infection Control and
Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

171

K100695

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

2012.12.31

Susan Runner DDS, MA 10:48:45

-05'00'

(Division Sign-Off)
Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K100695



Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room -WO66-G609
Silver Spring, MD 20993-0002

Mr. Dennis J. H. Seah
Collamatrix, Incorporated
1F, No. 50-1, Keyan Road, Jhunan Science Park
Miaoli County 350
TAIWAN

DEC 29 2010

Re: K100695
Device Name: CollaDental Barrier
Dated: December 20, 2010
Received: December 22, 2010

Dear Mr. Seah:

We have reviewed the information dated December 20, 2010, regarding the 510(k) notification K100695 previously submitted for the device referenced above. Based solely on the change or modification that you have described, it does not appear that you have significantly changed or modified the design, components, method of manufacture, or intended use of the device referenced above (see 21 CFR 807.81(a)(3)). Additionally, we did not review any data submitted with this add to file. It is, however, your responsibility to determine if the change or modification to the device or its labeling could significantly affect the device's safety or effectiveness and thus require submission of a new 510(k). Please refer to our guidance document entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device" at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm>. The information you have supplied will be added to the file.

Sincerely yours,

Anthony Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Services
Food and Drug Administration

Memorandum

Date: 1/7

From: DMC (HFZ-401)

Subject: Premarket Notification Number(s): K100695/A5

To: Division Director: OE/DAGID

The attached information has been received by the 510(k) DMC on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below.

Information does not change the status of the 510(k); no other action required by the DMC; please add to image file. (Prepare K-25) THIS DOES NOT APPLY TO TRANSFER OF OWNERSHIP. PLEASE BRING ANY TRANSFER OF OWNERSHIP TO POS.

Additional information requires a new 510(k); however, the information submitted is incomplete; (Notify company to submit a new 510(k); [Prepare the K30 Letter on the LAN]

No response necessary (e.g., hard copy of fax for the truthful and accuracy statement, 510(k) statement, change of address, phone number, or fax number).

CLIA CATEGORIZATION refers to laboratory test system devices reviewed by the Division of Clinical Laboratory Devices (HFZ-440)

Information requires a **CLIA CATEGORIZATION**; the complexity may remain the same as the original 510(k) or may change as a result of the additional information (Prepare a CAT letter)

Additional information requires a **CLIA CATEGORIZATION**; however, the information submitted is incomplete; (call or fax firm)

No response necessary

This information should be returned to the DMC within 10 working days from the date of this Memorandum.

Reviewed by: RSB

Date: 10-21-2011

[Signature]
NOV 9 2011

DLG
11/9

K100695/AS

Center for Devices and Radiological Health

Document Mail Center WO66-G609

10903 New Hampshire Avenue

Silver Spring, MD 20993-0002

January 05, 2011

Re: Information for CollaDental Barrier (K100695)

FDA CDRH DMC

JAN 07 2011

~~RECEIVED~~

Dear Dr. Betz,

Please find enclosed revised Indications for use statement and revised 510k summary required for the application of CollaDental Barrier.

Thank you.

Sincerely yours,



Dennis Seah

K-43

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. **Date Prepared**

March 3, 2010

2. **Submitter name and address**

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. **Contact person**

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. **Device names**

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. **Device classification**

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

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Page 1 of 3

COLLAMATRIX Co. Ltd.

Barrier has been tested for purity using standard purity testing procedures, sterilized by gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

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9. Biocompatibility

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All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

COLLAMATRIX Co. Ltd.

10. Conclusion

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Services
Food and Drug Administration

Memorandum

Date: ~~10/27/10~~ 12/27

From: DMC (HFZ-401)

Subject: Premarket Notification Number(s): K100695/A4

To: Division Director: DE/DA6FD

The attached information has been received by the 510(k) DMC on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below.

Information does not change the status of the 510(k); no other action required by the DMC; please add to image file. (Prepare K-25) THIS DOES NOT APPLY TO TRANSFER OF OWNERSHIP. PLEASE BRING ANY TRANSFER OF OWNERSHIP TO POS.

This is part of an ongoing 510(k) review
~~Additional information requires a new 510(k); however, the information submitted is incomplete; (Notify company to submit a new 510(k); [Prepare the K30 Letter on the LAN]~~

No response necessary (e.g., hard copy of fax for the truthful and accuracy statement, 510(k) statement, change of address, phone number, or fax number).

CLIA CATEGORIZATION refers to laboratory test system devices reviewed by the Division of Clinical Laboratory Devices (HFZ-440)

Information requires a CLIA CATEGORIZATION; the complexity may remain the same as the original 510(k) or may change as a result of the additional information (Prepare a CAT letter)

Additional information requires a CLIA CATEGORIZATION; however, the information submitted is incomplete; (call or fax firm)

No response necessary

This information should be returned to the DMC within 10 working days from the date of this Memorandum.

Reviewed by: RSB

Date: 12-27-2010

Please place in record. This file should remain on hold

RSB

K100695/A4

Food and Drug Administration

Center for Devices and Radiological Health

Document Mail Center WO66-G609

10903 New Hampshire Avenue

Silver Spring, MD 20993-0002

December 20, 2010

Re: Information for CollaDental Barrier (K100695)

FDA CDRH DMC

DEC 22 2010

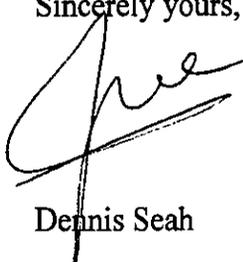
Dear Dr. Betz,

~~REMOVED~~

Please find enclosed revised Indications for use statement and revised 510k summary required for the application of CollaDental Barrier.

Thank you.

Sincerely yours,



Dennis Seah

K-48

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

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Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

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

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COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. **Date Prepared**

March 3, 2010

2. **Submitter name and address**

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
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3. **Contact person**

Name: Dennis J. N. Seah
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COLLAMATRIX Co. Ltd.

Barrier has been tested for purity using standard purity testing procedures, sterilized by gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

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Page 1 of 3

COLLAMATRIX Co. Ltd.

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Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

K100695/A1

September 27, 2010

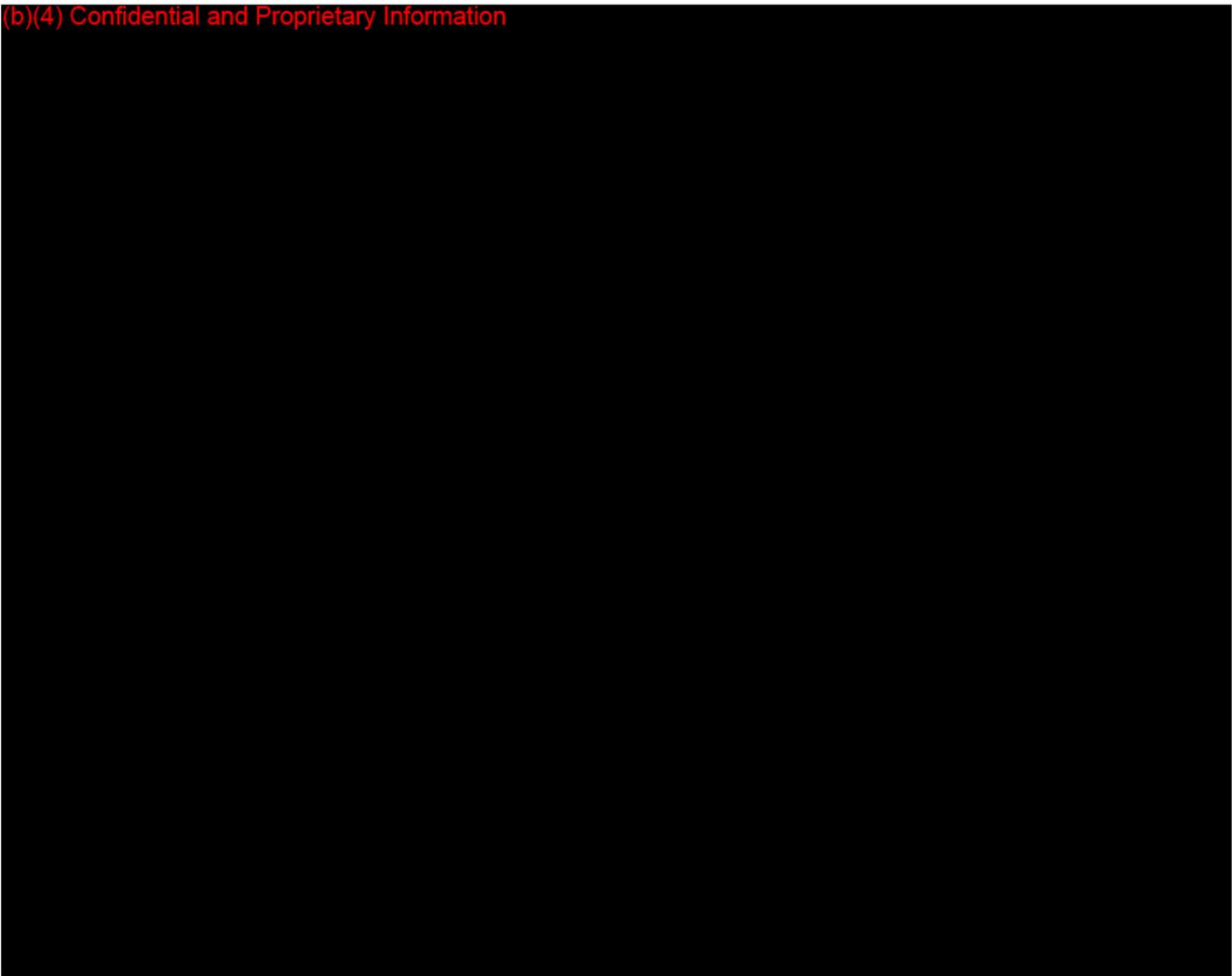
Re: Information for CollaDental Barrier (K100695)

FDA CDRH DMC
OCT 04 2010
Received

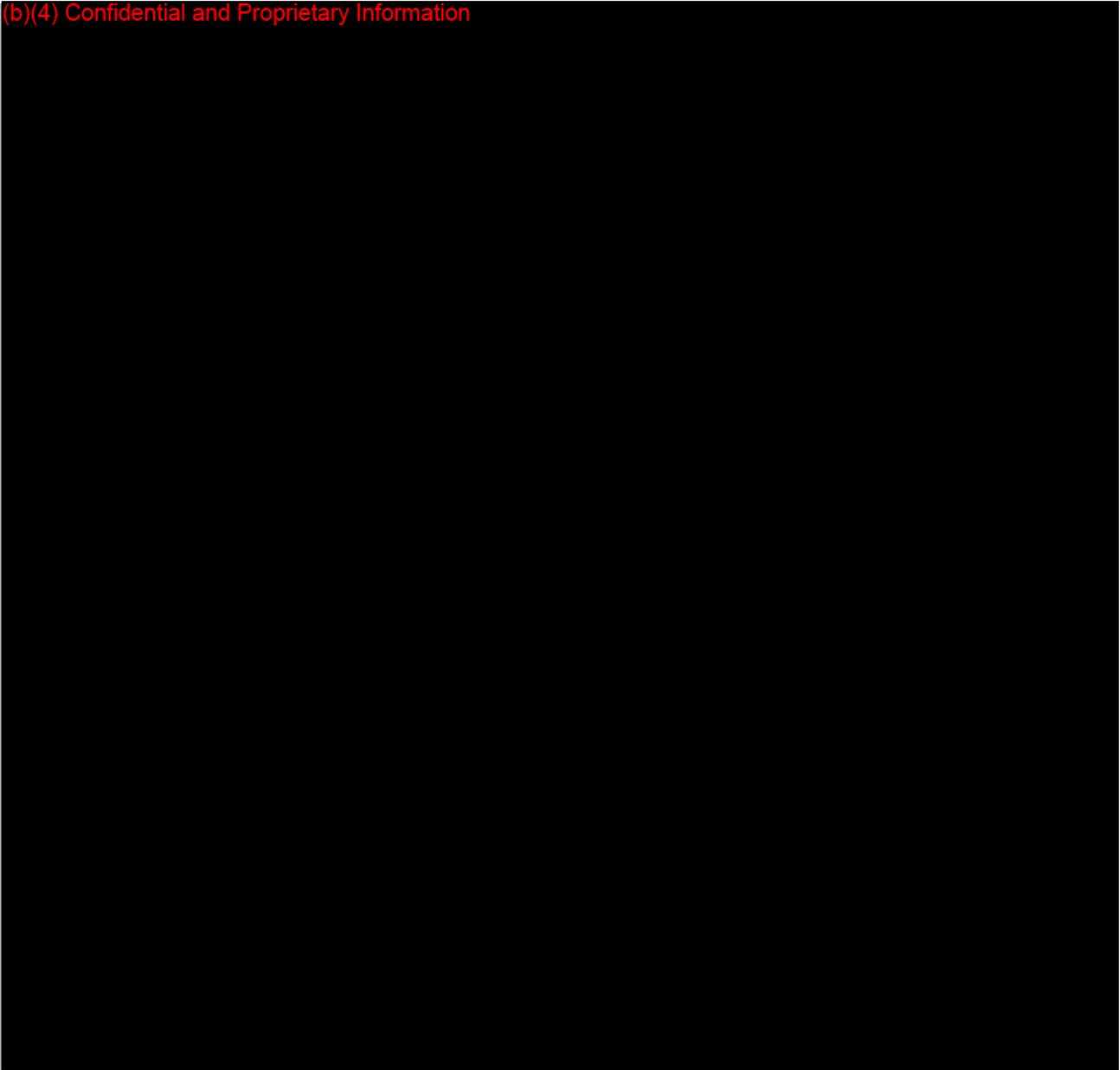
Dear Dr. Betz,

Please find enclosed information required for the application of CollaDental Barrier.

(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



Virus	Genóme type	Envelope	Size (nm)
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(b)(4) Confidential and Proprietary Information

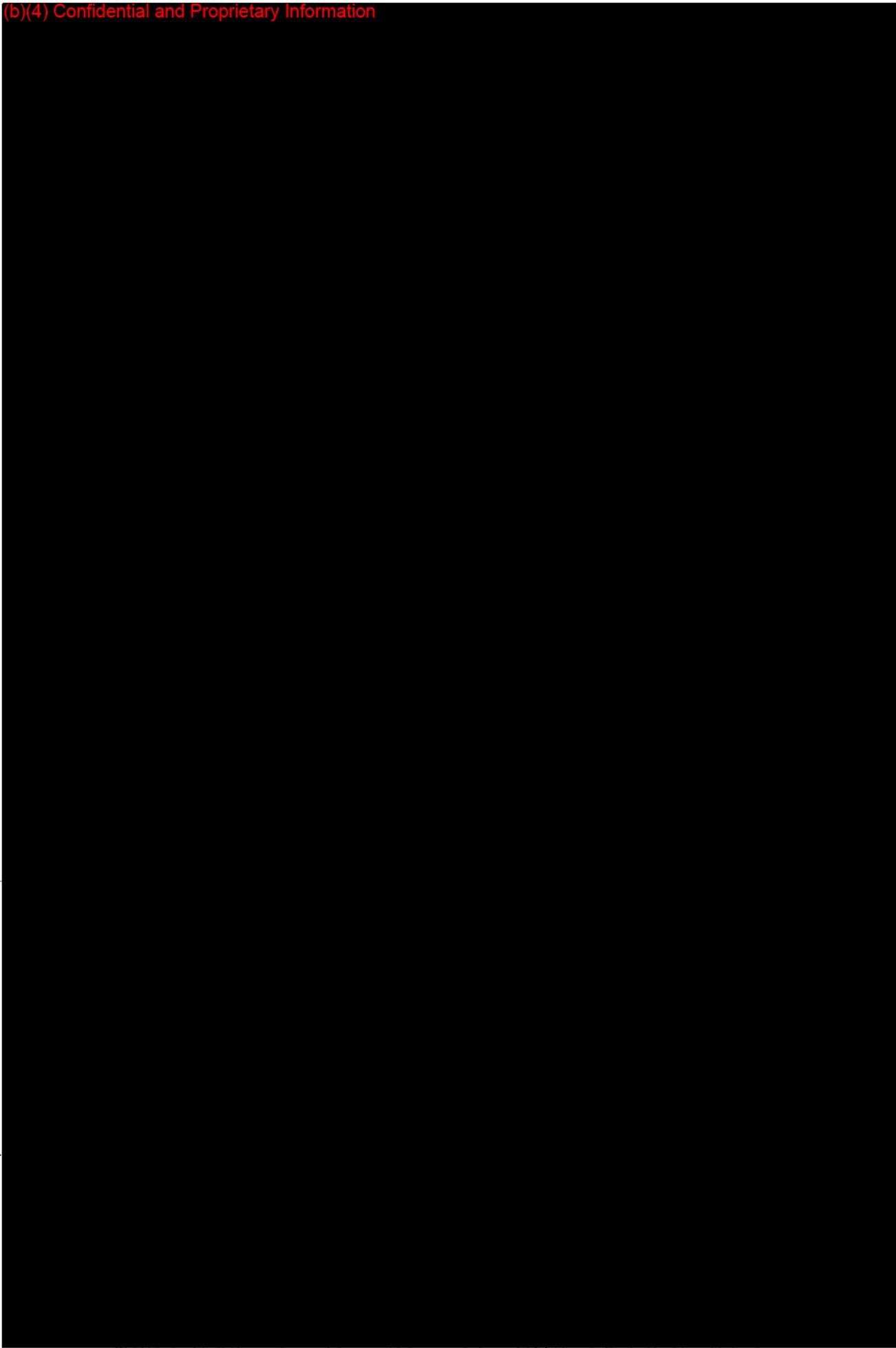


(b)(4) Confidential and Proprietary Information

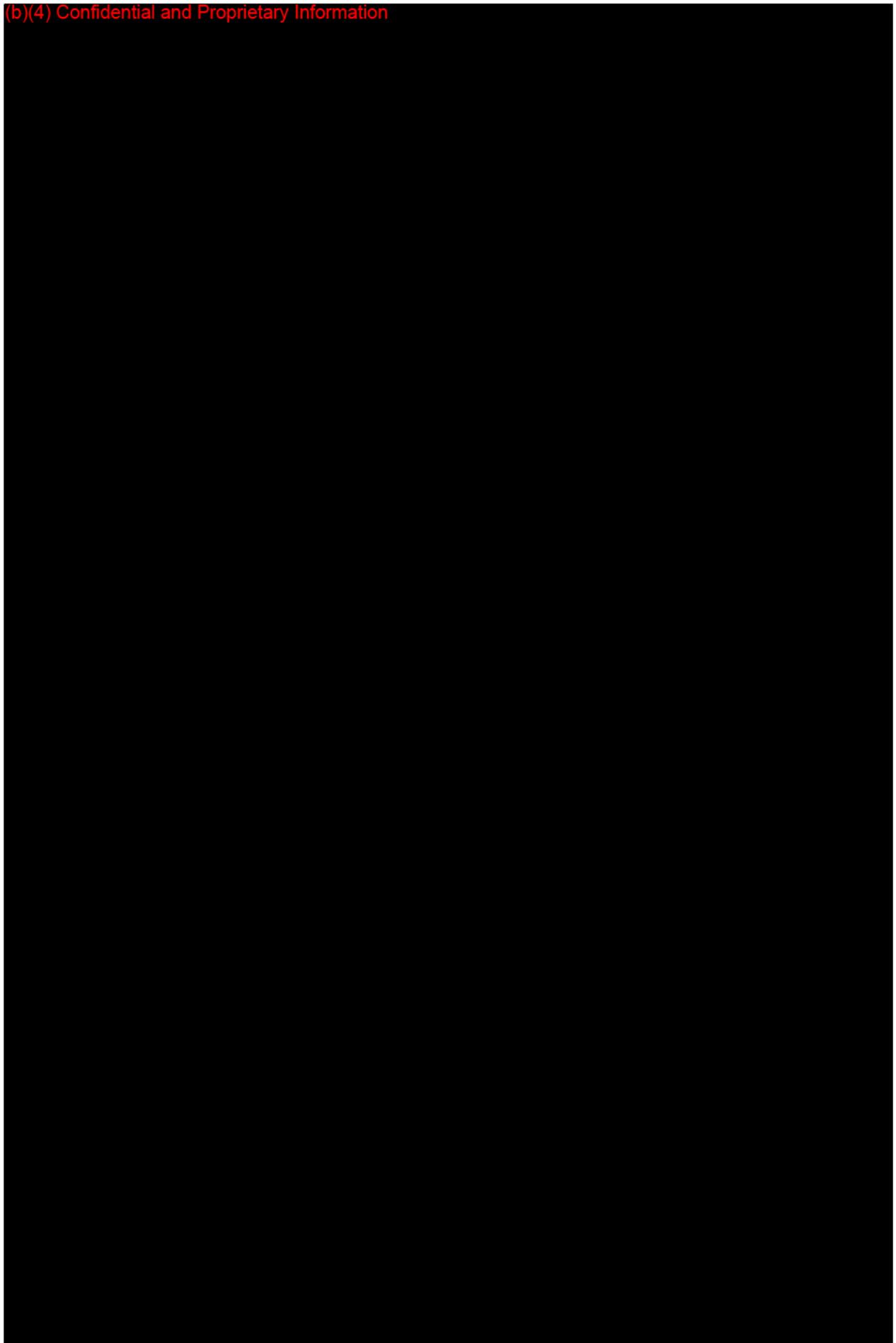


75

(b)(4) Confidential and Proprietary Information

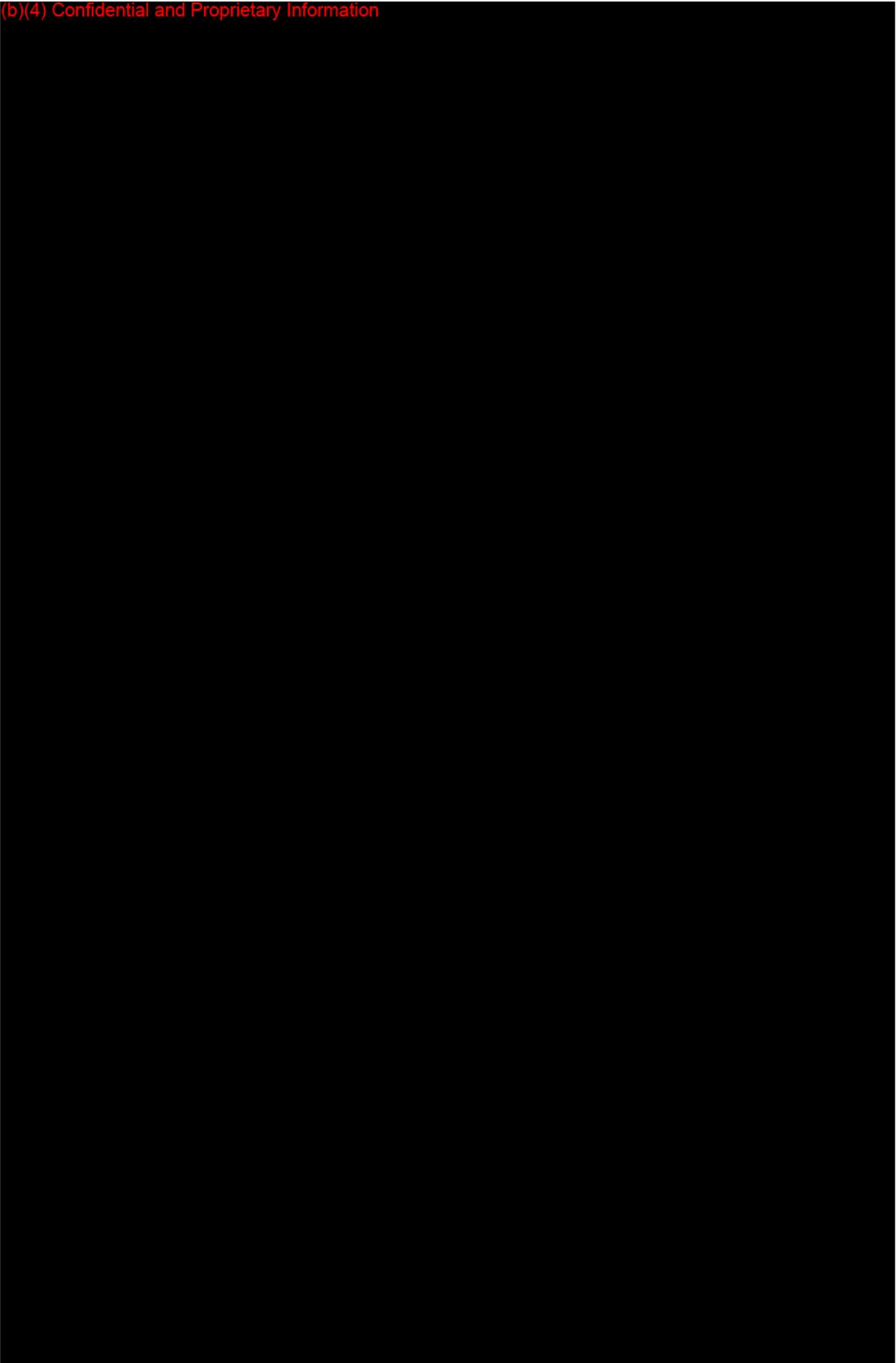


(b)(4) Confidential and Proprietary Information

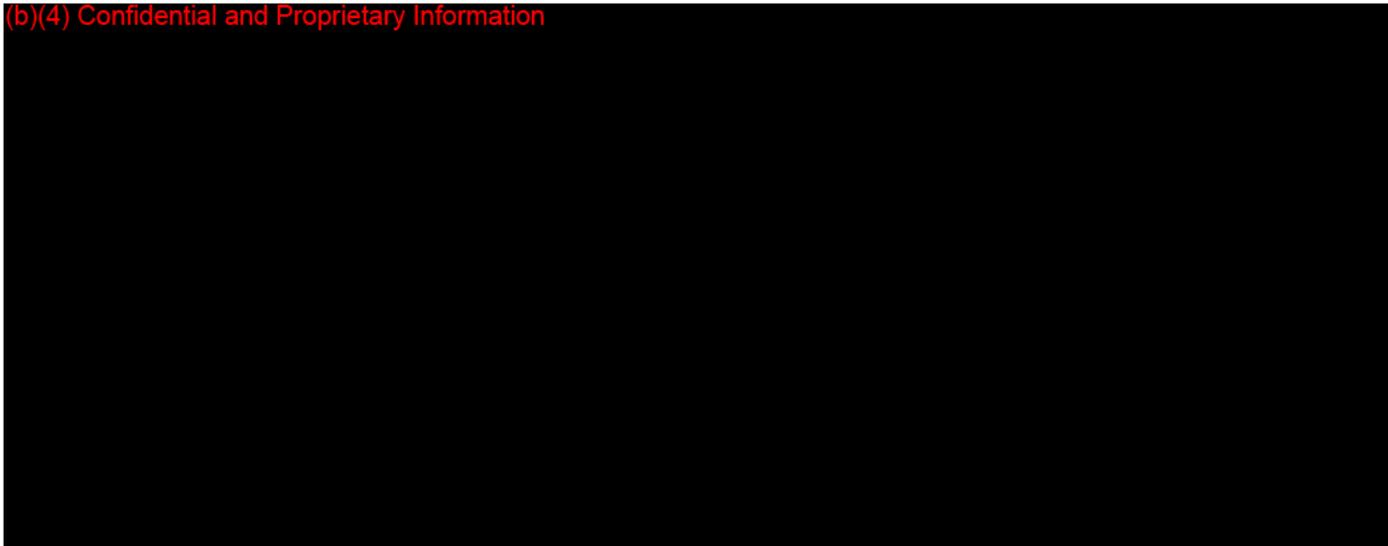


77

(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



Thank you.

Sincerely yours,

Dennis Seah

Jasper Chou for

Colla Dental Barrier 510 (k) content

1 Truthful and Accurate Statement

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT
[As required by 21 CFR 807.87(k)]

I certify that, in my capacity as Manager of Quality Assurance of Collamatrix Inc., I believe 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 omitted.

(Signature)

(Typed Name)

(Dated)

*(Premarket Notification [510(k)] Number)

2 General Information

1. Device name

- 1.1. Propriety name: CollaDental Barrier
- 1.2. Common name: Barrier, animal source, intraoral
- 1.3. Classification name: Bone grafting material

2. Registration number

- 2.1 Registration number: 3005841971
- 2.2 Address of manufacturing establishment

Collamatrix Inc.

1st floor, No. 50-1, Keyan Road, Jhunan Science Park,
Miaoli County, 350, Taiwan

3. Classification

Unclassified

4. Panel

Dental

5. Product code

NPL

6. Guidance and performance standards

- 6.1. ISO 10993 Biological Evaluation of Medical Devices.
- 6.2. ISO 11137:2006 Sterilization of health care products – Radiation.

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3 Statement of indications for use

510(k) Number (if known): _____

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

4 Substantial Equivalence Comparison

A. Predicate devices

CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices including:

- (1) BioMend Extend absorbable collagen membrane (K992216) manufactured by Integra LifeSciences corp.
- (2) BIO-GIDE® (K042197) manufactured by Ed. Geistlich Söhne AG für chemische Industrie.

B. Basis for Substantial Equivalence

1. Indications for use

- 1.1 CollaDental Barrier is intended for augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided tissue regeneration procedures in periodontal defects.
- 1.2 BioMend Extend absorbable collagen membrane is indicated for guided tissue regeneration procedures in periodontal defects to enhance regeneration of periodontal apparatus.
- 1.3 BIO-GIDE is indicated for simultaneous use of GBR-membrane and implants; augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects; guided tissue regeneration procedures in periodontal defects.

1.4 Therefore, indications for use of CollaDental Barrier is comparable to predicate device.

2. Technological characteristics

2.1 CollaDental Barrier is a monolayer, conformable, resorbable, non-friable, (b)(4) Confidential and Proprietary (b)(4) Confidential and Proprietary membrane.

2.2 BioMend Extend absorbable collagen membrane is a resorbable, non-friable, monolayer, (b)(4) Confidential and Proprietary Information membrane.

2.3 BIO-GIDE is a bilayer, resorbable non-crosslink membrane.

2.4 Therefore, CollaDental Barrier is similar in technological characteristics to predicate device.

3. Material

3.1 CollaDental Barrier comprises type I collagen obtained from porcine dermis.

3.2 BioMend Extend absorbable collagen membrane contains type I collagen obtained from bovine Achilles tendon.

3.3 BIO-GIDE contains type I and type III collagen obtained from porcine dermis.

3.4 Therefore, CollaDental Barrier is similar to predicate device with respect to materials of construction.

In summary, CollaDental Barrier is substantially equivalent to the predicate devices in terms of indication of use, technological characteristics and material used in manufacturing the device.

A table comparing the characteristics of CollaDental Barrier and predicate devices is provided in Table 1 (Attachment 4.1).

Comparison summary of CollaDental Barrier with predicate devices, BioMend Extend absorbable collagen membrane and BIO-GIDE Resorbable Bilayer Membrane

Device name	CollaDental Barrier	BioMend Extend absorbable collagen membrane	BIO-GIDE® resorbable bilayer membrane
Intended use	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus
Incorporate same basic design	Yes	Yes	Yes
Utilizes the same operating principle	Cell occlusive Implantable Resorbable	Cell occlusive Implantable Resorbable Hemostatic	Cell occlusive Implantable Resorbable Hemostatic
Incorporate same material	Yes. Type I Collagen	Yes. Type I collagen	Yes. Type I and type III Collagen
Biocompatibility	Yes	Yes	Yes
Sterilization process	Gamma irradiation	ETO	Gamma irradiation
Compatible sizes	Yes	Yes	Yes
Shelf life	36 months	24 months	36 months

5 Product Description

Description

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. Such a method of preventing epithelial migration into a specific area is known as guided tissue regeneration (GTR).

CollaDental barrier is a resorbable membrane made of type I collagen derived from pig. It is (b)(4) Confidential and Proprietary Information and takes about (b)(4) Confidential to fully resorb. It can inhibit migration of epithelial cells, promote the attachment of new connective tissue, are not antigenic.

CollaDental Barrier is a white to off white, nonfriable, conformable, resorbable, membrane consisting of primarily purified type I collagen derived from porcine dermis. CollaDental Barrier is (b)(4) Confidential thick (Figure 1). The average pore size is < (b)(4) Confidential (Figure 2). Device appears white to off white in dry state and translucent and non-slippery when wet. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the material is flexible and conforms to the contours of the defect site.

Degradation of CollaDental Barrier was evaluated in rat subcutaneous implantation. As shown in Figure 3, the membrane remained stable (b)(4) Confidential, was fully absorbed (b)(4) Confidential (Attachment 5.1). CollaDental Barrier is an odorless, hydrophilic product. It is water insoluble but lightly soluble in hot water and completely soluble in either acidic solution ($\text{pH} \leq 3$) or basic solution ($\text{pH} \geq 10$).

The porcine collagen is extracted from veterinary certified pigs and is carefully purified to avoid antigenic reactions. The collagen extraction process has been demonstrated to have the ability to substantially inactivate potential virus contaminant could be transmitted in the starting collagen-containing materials and to meet the requirement of sterility assurance level (SAL) equal to 10^{-6} . CollaDental Barrier is supplied sterile and for single use.

This device is available in three sizes 15mm x 20mm, 20mm x 30mm and 30mm x 40mm, respectively. CollaDental Barrier can be cut to any size or shape with scissors or scalpel in the wet and dry state, without tearing or fragmenting to meet the needs of the surgeon. CollaDental Barrier is individually housed in PET blister and sterilized by gamma irradiation.

(b)(4) Confidential and Proprietary Information

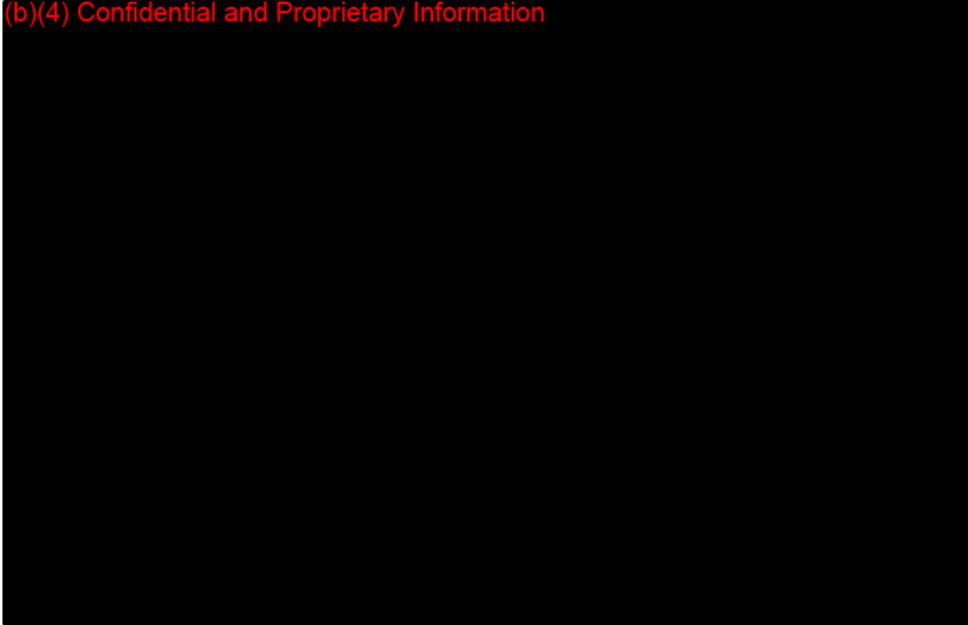


Figure 1 Scanning electron micrography image of CollaDental Barrier. The device has a dense surface and a multi-layer structure with thickness of (b)(4) Confidential and Proprietary

(b)(4) Confidential and Proprietary Information

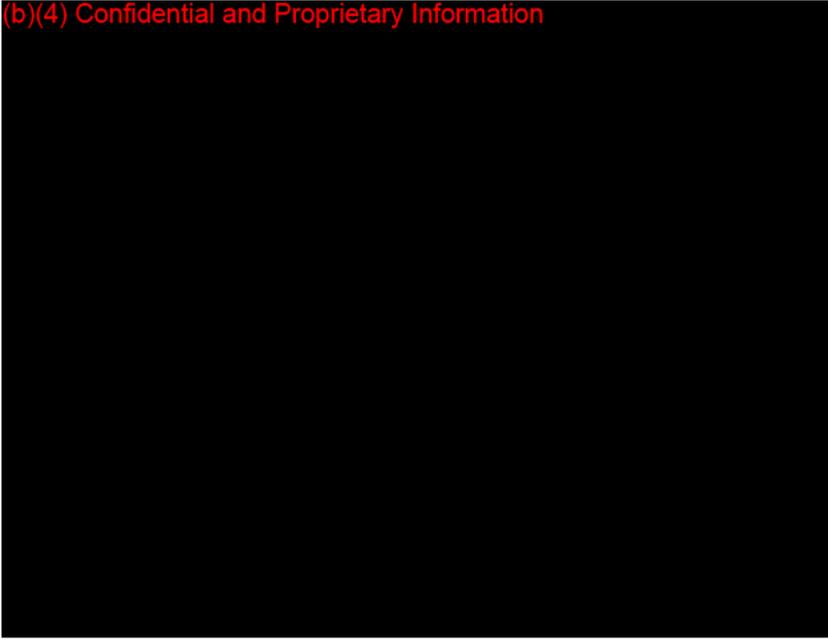


Figure 2 Scanning electron micrography image of CollaDental Barrier. The device has average pore size less than (b)(4) Confidential

(b)(4) Confidential and Proprietary Information

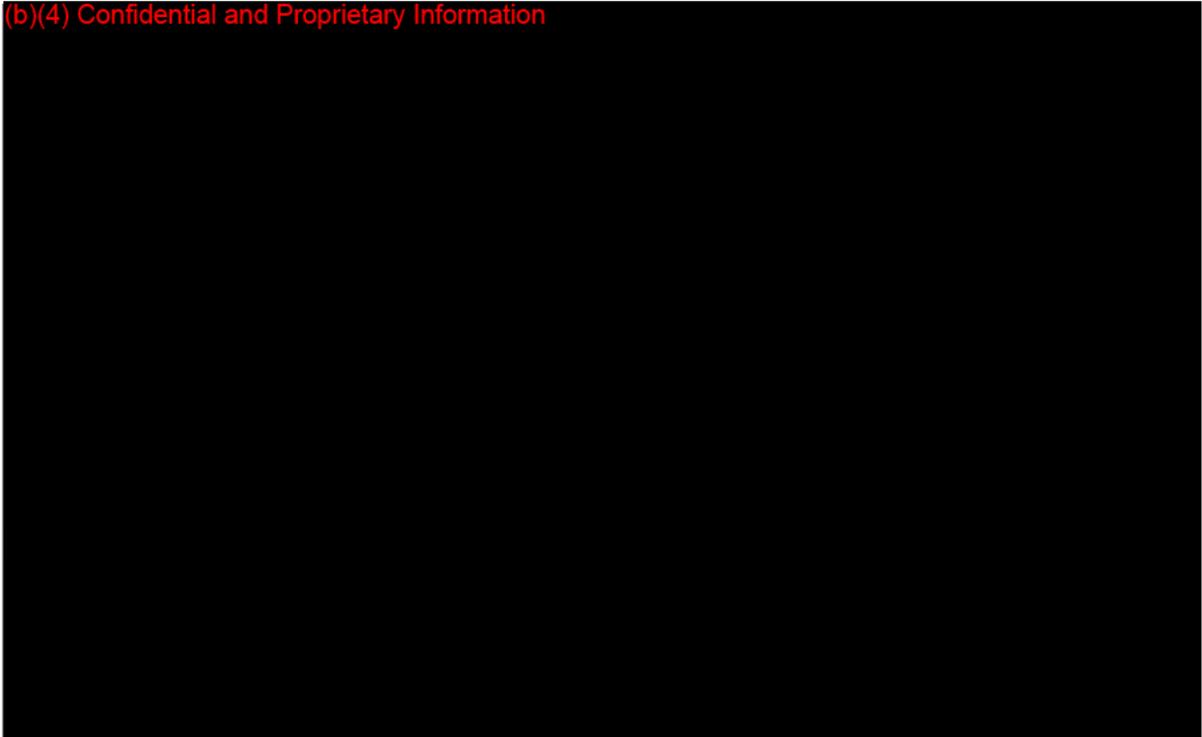


Figure 3 Change in surface area versus implantation time. CollaDental Barrier degradation profile, evaluated in rat subcutaneous implantation, demonstrated the device is degraded in (b)(4) Confidential

6 Manufacturing information

A. Materials

1. Collagen-containing tissues

Porcine hides are the principle material used in the manufacturing of CollaDental Barrier.

This material is harvested from pigs maintained under the appropriate (b)(4) Confidential

veterinary/animal welfare schemes. Extensive veterinary checks are made to the animals on

a regular basis throughout their life and both pre- and post-mortem to ensure they are

healthy and suitable for use. The animals are slaughtered by (b)(4) Confidential and Proprietary Information

slaughterhouse and are qualified for human consumption. Slaughtering of pigs and packing

of porcine hides are all provided by (b)(4) Confidential and Proprietary Information slaughterhouse

(b)(4) Confidential whereas packing and distribution of frozen porcine hides are handled by a (b)(4) Confidential

(b)(4) Confidential cold storage (b)(4) Confidential and Proprietary Information

2. (b)(4) Confidential and Proprietary the three hog species used. The type I collagen used in the device is prepared from the pig hides. No other animal tissues have been used.

3 How the health of herd is maintained and monitored.

3.1.1 Yes, the herd is closed.

3.1.2 Vaccination for (b)(4) Confidential and Proprietary Information (b)(4) Confidential is standard. The type of vaccine used is (b)(4) Confidential.

3.1.3 Veterinarian inspections are performed with the frequency of once a month.

3.1.4 Composition of the animal feed is composed of corn, barley, grain sorghum, oats, and wheat.

3.1.5 The abattoir is (b)(4) Confidential and Proprietary Information

3.1.6 No bovine origin or other animal derived material has been used in the preparation of CollaDental Barrier.

4 How the health of each animal is maintained and monitored.

4.1 The animal is sacrificed at the age of (b)(4) Confidential and Proprietary Information

4.2 Yes. Pre and post mortem are performed.

4.3 Animal material subjects to several tests as shown in the table. When the test results meet the acceptance criteria, the animal material is then qualified for further processing.

4.4 The following tests are performed (Table 1) to qualify porcine hides for further processing:

Table 1: Acceptance criteria for porcine hide's inspection

Tests	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

5. Validation of virus inactivation study

Study was performed to provide evidence that (a) the virus inactivation steps in the manufacturing process have the capability to substantially inactivate potential virus contaminant could be transmitted in the starting collagen-containing materials; (b) the virus inactivation steps in the manufacturing process has the capacity to inactivate and remove novel or yet undetermined virus contamination in the product. The results of inactivation meet the requirement of sterility assurance level (SAL) equal to 10^{-6} (Attachment 6.1).

6. Upon receipt, goods are inspected for proper documents and undergo visual inspection for any non-conformity. After which, porcine hides are stored (b)(4) Confidential and Proprietary Information or proceed to decontamination according to steps listed in Table 2 shown below.

Table 2: Cleaning SOP

Treatments
(b)(4) Confidential and Proprietary Information

7. Chemicals

7.1 Chemicals used in manufacturing CollaDental Barrier are tabulated in Table 3.

Table 3: Chemicals and specification

Items	Specification
(b)(4) Confidential and Proprietary Information	

7.2 Packaging of CollaDental Barrier

7.2.1 CollaDental Barrier is individually packaged in a polyethylene terephthalate (PET) blister pouch, heat-sealed with an aluminum foil and sterilized by gamma (γ)-irradiation.

B. Manufacture of CollaDental Barrier

1. Incoming inspection of collagen-containing animal tissues and other raw ingredients

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(b)(4) Confidential
and Proprietary
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are carried out to demonstrate the specification of each ingredient complies with quality requirements (Table 4). Certificate of Analysis and safety data sheet of each ingredient can be found in attachment 6.2

Table 4: Specification of ingredients

Items	Specifications
(b)(4) Confidential and Proprietary Information	

2. Disinfection of porcine collagen-containing tissues is carried out as described in Table 5 shown below.

Table 5: Cleaning steps and parameters for porcine tissues

Treatments	Parameters/conditions
(b)(4) Confidential and Proprietary Information	

3. Suspend disinfected tissues in (b)(4) Confidential solution containing (b)(4) Confidential and Proprietary (b)(4) Confidential (b)(4) (v/v). This acid/enzymatic extraction process is carried for at least (b)(4) Confidential with constant agitation (b)(4) Confidential. The extraction utilizes solubility of porcine collagen, which is predominantly found in pigskins, in acetic acid solution. Temperature is adjusted to (b)(4) Confidential and this temperature range is (b)(4) Confidential and Proprietary Information manufacturing process. 10mL solution is recovered for (b)(4) Confidential and Proprietary Information

4. After acid extraction, the acid soluble collagen-containing fraction is (b)(4) Confidential and Proprietary Information and then followed by (b)(4) Confidential to remove debris or large insoluble particulates. The filtered acid soluble solution is further clarified by (b)(4) Confidential and Proprietary Information

5. After clarification, the acid soluble collagen is precipitated by (b)(4) Confidential and Proprietary Information. A (b)(4) Confidential solution is prepared and (b)(4) Confidential and Proprietary Information the collagen-containing acid soluble fraction with its final concentration reaches (b)(4) Confidential (b)(4) Confidential. The formation of collagen-containing sludge, indicated by the appearance of (b)(4) Confidential and Proprietary Information, is facilitated by constant stirring (b)(4) Confidential of the solution. The solution is (b)(4) Confidential and Proprietary Information for additional (b)(4) Confidential to allow the precipitation of collagen.

6. The collagen-containing sludge is harvested by (b)(4) Confidential and Proprietary Information (b)(4) Confidential and followed by (b)(4) Confidential and Proprietary Information and then transferred to a filtration device to (b)(4) Confidential and Proprietary Information. After (b)(4) Confidential the collagen sludge can be (b)(4) Confidential and Proprietary Information (b)(4) Confidential. One gram of the collagen sludge is collected from each lot for in-process analysis including (b)(4) Confidential and Proprietary Information (b)(4) Confidential and Proprietary Information

7. Preparation of collagen membrane Dissolve collagen sludge in (b)(4) Confidential and by gently stirring at (b)(4) Confidential to generate a homogeneous solution with collagen concentration about (b)(4) Confidential. Pour the solution into (b)(4) Confidential and Proprietary and (b)(4) Confidential and Proprietary with collagen solution to a (b)(4) Confidential and Proprietary. The (b)(4) Confidential and Proprietary is then transferred to a (b)(4) Confidential refrigerated chamber with (b)(4) Confidential and Proprietary \leq (b)(4) Confidential. The (b)(4) Confidential process continues for (b)(4) Confidential until the solution is completely (b)(4) Confidential. The collagen membrane appears to be opaque, non-friable, off white and conformable.

8. Immerse (b)(4) Confidential and Proprietary in a solution containing (b)(4) Confidential solution and keep (b)(4) Confidential with constant agitation (b)(4) Confidential for (b)(4) Confidential, followed by rinsing the membrane thoroughly in excess (b)(4) Confidential and Proprietary to (b)(4) Confidential and Proprietary. The collagen membrane is then (b)(4) Confidential and Proprietary before transferred to a refrigerated lyophilizer. Vacuum is applied and, the vacuum is maintained at (b)(4) Confidential throughout the process. Lyophilization continues for (b)(4) Confidential. The resultant lyophilized membrane has a thickness of (b)(4) Confidential. The membrane is further processed to give different dimensions including 15mm x 20mm, 20mm x 30mm and 30mm x 40mm, respectively. Five pieces of air-dried product are collected for (b)(4) Confidential and Proprietary Information and viable count.

9. Filling and packaging of CollaDental Barrier are carried out in a class 10k clean room environment. CollaDental Barrier CollaDental Barrier is individually packaged in a polyethylene terephthalate (PET) blister, heat-sealed with a lidding material and sterilized by gamma (γ)-irradiation.

10. Five pieces of finished product are collected for sterility test and physical appearance inspection after γ -irradiation. Finished product release test is performed on every product lot. Semi-quantitative analysis of heavy metals (b)(4) Confidential is also carried out. The acceptance criterion for γ -irradiation products is sterile, validated by fluid (b)(4) Confidential and Proprietary Information and (b)(4) Confidential and Proprietary Information. The release/acceptance criteria for finished product are listed in table 6 shown below.

Table 6: Release/acceptance criteria for finished product inspection

Description	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

C. Environmental control

The clean room is equipped with an air shower room and with environmental temperature maintained at (b)(4) Confidential and the relative humidity (b)(4) Confidential. Particle count is performed (acceptance criterion: (b)(4) Confidential, (b)(4) Confidential, (b)(b)(4) Confidential) to monitor environmental cleanliness of the clean room as well as any leakage in HEPA filters. A positive pressure condition (acceptance criterion (b)(b)(4) Confidential) which monitors through a pressure gauge, is established and maintained to expel the back-flow of air from other compartments. Operators are required to wear appropriate clean room attire.

The Class 100 safety hood is equipped with UV light and HEPA filter that help to control airborne contaminants. Air quality monitoring is carried out by particle count (acceptance criterion (b)(4) Confidential and Proprietary Information) and air-borne microorganisms is detected by culture plate exposure using (b)(4) Confidential (acceptance criterion (b)(4) Confidential and Proprietary Information).

6-7
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D. Final testing

Final product release tests of CollaDental barrier include bioburden and physical appearance inspection. Table 7 summarizes the acceptance criteria for release tests.

Table 7: Release/acceptance criteria

Description	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

E. Cleaning

Cleaning/disinfection of the production line is carried out by a cleaning procedure comprises a lye solution wash and an acid solution wash. Rinsing with clean water is carried out in between each washing session. The washing conditions are tabulated in Table 8 shown below.

Table 8: Clean-in-Place parameters

Steps	Description/parameters
(b)(4) Confidential and Proprietary Information	

7 Labeling

All labeling information for CollaDental Barrier is supplied together with this application including

1. Pouch label (Attachment 7.1)
2. Package box label (Attachment 7.2)
3. Instruction for use (Attachment 7.3)

The content of the labeling information of CollaDental Barrier specifies the intended use, product claims, direction for use, contraindications, precautions and storage conditions that meet the requirements as defined in 21 CFR § 807.87

8 Controls

A. Quality assurance

1. Quality management system

The establishment is Good Manufacturing Practice certified as required by the regulatory agency of Taiwan. In addition, the establishment also implements a quality management system complies with the requirements of BS EN ISO 13485:2003 and is certified (b)(4) Confidential

(b)(4)
Confidential
d

by British Standards Institution management system.

2. Quality assurance program: QA program is implemented to assure that the product quality is consistently met. The entire program can be divided into four parts.

i. Raw materials

Quality of materials used directly or indirectly in the manufacturing of the device must be substantiated by incoming QC inspection according to each inspection SOP. Standard procedure of decontamination is established for source materials used in collagen extraction as described under section "Manufacturing information". Provisions of veterinary inspection licenses or certificates must be met prior to or accompanied with the delivery of the purchased items.

ii. Process controls

1. In process control at various manufacturing points is implemented to monitor the manufacturing parameters as well as the intermediates. This is to ensure that the quality requirements are consistently met and do not show deviation throughout the manufacturing process.

2. A closed production system is installed in order to reduce exposure to environmental change and minimized air-borne contamination.
 3. Vessels and piping lines are made of (b)(4) Confidential that comply with ASTM standard. All surfaces that come in contact with product(s) are mechanically polished to (b)(4) that residual substances left behind between different or similar production batches can be efficiently removed by a CIP cleaning process.
- iii. Personnel training
- Personnel working in the production site and QC laboratory received properly training to ensure that tasks are performed per SOPs. All records and test results are documented, filed to create a Device History Record of each product lot.
- iv. Environment management
- A well-maintained clean environment is important in controlling bioburden level in the product. In order to meet the standard of clean environment, Collamatrix manufacturing site divides into two zones. The first zone is a class 10K clean room where the production facilities are located. The second zone is a class 10K clean room where a class 100 Biosafety hood is housed. The handling and filling of CollaDental Barrier is performed in a class 10K clean room. In addition to routine cleaning procedure, a monitoring program comprising temperature, humidity, air-borne viable count, air-borne particle count and differential pressure between two clean zones are also included to maintain a clean and hygienic working environment.

3. **Validation of Systems and Equipments:** Utility systems, manufacturing equipments, manufacturing processes and analytical methodologies used in the production of CollaDental Barrier have been validated according to established written procedures. Procedures are in place to ensure the regular maintenance of equipment and the regular monitoring of environmental conditions within the production facilities.

B. Stability studies

The proposed shelf life of CollaDental Barrier is one month. Stability study of the device comprises real time stability at room temperature. The studies evaluate the effectiveness of terminal γ -sterilization by determining the bioburden level in the products. In addition, the color and the physical appearance of the product are also inspected.

Real-time study at room temperature condition (b)(4) is ongoing. Interim results of bioburden level for 1 month and physical appearance of the product revealed no deviation from the specification (Attachment 8.1).

C. Production batch/lot identification

Each production lot of CollaDental Barrier is assigned with an unique lot number for manufacturing and product traceability control. For example, lot number (b)(4) Confidential

(b)(4) Confidential and Proprietary Information

which means the CollaDental

Barrier lot was manufactured on (b)(4) Confidential and Proprietary Information

9 Performance

A. Biocompatibility tests

CollaDental Barrier was subjected to a battery of tests in accordance with Part-10993 of the International Standard Organization (ISO) Standard (Biological Evaluation of Medical Devices) and the United States Pharmacopeia (USP) methods.

CollaDental Barrier has been designed to meet the following requirements: (1) cytotoxicity study, (2) ISO modified intracutaneous study (irritation), (3) murine local lymph node assay (sensitization), (4) acute systemic toxicity study, (5) *Salmonella typhimurium* reverse mutation (Ames) test, (6) hemolytic study and (7) Endotoxin test.

1. Summary of cytotoxicity study

A single extract of CollaDental Barrier was prepared using single strength supplemented Minimum Essential Medium and tested on L-929 mouse fibroblast cells at standard culture conditions for 48 hours. CollaDental Barrier showed no evidence of causing cell lysis or toxicity. (Attachment 9.1)

2. Summary of ISO modified Intracutaneous study

Two extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution and sesame oil were injected intracutaneously into the dorsal sites of rabbits. Observations for erythema and edema were conducted after injection. CollaDental Barrier showed no evidence of causing any sign of irritation at the injection sites and the primary irritation index of CollaDental Barrier was negligible. (Attachment 9.2)

3. Summary of murine local lymph node assay

The delayed contact sensitization of CollaDental Barrier was tested in mice. Two extracts of CollaDental Barrier, prepared in 0.9% sodium chloride solution and dimethylsulfoxide, were used to dose on the dorsum of ear for 3 consecutive days. The radioactive counts in the lymph nodes draining were measured using scintillation counter. The Stimulatory Index of CollaDental Barrier was insignificant and considered non-sensitizing. (Attachment 9.3)

4. Summary of Acute systemic toxicity study

Two extracts of CollaDental Barrier, prepared in 0.9% sodium chloride solution and sesame oil, were injected either intravenously or intraperitoneally into mice. Sign of mortality or evidence of systemic toxicity from the extracts were not found. Therefore, CollaDental Barrier did not cause systemic toxicity in test animals. (Attachment 9.4)

5. Summary of genotoxicity study

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested for the genotoxicity activity using the *Salmonella typhimurium* reverse mutation (Ames) test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.5)

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution or sesame oil was tested for the genotoxicity activity using micronucleus test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.6)

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride or DMSO was tested for the genotoxicity activity using mouse lymphoma test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.7)

6. Summary of hemolysis study

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested for the hemolytic activity. Signs of hemolytic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause blood incompatibility. (Attachment 9.8)

7. Summary of Endotoxin test

The extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested the pyrogenic activity using Limulus ameocyte lysate (LAL) gelation assay. Sign of LAL reactivity from the extracts was not found. (Attachment 9.9)

B. Sterilization

CollaDental Barrier is sterilized by γ -irradiation. The terminal sterilization service was performed by China Biotech Corporation (FDA establishment registration number: 9681277), an ISO 13485:2003 and ISO 9001:2000 quality management systems certified contract sterilizer.

Sterilization of CollaDental Barrier was validated according to ISO 11137:2006 Sterilization of Health Care Products – Radiation. Dosimetry results revealed that the lowest dosage was (b)(4) and the highest was (b)(4) indicating that devices received sufficient sterilization dose (Attachment 9.10).

C. Sterility

CollaDental Barrier is sterilized by irradiation according to ISO 11137:2006. Sterility of CollaDental Barrier was verified using fluid thioglycollate medium (for bacteria) and Potato Dextrose agar (for yeasts and molds) per USP <71>. Results have consistently demonstrated that no microorganism was detected in the sterilized CollaDental Barrier. The effectiveness of γ -sterilization is validated and further substantiated by stability study. (Attachment 8.1)

10 510k Summary

A summary of the 510k safety and effectiveness information upon which the substantial equivalence of CollaDental Barrier is based is prepared to meet the requirements as defined in 21 CFR § 807. (Attachment 10.1)

Cell attachment and proliferation report

CMI-201003-3

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Report no:

CMI-201003-3

Study Title:

Cell proliferation and attachment

Test Article:

CollaDental Barrier

March, 2010

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Page no. 02/10

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1st Floor, No. 50-1, Keyen Road, Jhunan Township,
Miaoli County, 350, Taiwan

Study announcement:

1. This report could not be reprinted or adapted without the permission from (b)(4) Confidential and Proprietary Information and Collamatrix Inc.

Approved by

Date

Jasper Chau

2010. 3. 31

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The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

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SUMMARY

The purpose of this study was to evaluate the biological effects of CollaDental Barrier on cellular attachment and proliferation using (b)(4) Confidential and Proprietary . Under the test conditions described here, CollaDental Barrier may influence cell proliferation and differentiation.

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INTRODUCTION

The aim of this study was to evaluate the biological effects of CollaDental Barrier, as guided tissue regeneration (GTR) membrane, on the periodontal tissue attachment and proliferation. Degradable natural biopolymer such as collagen is recognized as promising GTR material, has attracted attention due to their excellent cell affinity, biodegradability and biocompatibility. These barrier membranes have been used to encourage appropriate progenitor cell populations at the wound site.

MATERIALS AND METHODS

Preparation of cell

A (b)(4) Confidential and Proprietary (b)(4) Confidential was used to examine the cellular responses to CollaDental Barrier. The culture medium was Dulbecco's Modification of Eagle's Medium (DMEM) supplemented with 10% fetal calf serum, 2mM L-glutamine and Pen/Strep antibiotic. The cells were cultured in a humidified incubator with 5% CO₂ at 37°C.

Proliferation assay

A 6-well plate was prepared, consisting of three wells of CollaDental Barrier membrane with dimension of 1cm x 1cm. Glass cover slips were placed in three wells as negative controls. Each well was seeded with MC3T3-E1 in DMEM at a cell density of (b)(4) cells per well. After incubation for (b)(4), the cell proliferation level was measured using an MTT assay.

Attachment assay

A 6-well plate was prepared, consisting of three wells of CollaDental Barrier membrane with dimension of 1cm x 1cm. Glass cover slips were placed in three wells as negative

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controls. Each well was seeded with MC3T3-E1 in DMEM at a cell density of (b) (4) cells per well. Plate was incubated at 37°C in humidified atmosphere containing 5% CO₂ for 24 hours before harvested for light microscopy inspection.

Light microscopy inspection

Following incubation, cell-seeded CollaDental Barrier membranes were rinsed with PBS and fixed with 10% Neutral Buffered Formalin and stained with haematoxylin. The membranes were evaluated under a light microscope and the number of cells attached per 0.25mm² was determined.

Statistical analyses

Light microscopic evaluation of cell attachment to coated and uncoated membranes was subjected to the Student's t test to determine levels of significant difference.

RESULTS

In this study, the proliferation of the (b)(4) Confidential cells was performed to assess the biological effects of CollaDental Barrier. The cell viability on the membranes after culturing for 3 days was quantified using an MTT assay. As shown in Figure 1, the cells on CollaDental Barrier proliferated to significantly higher degrees than those on the glass cover slips.

Light microscopic evaluation indicated that the glass cover slips showed sparse to non-existent cellular attachments. However, cell attachment was found significant ($P < 0.05$) on CollaDental Barrier membrane indicating CollaDental Barrier appeared to be conducive to cellular attachment (Table 1).

(b)(4) Confidential and Proprietary Information



Figure 1 Cell proliferation on CollaDental Barrier determined by MTT assay. Data are represented as mean \pm SD (n=3). ($p < 0.05$)

Table 1 Number of cell attached on CollaDental Barrier.

	Number of cell attached
CollaDental Barrier	(b)(4) Confidential and Proprietary
Negative control	(b)(4) Confidential and Proprietary Information

Data are represented as mean \pm SD (n=3). ($p < 0.05$)

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CONCLUSION

**(b)(4) Confidential and Proprietary
Information**

was used in this study to evaluate the biological effects of CollaDental Barrier in term of cellular attachment and proliferation. Under the test conditions described here, CollaDental Barrier is conducive for cellular proliferation and cell attachment.

Virus inactivation report

COLLAMATRIX

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Introduction

The primary concern of using animal-derived materials was the cross-species transfer of transmissible agents such as virus. The goal of this study was to evaluate the virus inactivation steps for the production of non-bovine derived extracellular matrix biomaterials for manufacturing medical devices and implantation applications. Avian feet and porcine hides were used as the source for biomaterial preparation. This aim of this study was to demonstrate the inactivation processes (1) (b)(4) Confidential and Proprietary Information (b)(4) Confidential and Proprietary Information (2) (b)(4) Confidential and Proprietary Information (b)(4) Confidential and Proprietary Information (3) could ensure that product quality was consistently maintained and met customers or regulatory requirements.

The inactivation steps comprised (b)(4) Confidential and Proprietary Information treatment, (b)(4) Confidential and Proprietary Information treatment and (b)(4) Confidential and Proprietary Information) and a (b)(4) Confidential and Proprietary Information

The virus inactivation achieved by the disinfection step and the (b)(4) Confidential and Proprietary Information digestion was validated using (b)(4) Confidential and Proprietary Information. Their molecular characteristics were summarized in Table 1. These viruses are the representatives of different genomic types and composition, envelope or sizes of viral contaminant that could present in animal tissues.

Table 1. Model viruses used for inactivation study

Virus	Genome type	Envelope	Size (nm)
(b)(4) Confidential and Proprietary Information			

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Materials and methods

Viruses and cells

The following virus-cell systems were used for viral propagation and titration: (b)(4) Confidential

(b)(4) Confidential and Proprietary Information

(b)(4) Confidential and Proprietary Information

The

(b)(4) Confidential and Proprietary Information

was used as a model virus for any endogenous uncharacterized retroviruses found in animals. These combinations were chosen because plaque formation and focus formation assays performed using these systems are commonly accepted as valid assays to evaluate viral inactivation for medical device regulatory approval.

(b)(4) Confidential and Proprietary Information were cultured in DMEM supplemented with 10% fetal bovine serum and 2 mM L-Glutamine. (b)(4) Confidential and Proprietary Information were maintained in RPMI 1640 supplemented with 10% fetal bovine serum and 2 mM L-Glutamine. (b)(4) Confidential and Proprietary Information were maintained in RPMI 1640 supplemented with 10% fetal bovine serum. All cells were maintained in a humidified chamber at 37°C, with 5% CO₂.

Samples preparation and spiking

Frozen porcine hide prepared from the market weight pigs with hair and fat had been removed was thawed at room temperature before use. Hides were washed thoroughly in sterile water to remove debris or blood. 10 grams of tissues were randomly injected with (b)(4) Confidential and Proprietary Information solution (b)(4) Confidential and Proprietary Information), suspended in culture medium to a concentration approximately (b)(4) Confidential and Proprietary Information plaque-forming unit (PFU).

Disinfection steps

After spiking with virus-containing medium, hides were thoroughly rinsed with sterile water and then followed by the treatment with (b)(4) Confidential and Proprietary Information (b)(4) Confidential and Proprietary Information in a sequential order at (b)(4) Confidential and Proprietary Information. Treatment parameters were summarized in Table 2. Three samples of tissue for each virus were tested.

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After air-dried, the disinfected tissues were homogenized and the residual virus activity was measured by plaque-formation assays.

Table 2. Procedures and details of the disinfection treatment

Steps	Final concentration	Duration (min)
(b)(4) Confidential and Proprietary Information		

(b)(4) Confidential and Proprietary Information

Homogenized spiked samples were suspended ((b)(4) Confidential and Proprietary) in an aqueous solution containing (b)(4) Confidential and Proprietary and (b)(4) Confidential and Proprietary. The suspension was incubated at (b)(4) Confidential and Proprietary with constant stirring for (b)(4) Confidential and Proprietary.

Viral plaque assay

(b)(4) Confidential and Proprietary Information

(b)(4) Confidential and Proprietary Information

cultured in triplicate in six-well plate to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were ten fold serially diluted in MEM cell culture medium. Plates were incubated at 37°C, 5% CO₂ for 1 hr with gentle rocking at 20 min interval to facilitate absorption. Following absorption, plates were overlaid with 0.5% Sea Plaque agarose containing dissolved in MEM medium and continua to grow until plaque formation was observed in positive control (4~5 days post-infection). Infected cells were fixed in formaldehyde solution for 12 hrs. Fixative and agarose were gently removed before the addition of plaque-staining dye, crystal violet blue. The 0.1% staining dye was prepared by dissolving the dye in ethanol. The lightly stained plaque against the densely stained dark background was calculated and expressed as plaque-forming unit.

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(b)(4) Confidential and Proprietary Information assay (b)(4) Confidential cultured in triplicate in six-well plates to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were ten fold serially diluted in RPMI culture medium. After infection, the plaques were counted by eye under the microscope after 2 days post-infection.

(b)(4) Confidential and Proprietary Information assay (b)(4) Confidential and Proprietary cultured in triplicate in six-well plates to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were tenfold serially diluted in RPMI 1640 cell culture medium. Plates were incubated at 37°C, 5% CO₂ for 1 hr with gentle rocking at 20 min interval to facilitate absorption. Following absorption, culture medium was replaced with fresh RPMI 1640 containing 1µg/ml hexadimethrine bromide to facilitate infection. The culture medium was replaced with fresh medium after 72 hours post-infection and continued to grow for another 5 days. After 8 days, foci observed as clustered and remained attached to the culture plate were counted and expressed as viral titer.

Results

Spike recovery of virus following injection into tissue samples before the inactivation steps was performed to show that virus remained viable after injection into the tissues. Virus titers were not significantly affected in the culture system (Table 3. *Spike recovery*). After confirming the stability of the virus in the culture system, these value readings were used as the basis for inactivation studies.

Inactivation studies utilizing spiking experiments with (b)(4) Confidential and Proprietary Information were performed to give a quantitative estimate of viral inactivation.

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Table 3. Validation of viral inactivation

	Reduction log ₁₀
	(b)(4) Confidential and Proprietary Information
Treatments	
Spike recovery	
Disinfection step	
Total clearance	

	* Reduction log ₁₀
	(b)(4) Confidential and Proprietary Information
Treatments	
Spike recovery	
(b)(4) Confidential and Proprietary Information	
Total clearance	

Overall total clearance	(b)(4) Confidential and Proprietary Information
-------------------------	---

* Calculation of log reduction value = $[(C1 \times V1) / (C2 \times V2)]$, *C1, V1* initial viral concentration and volume, *C2, V2* postprocessing viral concentration and volume.

Collagen purity report

CMI-200912-11
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Report no:

CMI-200912-11

Study Title:

Analysis of purity of the porcine collagen

Test Article:

Non-crosslinked collagen sponge

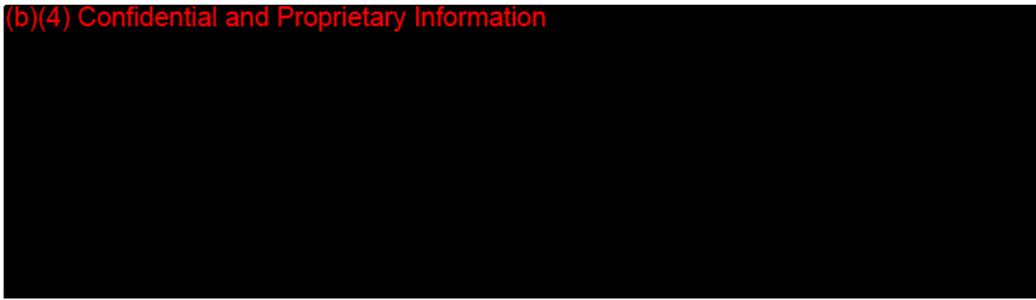
December, 2009

CMI-200912-11
Page no. 02/10

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

1. This report is valid for the test article (page 3) only.
2. This report could not be reprinted or adapted without the permission from (b)(4) Confidential and Proprietary Information and Collamatrix Inc.

Approved by

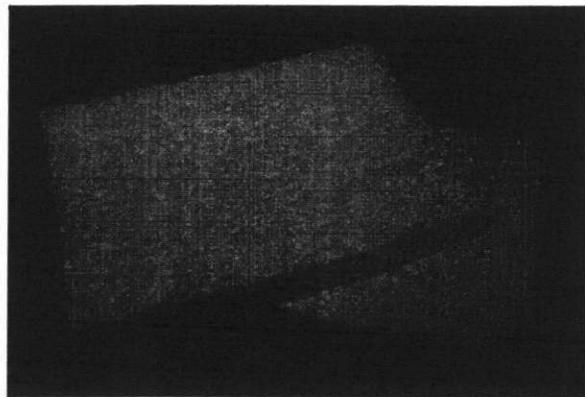
Date

Scott Shaw

2009. 12. 20

CMI-200912-11
Page no. 03/10

Information for Test Article

Name	Non-crosslinked collagen sponge
Package	-
External feature	Sponge-like
Color	White
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Note	-
Photo	

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SUMMARY

Purity of porcine collagen was determined by both amino acid analysis and SDS-PAGE.

Amino acid analysis showed that the amino acid composition of porcine collagen

contained about (b)(4) Confidential and Proprietary Information and trace amount (b)(4) Confide

(b)(4) Confidential of (b)(4) Confidential and Proprietary ; indicated no non-collageneous protein is found in the

collagen preparation. SDS-PAGE of the non-crosslinked collagen sponge revealed the

electrophoretic profile of porcine collagen comprising monomeric α forms, polymeric β

and γ forms. No other low molecular weight protein band was observed indicated the

integrity of porcine collagen was not compromised during the manufacturing process.

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INTRODUCTION

Collagen derived from porcine hides was purified and lyophilized into sponge configuration. Non-collagenous proteins found in the hides could contaminate and thus affect the purity of the collagen preparation. Collagen is inheritably unstable; the structural integrity of collagen could be compromised during the purification process. Therefore, amino acid analysis and SDS-PAGE were performed to determine the purity and to characterize of the integrity of collagen in the lyophilized sponges.

MATERIALS AND METHODS

Amino acid composition analysis

1. Dissolve 2g of the lyophilization collagen sponge in (b)(4) Confidential and Proprietary Information at (b)(4) Confidential and Proprietary Information
2. The acid-soluble fraction was separated by a (b)(4) Confidential and Proprietary and the amino acid composition of the collagen was analyzed by (b)(4) Confidential and Proprietary Information

Protein gel electrophoresis

1. Lyophilized collagen was prepared from (b)(4) Confidential and Proprietary solubilization, followed by precipitation and lyophilization. Three samples were used in this study.
2. Dissolve 1g of the lyophilization collagen sponge in (b)(4) Confidential and Proprietary Information with constant agitation for (b)(4) Confidential
3. Harvest the acid-soluble fraction and analyzed by SDS-polyacrylamide gel electrophoresis on an 8% SDS-gel.

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EVALUATION CRITERIA

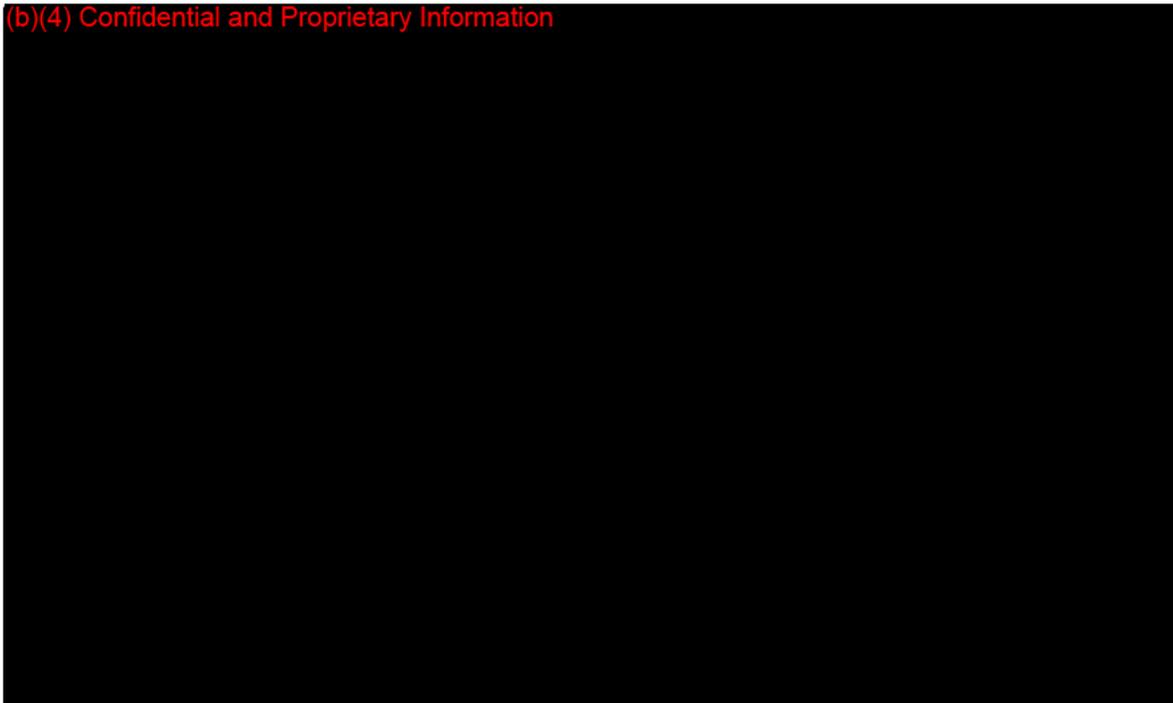
Requirements	Acceptance criteria
1. Amino acid composition	(b)(4) Confidential and Proprietary Information
2. Purity by SDS-PAGE	(b)(4) Confidential and Proprietary Information

RESULTS

Amino acid composition analysis

Amino acid composition analysis showed the residues of (b)(4) Confidential and Proprietary Information were (b)(4) Confidential and Proprietary (b)(4) Confidential and Proprietary (b)(4) Confidential and Proprietary. Trace amount of (b)(4) Confidential and Proprietary and (b)(4) Confidential and Proprietary were detected in the purified collagen. The elution profile of porcine collagen amino acid was shown in Figure 1 and its composition per 1000 residues was summarized in Table 1.

(b)(4) Confidential and Proprietary Information



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Table 1. Amino acid composition of collagen extracted from porcine hides.

Amino acid	Residues
(b)(4) Confidential and Proprietary Information	

Protein electrophoresis

Three lyophilized collagen sponge samples were analyzed by 8% SDS-PAGE (Figure 2). Type I collagen comprises two $\alpha 1$ monomers and one $\alpha 2$ monomer, which constitute a typical triple helical structure of collagen. Two protein bands corresponding to monomeric $\alpha 1$ and $\alpha 2$ with faster mobility rate were found (Figure 2, $\alpha 1$ and $\alpha 2$). Since the ratio of $\alpha 1$ and $\alpha 2$ was 2:1, the $\alpha 1$ band was more intense than the $\alpha 2$ band. Collagen molecules undergo both intra- and inter-molecular polymerization and resulted in high molecular weight structures. These polymeric structures are known as β and γ forms. These structures migrate slowly due to its sheer sizes as shown in Figure 2, β and γ .

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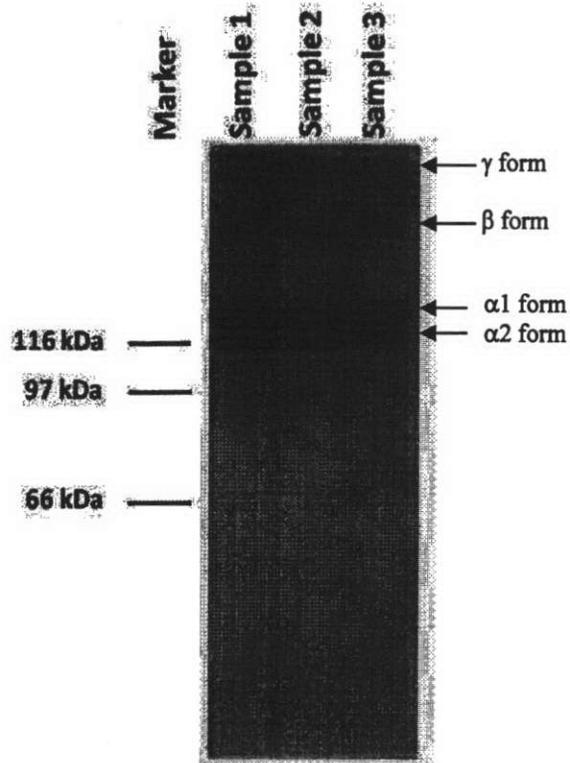


Figure 2 Analysis of lyophilized collagen by 8% SDS-PAGE. *Lanes 1 to 3* Collagen sponge obtained from three different samples.

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CONCLUSION

Result of amino acid analysis revealed the ratio of glycine, proline and hydroxyproline conformed to typical collagen composition. Trace amount of tyrosine and cysteine residues detected in porcine collagen preparation suggested that non-collagenous proteins were not present or at negligible level. In addition to amino acid analysis, SDS-PAGE of the lyophilized collagen sponges revealed the monomeric α forms, polymeric β and γ forms and no low molecular weight product was found indicated that no degradation was observed and the structural integrity of collagen molecules were preserved.

Colla Dental packaging report

COLLAMATRIX TAIWAN LTD.

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Prepared by Jasper Chan

COLLAMATRIX TAIWAN LTD.

Packaging Test Report	Date	20100715
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Objective

The objective of this test is to evaluate package integrity of CollaDental products. The packaging requirements must be able to (1) maintain intact sealing throughout the shelf life of the gamma ray sterilized products and (2) able to tolerate conditions such as shock or vibration, encountered during shipping and transportation.

Introduction

CollaDental products are single use collagen-based devices intended for dental surgery. In order to protect the dressing from potential contaminations, dressing is individually packaged in a PET blister pouch sealed with porous barrier lidding material and terminally sterilized by gamma-irradiation.

The porous barrier lidding material is composed of (b)(4) Confidential and Proprietary Information with thickness

about (b)(4) Confidential and Proprietary Information. The adhesive system used on the lidding material is (b)(4) Confidential and Proprietary Information.

(b)(4) Confidential and Proprietary Information The heat seal condition is (b)(4) Confidential and Proprietary Information.

The packaging and sealing requirement of CollaDental products are (b)(4) Confidential and Proprietary Information.

(b)(4) Confidential vacuum decay test time. The evaluation of packaging of CollaDental products is performed according to ASTM F 2338 - Standard Test Methods for Non-destructive Detection of Leaks in Packages by Vacuum Decay Method.

COLLAMATRIX TAIWAN LTD.

Packaging Test Report	Date	20100715
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Test products/samples**Test for packaging and seal integrity**

Items	Quantity	Remark
1. CollaDental Matrix	10 pieces	1 piece in one PET blister pouch
2. CollaDental Barrier	10 pieces	1 piece in one PET blister pouch
3. CollaDental Graft	10 pieces	0.5g/vial in one PET blister pouch

Test for package and seal integrity after gamma sterilization

Items	Quantity	Remark
1. CollaDental Matrix	20 pieces	1 piece in one PET blister pouch
2. CollaDental Barrier	20 pieces	1 piece in one PET blister pouch
3. CollaDental Graft	20 pieces	0.5g/vial in one PET blister pouch

Test for package and seal integrity after transportation simulation

Items	Quantity	Remark
1. CollaDental Matrix	20 pieces	1 piece in one PET blister pouch
2. CollaDental Barrier	20 pieces	1 piece in one PET blister pouch
3. CollaDental Graft	20 pieces	0.5g/vial in one PET blister pouch

Methods**Vacuum decay method**

ASTM F 2338 Standard Test Methods for Non-destructive Detection of Leaks in Packages by Vacuum Decay Method.

1. Install test chamber for package to be tested.
2. Make adjustments to ensure sufficiently tight seal of the upper lid and lower chamber package nest when the test chamber is in the closed position.
3. Check the vacuum pump.
4. Place the assembled package into the lower chamber package nest and close the test chamber.

5. Start the test, set the target vacuum of (b)(4) Confidential and P i t
Questions? Contact FDA/CDRH/OCE/DID S@fda.hhs.gov or call 301-796-8118.

COLLAMATRIX TAIWAN LTD.

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6. Note the pass or fail indicator and document the results.
7. Set aside fail package for further evaluation.
8. Select another package and repeat the test process.

Acceptance criteria

Each test result is valid only when the following conditions are satisfied simultaneously:

1. (b)(4) Confidential and Proprietary Information
2. [Redacted]
3. [Redacted]

Results

The result of leak detection of CollaDental package for different test conditions is summarized in Table 1 Trays with porous barrier lidding leak detection results, Table 2 Effect of gamma-irradiation on package leak detection and Table 3 Effect of shipping and transportation simulation on package leak detection respectively.

Table 1 Trays with porous barrier lidding leak detection results

Lidding material	Bonding adhesive	Package description	Package Qty	Replicate tests	FAILED	PASSED	Accuracy
ML ^a	C ^b	Sponge	10	20	0	20	100%
ML	C	Film	10	20	0	20	100%
ML	C	Particle	10	20	0	20	100%

(b)(4) Confidential and Proprietary Information

Table 2 Effect of gamma-irradiation on package leak detection

Lidding material	Bonding adhesive	Package description	Package Qty	Replicate tests	FAILED	PASSED	Accuracy
ML ^a	C ^b	Sponge	20	5	0	20	100%
ML	C	Film	20	5	0	20	100%
ML	C	Particle	20	5	0	20	100%

COLLAMATRIX TAIWAN LTD.

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Table 3 Effect of shipping and transportation simulation on package leak detection

Lidding material	Bonding adhesive	Package description	Package Qty	Replicate tests	FAILED	PASSED	Accuracy
ML ^a	C ^b	Sponge	20	5	0	20	100%
ML	C	Film	20	5	0	20	100%
ML	C	Particle	20	5	0	20	100%

Discussion

CollaDental contains three products, Matrix, Barrier and Graft which is individually housed in a PET blister pouch, sealed with porous barrier lidding material. Table 1, 2 and 3 summarize the results for packaging integrity of CollaDental after the packages were subject to (1) standard testing condition, (2) gamma-irradiation and (3) gamma-irradiation and shipping/transportation simulation respectively. Each product has passed the leak detection test using vacuum decay method. In conclusion, the packaging of CollaDental is intact and remains sealed under the test conditions according to ASTM standard F 2338.

Revised SIK summary

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. **Date Prepared**

March 3, 2010

2. **Submitter name and address**

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. **Contact person**

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. **Device names**

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. **Device classification**

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

6. **Device description**

CollaDental Barrier is a nonfriable, resorbable membrane made of purified type I collagen derived from pig skin using standardized controlled manufacturing process. The collagen is obtained from veterinary certified pigs and purified to avoid its antigenicity. CollaDental Barrier is sterilized by gamma irradiation and for single use only. It is flexible and

COLLAMATRIX Co. Ltd.

conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

CollaDental Barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

8. Statement of Substantial equivalence

CollaDental Barrier is a device similar to predicate devices that are previously approved by the agency. CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices, BioMend Extend absorbable collagen membrane (K992216) and BIO-GIDE® (K042197), each of which has been determined by FDA to be substantially equivalent to preamendment devices. CollaDental Barrier has the following similarities to the predicate devices in terms of indication for use, technological characteristics, material use and the process for sterilization. In summary, CollaDental Barrier is substantially equivalent to the predicate devices under the 510(k) regulations.

9. Biocompatibility

CollaDental Barrier has been demonstrated to be safe. To support the biocompatibility of this product, safety tests were conducted in accordance with ISO 10993 Part 1 Biological Evaluation of Medical Devices.

All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

10. Conclusion

COLLAMATRIX Co. Ltd.

CollaDental Barrier is essentially equivalent in indication for use, technological characteristics and material to the commercially available predicate device, and therefore meets the requirements as defined in 21 CFR § 807.

Revised Instruction for Use

CollaDental Barrier

Instruction For Use

COMPOSITION:

CollaDental Barrier is made of porcine type I collagen obtained by standardized, controlled manufacturing processes. The collagen is extracted from veterinary certified pigs and is carefully purified to avoid antigenic reactions. CollaDental Barrier is sterilized by γ -irradiation.

ACTION / PROPERTIES:

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone. CollaDental Barrier is resorbed within 18 weeks. It retains its structural integrity even when wet and be fixed by sutures or pins.

INDICATIONS:

CollaDental Barrier is indicated for:

- Augmentation around implants placed in immediate extraction sockets.
- Augmentation around implants placed in delayed extraction sockets.
- Alveolar ridge reconstruction for prosthetic treatment.
- Filling of bone defects after root resection, cystectomy, removal of retained teeth.
- Guided bone regeneration in dehiscence defects.
- Guided tissue regeneration procedures in periodontal defects.

Caution: Federal law restricts this device to sale by or on the order of a dentist

CollaDental Barrier has to be used in combination with space-making bone graft materials, e.g., autogenous bone or bone filler.

INSTRUCTIONS FOR USE:

The general principles of sterile handling and patient medication must be followed when using CollaDental Barrier:

- The bone defect is exposed by a mucoperiosteal flap and basic surgical**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOI@FDA.HHS.GOV or call 301-796-8118.

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procedures (e.g., curettage) are undertaken.

- The bone defect is filled with a space-making material, e.g., autogenous bone or bone filler. The defect should not be overfilled.
- The size of CollaDental Barrier is adapted by scissors according to the exposed defect. The membrane should overlap the walls of the defect by at least two millimeters to allow complete bone contact and to prevent gingival connective tissue invasion below the material.
- CollaDental Barrier is applied over the defect without further treatment and held in place with moderate pressure. The period of time necessary to apply pressure will vary with the degree of bleeding. Adherence to the bone surface is achieved by gel formation of the collagen fibres with blood.
- Complete penetration of the membrane by blood and exudate allows close adaptation and adhesion of the membrane to bony structures and makes the formation of a blood clot possible.
- Salivary and other contamination to the material and surgical site should be minimized to avoid bacterial contamination.
- Fixation may be indicated to avoid membrane displacement due to loading or mobilization.
- The mucoperiosteal flap is sutured over the collagen membrane (e.g., single sutures and deep mattress sutures).
- The wound should be closed completely to avoid accelerated resorption due to membrane exposure.

Special instructions for use in periodontology

- A basic requirement for successful periodontal treatment includes eradicating the underlying bacterial infection as well as adequate oral hygiene. Therefore, prior to surgical intervention, patients must receive a hygiene phase of treatment, consisting of oral hygiene instructions, scaling and root planning, and occlusal adjustment when indicated. A postoperative maintenance phase can help to ensure long-term therapeutic success.
- In order to avoid the formation of a long junctional epithelium, CollaDental Barrier must be adapted closely to the tooth (e.g. with additional fixation using suture material).

POST-OPERATIVE CARE:

- The patient should be monitored closely.
- If the membrane becomes exposed, the dehiscence usually heals by itself within several weeks. Membrane removal is usually not necessary. However, to

minimize bacterial contamination rinsing with bactericidal solutions are recommended.

- In the event that early membrane removal is necessary, the tissues adjacent to the membrane should be anesthetized with a local anesthetic. An incision should then be made immediately adjacent to the residual membrane. Following careful reflection of the surrounding tissue, the remaining portion of the membrane can be excised and the area curetted to remove any inflamed or infected tissue.
- To allow for undisturbed bone regeneration underneath the membrane surgical reentry should not be done before 4 to 6 months postoperatively.

LIMITATIONS FOR USE:

Contraindications Due to the adherence to the bone tissue and the elasticity of CollaDental Barrier, bone augmentation material is required to create and maintain space for bone formation. CollaDental Barrier is therefore not indicated for single use in guided bone regeneration (GBR) without any space-making material. CollaDental Barrier should not be placed where active infection exists. Before placement, the surgeon should be confident that any active or recent infection has been properly treated.

The material has not been tested on pregnant women.

This material has not been tested on patients with age < 18 years.

PRECAUTIONS:

1. The content of the double blister is designed for single use only. Do not re-sterilize CollaDental Barrier.
2. In case of membrane exposure during the healing phase the resorption time may be accelerated.
3. If endosseous implants are involved, the membrane should be used only in combination with a stable implant and not in lieu of achieving primary implant stability.
4. Absolute stability of the membrane is important for guided bone regeneration and is a vital condition for therapeutic success, and that the smallest movement on the tissue underneath is to be avoided. Use of bone tacks or sutures to immobilize membranes around dental implants.

ADVERSE REACTIONS:

Adverse reactions after the use of CollaDental Barrier have not been observed. Since CollaDental Barrier is a collagen product allergic reactions may not be totally

excluded. However, the following potential side effects may be noticed due to the surgical intervention; dehiscence, hematoma, pain, increased sensitivity and pain, redness, and inflammation.

STORAGE AND HANDLING:

1. Do not use after expiry date.
2. Store at dry clean place.
3. The membrane should be handled using sterile gloves or sterile instruments. The membrane is sterile unless the package has been opened, damaged, or otherwise contaminated.

PRESENTATION: CollaDental Barrier is packed in sterile blister.

Revised

color box 1521

COLLADENTAL Barrier

PRECAUTIONS

1. This device is for single use only. Discard all unused and opened portions of CollaDental Barrier.
2. Device is sterile if the package is dry, undamaged and unopened. Do not use if the package seal is broken or damaged.

STORAGE

1. This device should be stored at dry clean place.
2. Avoid direct sunlight and heat.
3. Keep out of reach of children.

For additional information, please see enclosed instructions for use.

Manufactured by

Collamatrix Inc.

No.50-1; Keyan Road, Jhunan Science Park

Miaoli County, 350, Taiwan

Tel: +886 2 7711 3699

www.collamatrix.com

STERILE R



Tensile strength test report

COLLAMATRIX

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Conclusion.....	2

Prepared by Jasper Chen

COLLAMATRIX

Tensile strength Report	Date	20100720
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Objective

The objective of this test is to determine the tensile strength of CollaDental Barrier.

Introduction

CollaDental Barrier is a resorbable barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. CollaDental Barrier is crosslinked and takes about eighteen weeks to fully resorb. A tensile test is employed to test the strength of CollaDental Barrier.

Samples

Samples	Dimension	Quantity
1. CollaDental Barrier sample -1	10 x 4 mm	3 pieces
2. BIO-GIDE® resorbable bilayer membrane	10 x 4 mm	3 pieces
3. BioMend Extend collagen membrane	10 x 4 mm	3 pieces

Method

Tensile Machine: Universal test machine

Each measurement was made in triplicate.

Conditioning/Pretreatment: (b)(4) minimum at (b)(4) Confidential and Proprietary Information

Temperature and Humidity: (b)(4) Confidential and Proprietary Information

Crosshead Speed: (b)(4) Confidential

Evaluation: The sample was stretched to failure

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Results

The results of maximum breaking force of CollaDental Barrier comparing to its predicates, BioGide and BioMend, are summarized in Table1.

Table 1 Tensile strength of three collagen membranes.

Samples	Tensile strength (Mpa)
1. CollaDental Barrier	(b)(4) Confidential and Proprietary Information
2. BIO-GIDE® membrane	
3. BioMend Extend membrane	

Conclusion

CollaDental Barrier samples exhibit tensile strength equivalent to BioGIDE membrane and BioMend Extend membrane.

CIP cleaning validation report

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

	Cleaning validation report	Date	20070610
Prep by	Quality Assurance	Page	1/2

1 Summary

This document is intended to present the results of an automated procedure Clean-In-Place (CIP) cleaning procedure for equipments used in the manufacture of collagen-based products. Sampling is conducted by (b)(4) Confidential and Proprietary Information. The effectiveness of CIP cleaning is analysed based on the removal of contaminants associated with previous products, residues of cleaning agents as well as the control of potential microbial contaminants.

2 Results

(a) Three (3) consecutive applications of the cleaning procedure were performed and shown to be successful in order to prove that the method is validated.

(b) 1 hour interval between the end of production and the beginning of the cleaning procedures; cleaning procedures was used.

(c) Environment temperature: (b)(4) Confidential

(d) Relative humidity: (b)(4) Confidential and

(e) Data

	Test 1	Test 2	Test 3	Acceptance criteria	Pass/Fail
Bioburden	(b)(4) Confidential and Proprietary Information				
pH					
Total protein					

膠原科技股份有限公司
COLLAMATRIX TAIWAN LTD.

Cleaning validation report		Date	20070610
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3 Conclusions

(a) No deviation in term of operation protocols, environment controls and personnel were observed during CIP cleaning process.

(b) Based on the data collected, the assessment of the CIP cleaning process meets the requirement stated in the acceptance criteria and therefore validated.

4 Annex

4.1 Bioburden data

4.2 pH data

4.3 Total protein

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: Bioburden

Product:

1. Lot number:

原料/樣品檢驗

巡迴檢驗

成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	原	Scott
2. Direct plate out method	<input type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted	合	Scott
	<input type="checkbox"/> _____ dilution		
4. Perform filtration per SOP	OK	合	Scott
5. Perform direct plate out per SOP			
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE	合	Scott
7. [] Incubate at 35°C±2°C (48 hrs) for bacteria	<input checked="" type="checkbox"/> TSA		
8. [] Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input type="checkbox"/> PDA		
	<input type="checkbox"/> YM broth		
	<input type="checkbox"/> Other: _____		
	<input checked="" type="checkbox"/> 35°C±2°C		
	<input type="checkbox"/> 23°C±3°C (RT)		
9. Check number of colony forming unit (CFU):	<input type="checkbox"/> Not detected	合	Scott
	<input checked="" type="checkbox"/> < 150 cfu		
	<input type="checkbox"/> 150-250 cfu		
	<input type="checkbox"/> TNTC		
10. Determine total viable count: CFU/mL CFU/g	(b)(4) Confidential and Proprietary Information	合	Scott
	_____ CFU/g		
11. Comments	pass	合	Scott
(b)(4) Confidential and Proprietary Information			

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: Bioburden

Product: *CTP*

1. Lot number: */*

原料/樣品檢驗

巡迴檢驗

成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	<i>合</i>	<i>Scott</i>
2. Direct plate out method	<input checked="" type="checkbox"/> Plate out	<i>合</i>	<i>Scott</i>
3. Dilution fold	<input checked="" type="checkbox"/> undiluted <input type="checkbox"/> _____ dilution	<i>合</i>	<i>Scott</i>
4. Perform filtration per SOP	<i>OK</i>	<i>合</i>	<i>Scott</i>
5. Perform direct plate out per SOP		<i>合</i>	<i>Scott</i>
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE <input checked="" type="checkbox"/> TSA <input type="checkbox"/> PDA <input type="checkbox"/> YM broth <input type="checkbox"/> Other: _____	<i>合</i>	<i>Scott</i>
7. [] Incubate at 35°C±2°C (48 hrs) for bacteria	<input checked="" type="checkbox"/> 35°C±2°C		
8. [] Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input type="checkbox"/> 23°C±3°C (RT)		
9. Check number of colony forming unit (CFU):	<input type="checkbox"/> Not detected <input checked="" type="checkbox"/> <150 cfu <input type="checkbox"/> 150-250 cfu <input type="checkbox"/> TNTC	<i>合</i>	<i>Scott</i>
10. Determine total viable count : CFU/mL CFU/g	(b)(4) Confidential and Proprietary Information _____ CFU/g	<i>合</i>	<i>Scott</i>
11. Comments	<i>pass</i>	<i>合</i>	<i>Scott</i>

(b)(4) Confidential and Proprietary Information

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膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: Bioburden

Product: *CIP*

1. Lot number: */* 原料/樣品檢驗 巡迴檢驗 成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	<i>余</i>	<i>Scott</i>
2. Direct plate out method	<input checked="" type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted <input type="checkbox"/> _____ dilution	<i>余</i>	<i>Scott</i>
4. Perform filtration per SOP	<i>OK</i>		
5. Perform direct plate out per SOP		<i>余</i>	<i>Scott</i>
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE <input checked="" type="checkbox"/> TSA <input type="checkbox"/> PDA <input type="checkbox"/> YM broth <input type="checkbox"/> Other: _____	<i>余</i>	<i>Scott</i>
7. [] Incubate at 35°C±2°C (48 hrs) for bacteria	<input checked="" type="checkbox"/> 35°C±2°C		
8. [] Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input type="checkbox"/> 23°C±3°C (RT)		
9. Check number of colony forming unit (CFU):	<input type="checkbox"/> Not detected <input checked="" type="checkbox"/> < 150 cfu <input type="checkbox"/> 150-250 cfu <input type="checkbox"/> TNTC	<i>余</i>	<i>Scott</i>
10. Determine total viable count: CFU/mL CFU/g	(b)(4) Confidential and Proprietary Information _____ CFU/g	<i>余</i>	<i>Scott</i>
11. Comments	<i>pass</i>	<i>余</i>	<i>Scott</i>

(b)(4) Confidential and Proprietary Information

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: pH

C2P

1. Lot number: /

巡迴檢驗

成品檢驗

樣品

Reagent and Standard Preparation	Parameters	Operator	Verifier
Samples= 20ml = 30ml	30ml	Seah	Scott
Check sample's temperature (Note: Equilibrate sample at room temperature prior to measurement)	26 °C	Seah	Scott
Calibration standards	Tick:		
1. pH 4.0	[] pH 4.0		Scott
2. pH 7.0	[✓] pH 7.0	Seah	
3. pH 9.0	[✓] pH 9.0		
Wash probe with deionized water	OK	Seah	Scott
Insert probe into sample. Submerge the probe to cover the "white opening"	OK	Seah	Scott
Wait until [√A] stop blinking	OK	Seah	Scott
Rinse probe with deionized water and blot with tissue paper	OK	Seah	Scott
Insert probe into container with KCl solution	OK	Seah	Scott
Conclusions: <div style="background-color: black; color: red; padding: 2px;">(b)(4) Confidential and Proprietary Information</div>	pass	Seah	Scott

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: pH

Ccp

1. Lot number: /

巡迴檢驗

成品檢驗

樣品

Reagent and Standard Preparation	Parameters	Operator	Verifier
Samples= 20ml ~ 30ml	30ml	Seah	Scott
Check sample's temperature <small>(Note: Equilibrate sample at room temperature prior to measurement)</small>	26 °C	Seah	Scott
Calibration standards	Tick:		
1. pH 4.0	[] pH 4.0		
2. pH 7.0	[✓] pH 7.0	Seah	Scott
3. pH 9.0	[✓] pH 9.0		
Wash probe with deionized water	OK	Seah	Scott
Insert probe into sample. Submerge the probe to cover the "white opening".	OK	Seah	Scott
Wait until [√A] stop blinking	OK	Seah	Scott
Rinse probe with deionized water and blot with tissue paper	OK	Seah	Scott
Insert probe into container with KCl solution	OK	Seah	Scott
Conclusions:	pass	Seah	Scott

(b)(4) Confidential and Proprietary Information

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: pH

C2P

1. Lot number:

巡迴檢驗
 成品檢驗
 樣品

Reagent and Standard Preparation	Parameters	Operator	Verifier
Samples= 20ml - 30ml	30	Seal	Scott
Check sample's temperature <small>(Note: Equilibrate sample at room temperature prior to measurement)</small>	25 °C	Seal	Scott
Calibration standards 1. pH 4.0 2. pH 7.0 3. pH 9.0	Tick: [] pH 4.0 [✓] pH 7.0 [✓] pH 9.0	Seal	Scott
Wash probe with deionized water	ok	Seal	Scott
Insert probe into sample. Submerge the probe to cover the "white opening"	ok	Seal	Scott
Wait until \sqrt{A} stop blinking	ok	Seal	Scott
Rinse probe with deionized water and blot with tissue paper	ok	Seal	Scott
Insert probe into container with KCl solution	ok	Seal	Scott
Conclusions: <div style="background-color: black; color: red; padding: 2px; display: inline-block;">(b)(4) Confidential and Proprietary Information</div>	pass	Seal	Scott

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: Protein assay

Product: *CIP validation*

1. Lot number: */*

巡迴檢驗

成品檢驗

Reagent and Standard Preparation	Results	Operator	Verifier
Dilute Internal Reference according to the table. Use new tip for every dilution. Vortex between each dilution	<i>OK</i>	<i>Seah</i>	<i>Scott</i>
Working reagent needed for duplicate = mL	Σ : <i>10.0</i> ml	<i>Seah</i>	<i>Scott</i>
Reagent A = mL Reagent B = mL	A: <i>10</i> ml B: <i>0.2</i> ml		
Switch ON the spectrophotometer; Set λ to 562 nm	λ : <i>562</i> nm	<i>Seah</i>	<i>Scott</i>
Add 50 μ L of unknown and standards to each tube	Temp: <i>60</i> °C		
Mix Reagent B to reagent A thoroughly. Add 1 mL of the working reagent to each tube carefully	Time: <i>30</i> min	<i>Seah</i>	<i>Scott</i>
Incubate samples at 60°C water bath for 30 min	<i>OK</i>	<i>Seah</i>	<i>Scott</i>
Calibrate and zero spectrophotometer with cuvette filled with pure water as blank in duplicates.	<i>OK</i>	<i>Seah</i>	<i>Scott</i>
Measure the absorbance of all the samples within 10 min Write down all the readings clearly and precisely	<i>OK</i>	<i>Seah</i>	<i>Scott</i>
Subtract the readings from the blank. Plot a curve using blank-corrected 562 nm measurements of the internal reference in mg/mL	Blank @ 562nm: <i>0.163 0.167</i>	<i>Seah</i>	<i>Scott</i>
Determine the linear equation using standards and compute protein concentration of the unknown samples	<i>OK</i>	<i>Seah</i>	<i>Scott</i>
Attach a spreadsheet that contains: (1) absorbance of standards and unknown samples [<i>✓</i>] (3) Curve, equation and parameters derived from the standards [<i>✓</i>] (4) Deduce protein concentration of each unknown [<i>✓</i>]	<i>Ref to attachment</i>	<i>Seah</i>	<i>Scott</i>
(b)(4) Confidential and Proprietary Information	<i>Pass</i>	<i>Seah</i>	<i>Scott</i>

Statement

Assurance Statement

I assure, in my capacity as Manager of Quality Assurance of Collamatrix Inc.,

- (1) That the equipment used to process the porcine materials used in your products is dedicated only to the processing of porcine materials;
- (2) That the equipment used to process the porcine materials used in your products has never been used to process bovine materials;
- (3) That the equipment used to process the porcine materials used in your will never be used to process bovine materials between processing lots of porcine materials for this product.

SZAH JUNZ NAM

(Typed Name)

2010. 8. 31

(Dated)

Food and Drug Administration

K100695 / A2

Center for Devices and Radiological Health

Document Mail Center WO66-G609

10903 New Hampshire Avenue

FDA CDRH DMC

Silver Spring, MD 20993-0002

NOV 3 2010

November 01, 2010

Received K40

Re: Information for CollaDental Barrier (K100695)

Dear Dr. Betz,

Please find enclosed information required for the application of CollaDental Barrier.

1. You provided cell attachment and proliferation testing in Supplement 001 to support claims that your membranes promote cellular attachment and proliferation. The testing supplied demonstrates that some (b)(4) Confidential and [REDACTED] will stick to your membranes better than on a glass cover slide. This testing does not address cell attachment and proliferation in human subjects. Please remove this claim or provide more substantive evidence to support your claim.

Answer: The “promote cellular attachment and proliferation” claim has been removed. Please refer to Page 5-1 of attachment 1 entitled “Revised CollaDental Barrier 510(K)”.

2. Your supplement contains a revised 510(k) Summary that still does not conform to 21 CFR 807.92. Your Summary did not discuss the technology behind the use of barrier membranes or information about purity and viral testing. You can state that your products have been tested for purity using standard purity testing procedures. Likewise, you can state that your product sterilization procedures have been tested to assure that viruses affecting porcine materials have been killed. Unless you believe that identifying the test viruses used in your sterilization testing constitutes confidential information, you can, but do not have to include this information in your 510(k) Summary. Please submit a revised 510(k) Summary that addresses these concerns.

Answer: 510(k) Summary has been revised accordingly. Please refer to attachment 2 entitled “Revised 510(k) Summary”.

3. Your supplement contains information about your device packaging and its testing. However, it does not identify a shelf life for your membranes. Please identify a shelf life for your devices. Please submit revised device labeling that includes a shelf life statement.

Answer: Labeling information has been revised accordingly. Please refer to attachment 3 entitled "Revised IFU".

4. The device package label submitted in your supplement contains symbols that are not recognized by the FDA Office of Device Evaluation. 21 CFR 801.15(c)(1) states that labeling in English. Please revise your packaging labels to include English explanations of symbols.

Answer: Labeling information with english explanations of symbols has been revised accordingly. Please refer to attachments 4.1 and 4.2 entitled "Revised Pouch label" and "Revised Color box label", respectively.

Thank you.

Sincerely yours,



Dennis Seah

Attachment 1 Revised CollaDental Barrier 510(K) content

5 Product Description

Description

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. Such a method of preventing epithelial migration into a specific area is known as guided tissue regeneration (GTR).

CollaDental barrier is a resorbable membrane made of type I collagen derived from pig. It is glutaraldehyde crosslinked and takes about eighteen weeks to fully resorb. It can inhibit migration of epithelial cells and is not antigenic.

CollaDental Barrier is a white to off white, nonfriable, conformable, resorbable, membrane consisting of primarily purified type I collagen derived from porcine dermis. CollaDental Barrier is (b)(4) (b)(4) (Figure 1). The average pore size is (b)(4) (Figure 2). Device appears white to off white in dry state and translucent and non-slippery when wet. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the material is flexible and conforms to the contours of the defect site.

Degradation of CollaDental Barrier was evaluated in rat subcutaneous implantation. As shown in Figure 3, the membrane remained stable for (b)(4), was fully absorbed in (b)(4) Confidential and Proprietary Information (Attachment 5.1). CollaDental Barrier is an odorless, hydrophilic product. It is water insoluble but lightly soluble in hot water and completely soluble in either acidic solution ($\text{pH} \leq 3$) or basic solution ($\text{pH} \geq 10$).

Attachment 2 Revised 510(k) Summary

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. Date Prepared

March 3, 2010

2. Submitter name and address

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. Contact person

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. Device names

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. Device classification

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

6. Device description

CollaDental Barrier is a nonfriable, resorbable membrane made of purified type I collagen derived from pig skin using standardized controlled manufacturing process. The collagen is obtained from veterinary certified pigs and purified to avoid its antigenicity. The manufacturing process complies with the standards for virus inactivation. The CollaDental

COLLAMATRIX Co. Ltd.

Barrier has been tested for purity using standard purity testing procedures, sterilized by gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

CollaDental Barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

8. Statement of Substantial equivalence

CollaDental Barrier is a device similar to predicate devices that are previously approved by the agency. CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices, BioMend Extend absorbable collagen membrane (K992216) and BIO-GIDE® (K042197), each of which has been determined by FDA to be substantially equivalent to preamendment devices. CollaDental Barrier has the following similarities to the predicate devices in terms of indication for use, technological characteristics, material use and the process for sterilization. In summary, CollaDental Barrier is substantially equivalent to the predicate devices under the 510(k) regulations.

9. Biocompatibility

CollaDental Barrier has been demonstrated to be safe. To support the biocompatibility of this product, safety tests were conducted in accordance with ISO 10993 Part 1 Biological Evaluation of Medical Devices.

All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

COLLAMATRIX Co. Ltd.

10. Conclusion

CollaDental Barrier is essentially equivalent in indication for use, technological characteristics and material to the commercially available predicate device, and therefore meets the requirements as defined in 21 CFR § 807.

Attachment 3 Revised IFU

CollaDental Barrier

Instruction For Use

COMPOSITION:

CollaDental Barrier is made of porcine type I collagen obtained by standardized, controlled manufacturing processes. The collagen is extracted from veterinary certified pigs and is carefully purified to avoid antigenic reactions. CollaDental Barrier is sterilized by γ -irradiation.

ACTION/PROPERTIES:

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone. CollaDental Barrier is resorbed within 18 weeks. It retains its structural integrity even when wet and be fixed by sutures or pins.

INDICATIONS:

CollaDental Barrier is indicated for:

- Augmentation around implants placed in immediate extraction sockets.
- Augmentation around implants placed in delayed extraction sockets.
- Alveolar ridge reconstruction for prosthetic treatment.
- Filling of bone defects after root resection, cystectomy, removal of retained teeth.
- Guided bone regeneration in dehiscence defects.
- Guided tissue regeneration procedures in periodontal defects.

CAUTION: Federal law restricts this device to sale by or on the order of a dentist or physician.

CollaDental Barrier has to be used in combination with space-making bone graft materials, e.g., autogenous bone or bone filler.

INSTRUCTIONS FOR USE:

The general principles of sterile handling and patient medication must be followed when using CollaDental Barrier:

- The bone defect is exposed by a mucoperiosteal flap and basic surgical

procedures (e.g., curettage) are undertaken.

- The bone defect is filled with a space-making material, e.g., autogenous bone or bone filler. The defect should not be overfilled.
- The size of CollaDental Barrier is adapted by scissors according to the exposed defect. The membrane should overlap the walls of the defect by at least two millimeters to allow complete bone contact and to prevent gingival connective tissue invasion below the material.
- CollaDental Barrier is applied over the defect without further treatment and held in place with moderate pressure. The period of time necessary to apply pressure will vary with the degree of bleeding. Adherence to the bone surface is achieved by gel formation of the collagen fibres with blood.
- Complete penetration of the membrane by blood and exudate allows close adaptation and adhesion of the membrane to bony structures and makes the formation of a blood clot possible.
- Salivary and other contamination to the material and surgical site should be minimized to avoid bacterial contamination.
- Fixation may be indicated to avoid membrane displacement due to loading or mobilization.
- The mucoperiosteal flap is sutured over the collagen membrane (e.g., single sutures and deep mattress sutures).
- The wound should be closed completely to avoid accelerated resorption due to membrane exposure.

SPECIAL INSTRUCTIONS FOR USE IN PERIODONTOLOGY:

- A basic requirement for successful periodontal treatment includes eradicating the underlying bacterial infection as well as adequate oral hygiene. Therefore, prior to surgical intervention, patients must receive a hygiene phase of treatment, consisting of oral hygiene instructions, scaling and root planning, and occlusal adjustment when indicated. A postoperative maintenance phase can help to ensure long-term therapeutic success.
- In order to avoid the formation of a long junctional epithelium, CollaDental Barrier must be adapted closely to the tooth (e.g. with additional fixation using suture material).

POST-OPERATIVE CARE:

- The patient should be monitored closely.
- If the membrane becomes exposed, the dehiscence usually heals by itself within several weeks. Membrane removal is usually not necessary. However, to

minimize bacterial contamination rinsing with bactericidal solutions are recommended.

- In the event that early membrane removal is necessary, the tissues adjacent to the membrane should be anesthetized with a local anesthetic. An incision should then be made immediately adjacent to the residual membrane. Following careful reflection of the surrounding tissue, the remaining portion of the membrane can be excised and the area curetted to remove any inflamed or infected tissue.
- To allow for undisturbed bone regeneration underneath the membrane surgical reentry should not be done before 4 to 6 months postoperatively.

LIMITATIONS FOR USE:

Contraindications Due to the adherence to the bone tissue and the elasticity of CollaDental Barrier, bone augmentation material is required to create and maintain space for bone formation. CollaDental Barrier is therefore not indicated for single use in guided bone regeneration (GBR) without any space-making material. CollaDental Barrier should not be placed where active infection exists. Before placement, the surgeon should be confident that any active or recent infection has been properly treated.

CollaDental Barrier has not been tested on pregnant women.

CollaDental Barrier has not been tested on patients with age < 18 years.

PRECAUTIONS:

1. The content of the double blister is designed for single use only. Do not re-sterilize CollaDental Barrier.
2. In case of membrane exposure during the healing phase the resorption time may be accelerated.
3. If endosseous implants are involved, the membrane should be used only in combination with a stable implant and not in lieu of achieving primary implant stability.
4. Absolute stability of the membrane is important for guided bone regeneration and is a vital condition for therapeutic success, and that the smallest movement on the tissue underneath is to be avoided. Use of bone tacks or sutures to immobilize membranes around dental implants.

ADVERSE REACTIONS:

Adverse reactions after the use of CollaDental Barrier have not been observed. Since CollaDental Barrier is a collagen product allergic reactions may not be totally

excluded. However, the following potential side effects may be noticed due to the surgical intervention; dehiscence, hematoma, pain, increased sensitivity and pain, redness, and inflammation.

STORAGE AND HANDLING:

1. CollaDental Membrane has a recommended shelf-life of 3 years.
2. Do not use after expiry date.
3. Store at dry clean place.
4. The membrane should be handled using sterile gloves or sterile instruments. The membrane is sterile unless the package has been opened, damaged, or otherwise contaminated.

PRESENTATION: CollaDental Barrier is packed in sterile blister.

Attachment 4.1 Revised Pouch label

COLLADENTAL Barrier

PRECAUTIONS

1. This device is for single use only. Discard all unused and opened portions of CollaDental Barrier.
2. Device is sterile if the package is dry, undamaged and unopened. Do not use if the package seal is broken or damaged.

STORAGE

1. This device should be stored at dry clean place.
2. Avoid direct sunlight and heat.
3. Keep out of reach of children.

For additional information, please see enclosed instructions for use.

Manufactured by
Collamatrix Inc.
No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan
Tel: +886 2 7711 3699
www.collamatrix.com



Recycle symbol



Sterilized by γ -irradiation



Keep dry



Do not reuse

Attachment 4.2 Revised Color box label

COLLADental Barrier

Catalog number: CD011

Do not reuse/resterilize.

Do not use if individual package is damaged/opened.

LOT :

EXP :

Collamatrix Inc.

1F, No.50-1, Keyan Road, Jhunan Science Park

Miaoli County, 350, Taiwan



Sterilized by γ -irradiation



Consults instruction for use



Keep dry



Do not reuse



Incomplete Response

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name

Robert S. Betz MD

Subject: 510(k) Number

K100695/S1

To: The Record

Convert 5001 to A001

Please list CTS decision code

Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPreMarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

Hold (Additional Information or Telephone Hold).

Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Reset review clock

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	Attach IFU		
510(k) Summary /510(k) Statement	Attach Summary		
Truthful and Accurate Statement.	Must be present for a Final Decision		
Is the device Class III?			
If yes, does firm include Class III Summary?	Must be present for a Final Decision		
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)			
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPreMarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC)			
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			
Is this device intended for pediatric use only?			
Is this a prescription device? (If both prescription & OTC, check both boxes.)			
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			
Is clinical data necessary to support the review of this 510(k)?			
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If not, then applicant must be contacted to obtain completed form.)			
Does this device include an Animal Tissue Source?			
All Pediatric Patients age <=21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days -< 2 years old)			
Child (2 years -< 12 years old)			
Adolescent (12 years -< 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)

Nanotechnology

Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, <http://www.fda.gov/cdrh/comp/guidance/169.html>) *Contact OC.*

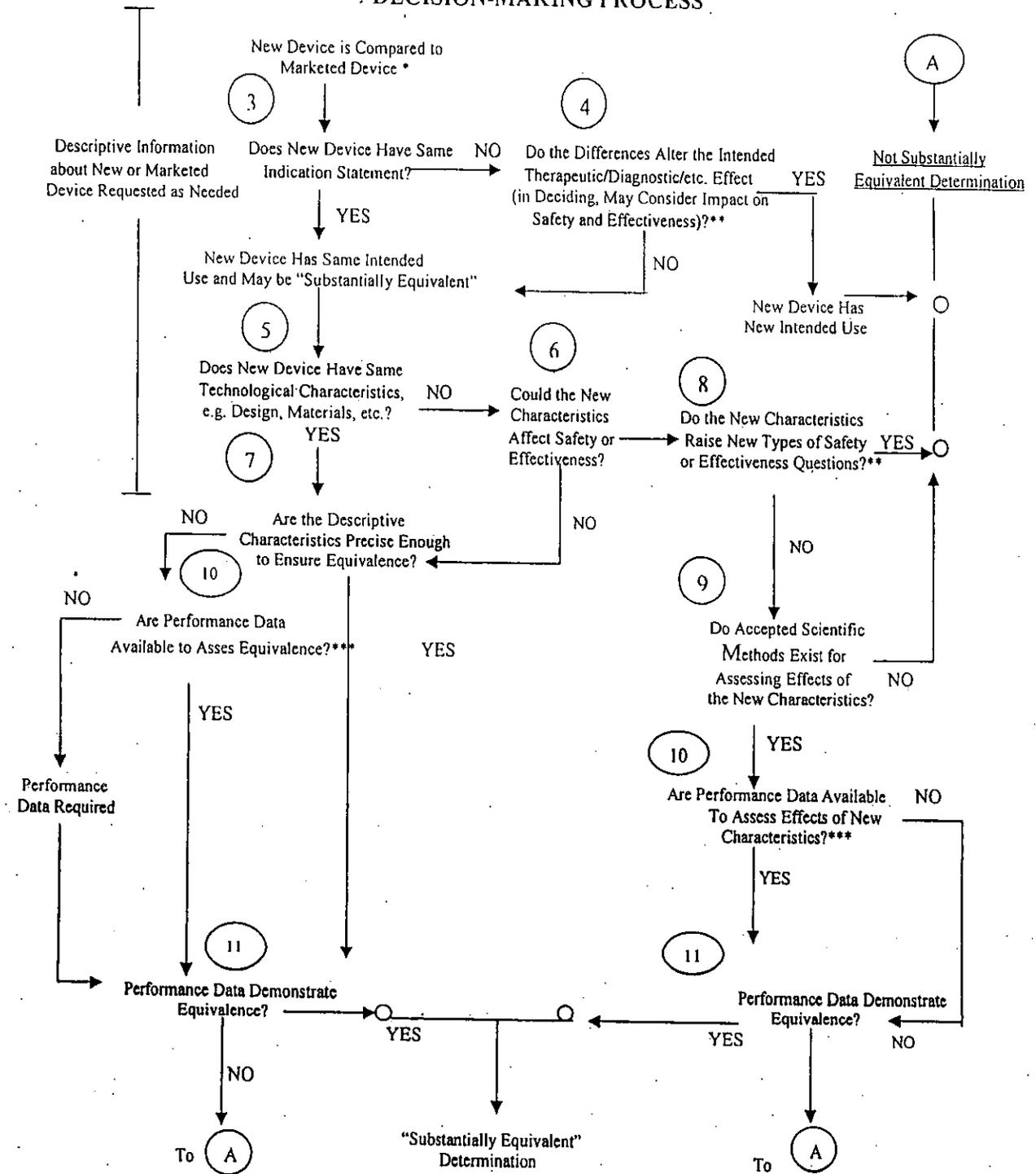
Regulation Number	Class*	Product Code
-------------------	--------	--------------

Additional Product Codes: _____ (*If unclassified, see 510(k) Staff)

Review: _____
(Branch Chief) (Branch Code) (Date)

Final Review: _____
(Division Director) (Date)

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



❖ 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 maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

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



DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
Traditional/Abbreviated

K100695/S001

Date: October 12, 2010
To: The Record
From: Robert S. Betz, D.D.S.

Office: ODE
Division: DAGID
Branch: DEDB

Device Name: CollaDental Barrier
510(k) Holder: Collamatrix, Inc.
Contact: Dennis J. N. Seah

Phone: 886-277-113299
Fax: 886-277-113599
E-mail: jnseah@collamatrix.com

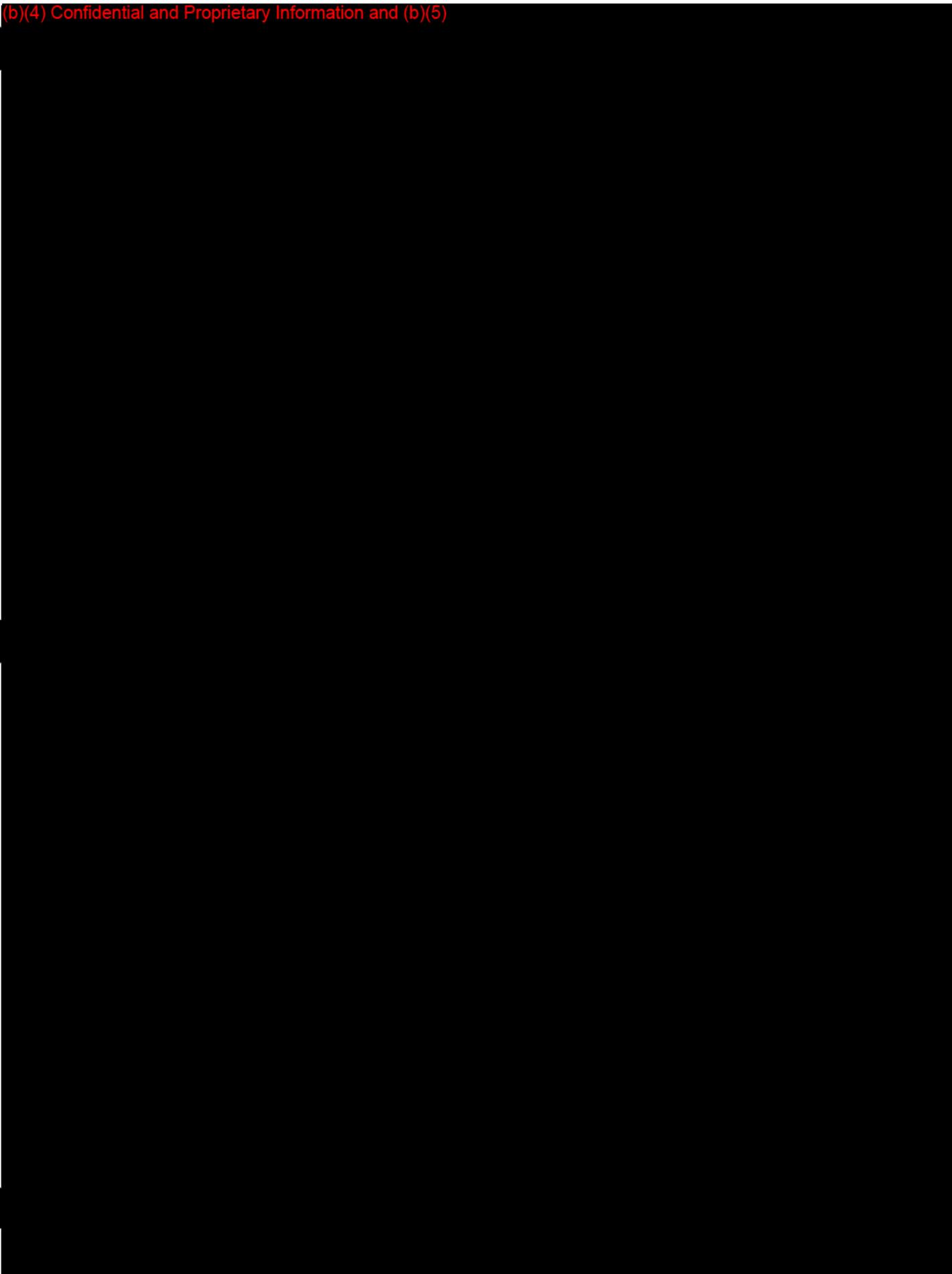
- I. Purpose and Submission Summary - This product is a collagen dental barrier material. Barrier membranes are Class II devices that have a Product Code of NPL. They are accessories to dental bone grafting materials which are described in 21 CFR 872.3930. Substantial equivalence is claimed to Integra Life Science's BioMend Extend (K992216), and BioGide (K042197). Conformance is claimed to:
1. ISO 11137 (Sterilization - Radiation),
2. ISO 10993 (Biological Evaluation of Medical Devices) Part 3 - Genotoxicity, carcinogenicity and reproductive toxicity.
3. ISO 10993 (Biological Evaluation of Medical Devices) Part 4 - Interaction with blood.
4. ISO 10993 (Biological Evaluation of Medical Devices) Part 5 - Cytotoxicity.
5. ISO 10993 (Biological Evaluation of Medical Devices) Part 10 - Irritation and sensitization.
6. ISO 10993 (Biological Evaluation of Medical Devices) Part 11 - Systemic toxicity.
7. ISO 2338 Package integrity using vacuum decay method.
8. USP 71 - Sterility test
9. USP 85 - Bacterial endotoxin testing

II. Administrative Requirements

Table with 4 columns: Requirement, Yes, No, N/A. Rows include: Indications for Use page (Indicate if: Prescription or OTC), Truthful and Accuracy Statement, 510(k) Summary or 510(k) Statement, Standards Forms.

(b)(4) Confidential and Proprietary Information and (b)(5)

(b)(4) Confidential and Proprietary Information and (b)(5)

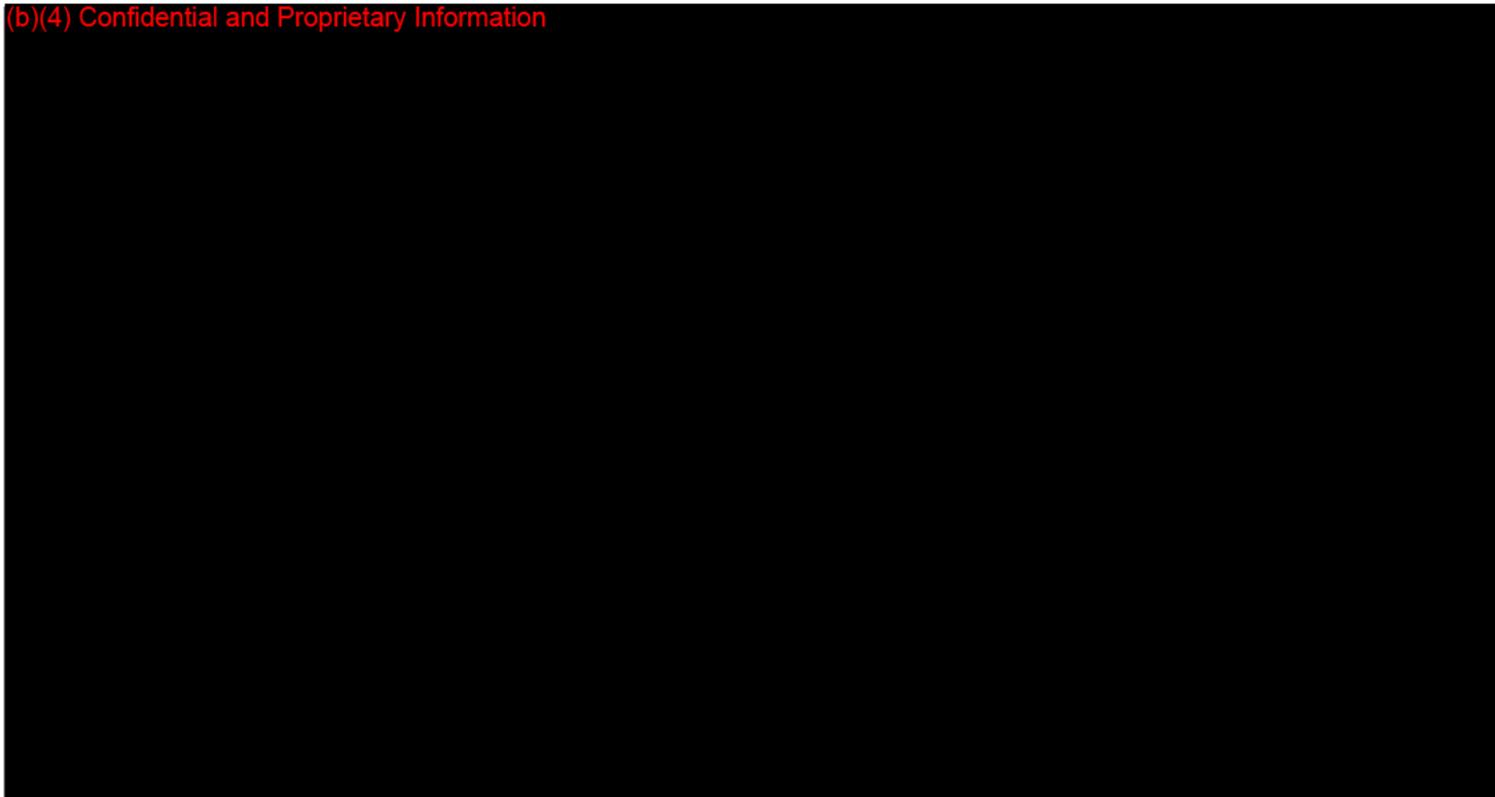


- V. **510(k) Summary/Statement** – The sponsor should submit either the 510(k) Statement or the 510(k) Summary but not both documents. The table below contains elements of these documents as described in 21 CFR 807.92 and .93.

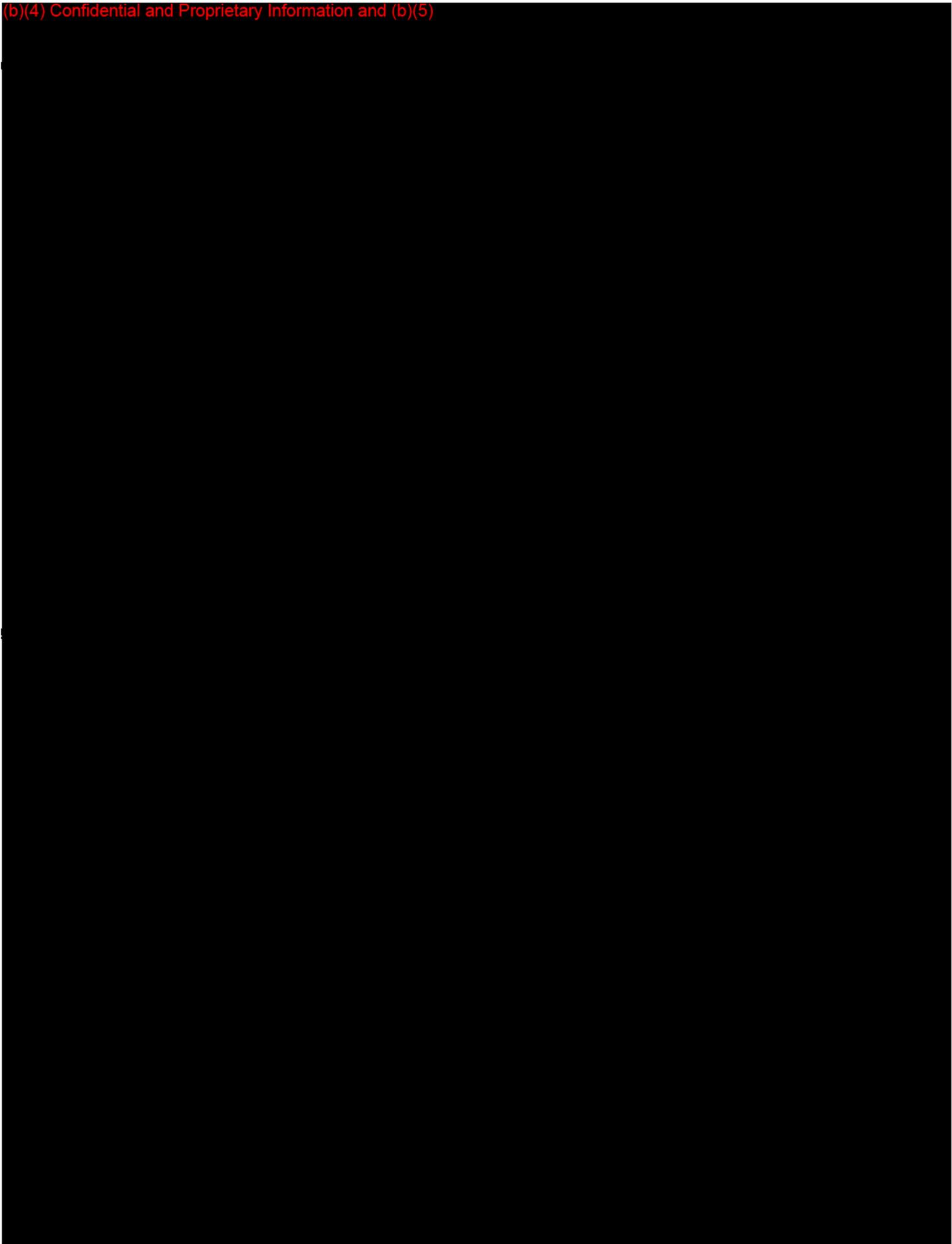
	YES	NO	N/A
510(k) Summary labeled as a 510(k) Summary	X		
Submitter's name, address, phone number, and contact person	X		
Date the summary was prepared	X		
The name of the device/trade name/common name/classification name	X		
An identification of the legally marketed Predicate	X		
Description of the subject device including functions, scientific concepts on which the device is based, physical and performance characteristics including design and material composition		X	
Statement of intended use, disease/condition, use population, if intended use not same as predicate, why differences are not critical and do not affect safety and effectiveness when used as labeled.		X	
Summary of technological characteristics and if different from those of predicate, how characteristics compare to those of predicate		X	
If performance data is submitted; description of nonclinical and clinical test data used to support SE decision. For clinical data, adverse events and complications observed relevant to SE decision.	X		
Conclusions drawn from clinical and nonclinical data indicating that the new device is safe and effective for its intended use and performs as well or better than predicate device.	X		
The 510(k) Summary is on a separate section of the document on a separate page not shares with any other section of 510(k)	X		
Any other information reasonably deemed necessary by the agency			X

The device description is incomplete and use population were not described.

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(b)(4) Confidential and Proprietary Information and (b)(5)



(b) (4)

IX. **Software, Electromagnetic Compatibility, and Electrical, Mechanical and Thermal Safety – (b) (4)**

X. **Performance Testing – Bench – (b)(4)**

XI. **Performance Testing – Animal, Clinical – (b)(4)**

XII. **Predicate Device Comparison and Substantial Equivalence Discussion – (b)(4)**

[Redacted]

(b)(4)

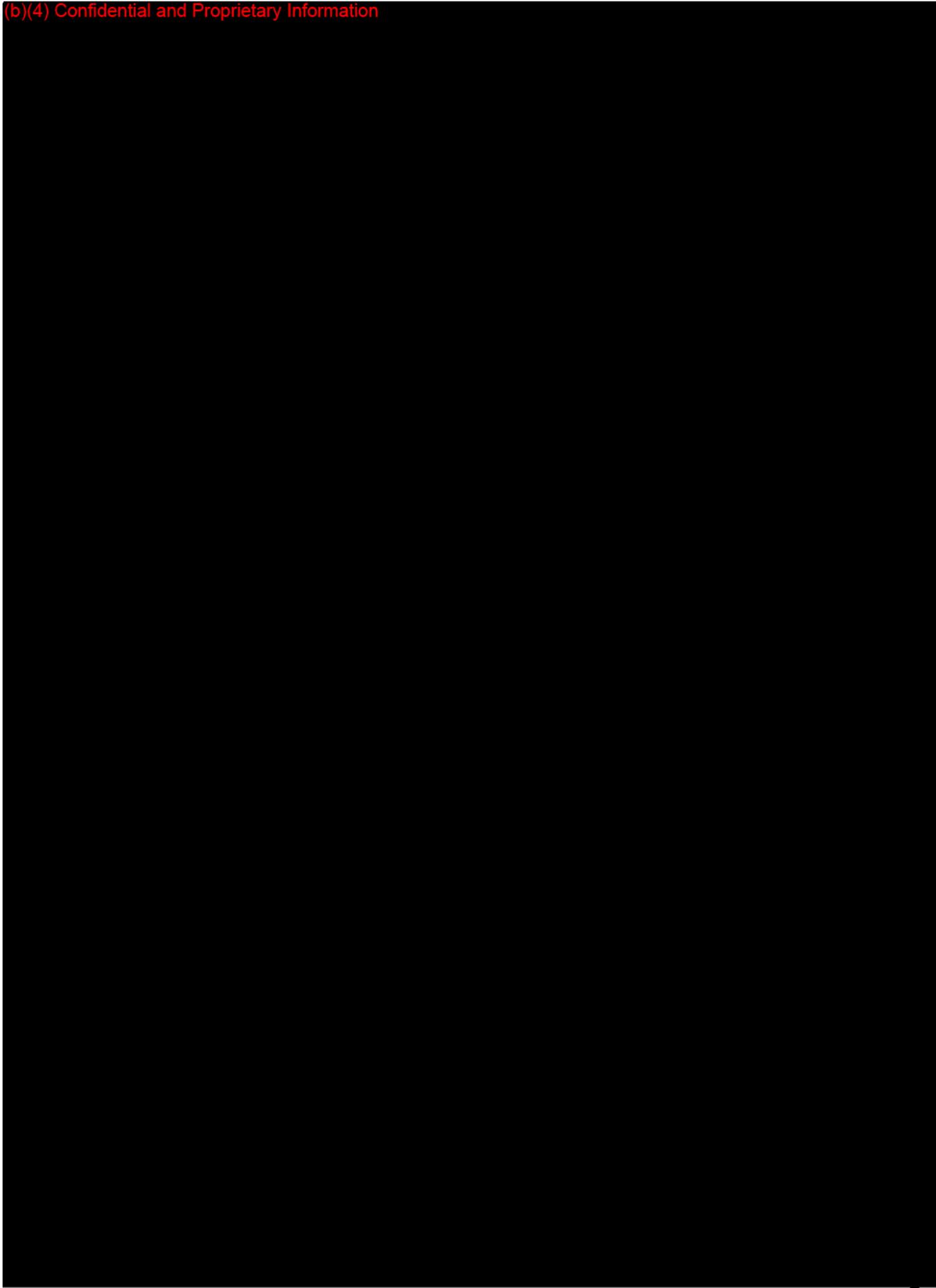
	Yes	No
1. Same Indication Statement?	X	If YES = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?		If YES = Stop NSE
3. Same Technological Characteristics?	*	If YES = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?	?	If YES = Go To 6
5. Descriptive Characteristics Precise Enough?	*	If NO = Go To 8 If YES = Stop SE
6. New Types Of Safety Or Effectiveness Questions?	*	If YES = Stop NSE
7. Accepted Scientific Methods Exist?	X	If NO = Stop NSE
8. Performance Data Available?	*	If NO = Request Data
9. Data Demonstrate Equivalence?	*	Final Decision:

* Deficiencies noted - have been sent to the sponsor.

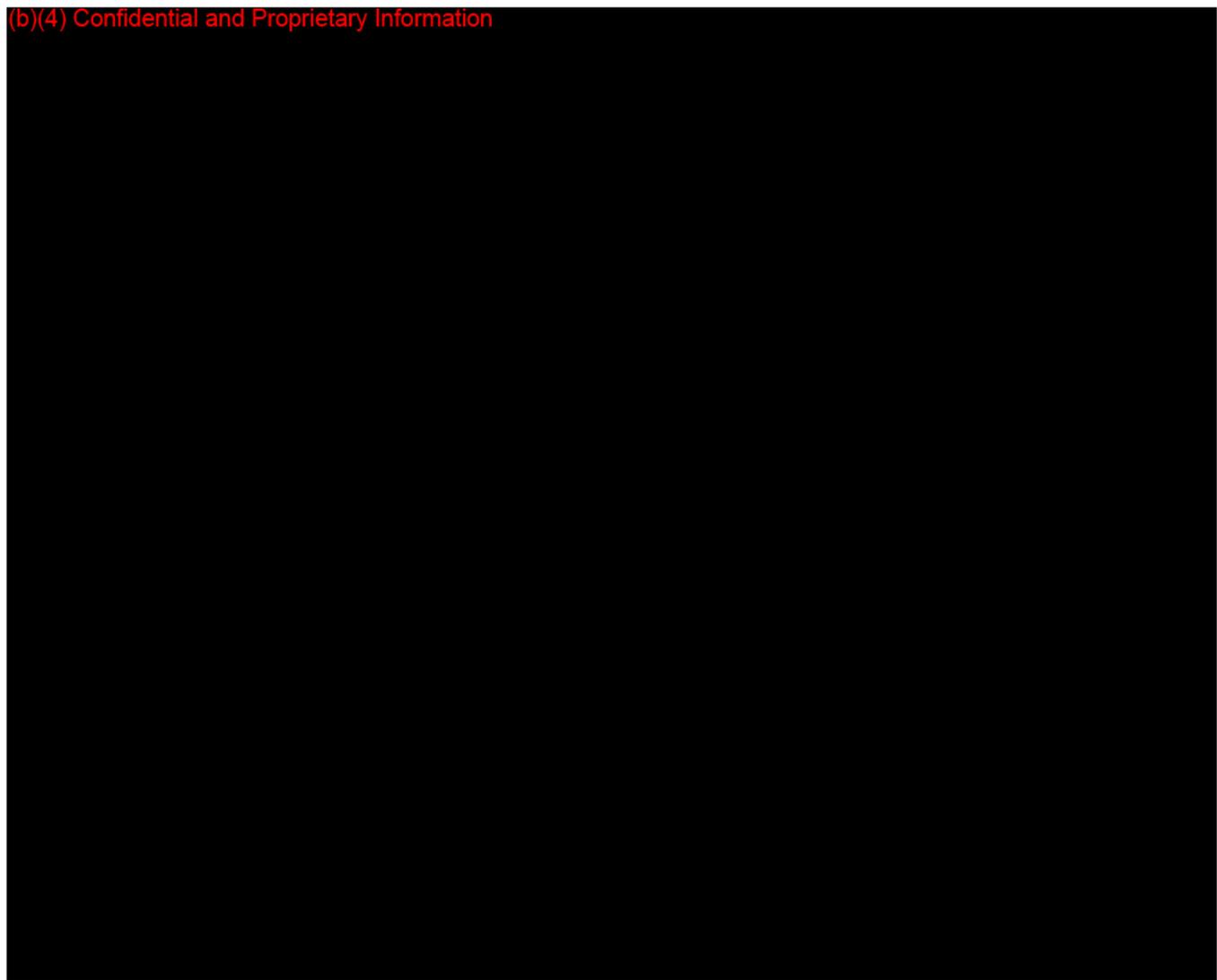
XIII. **Deficiencies (b)(4)**

64

(b)(4) Confidential and Proprietary Information

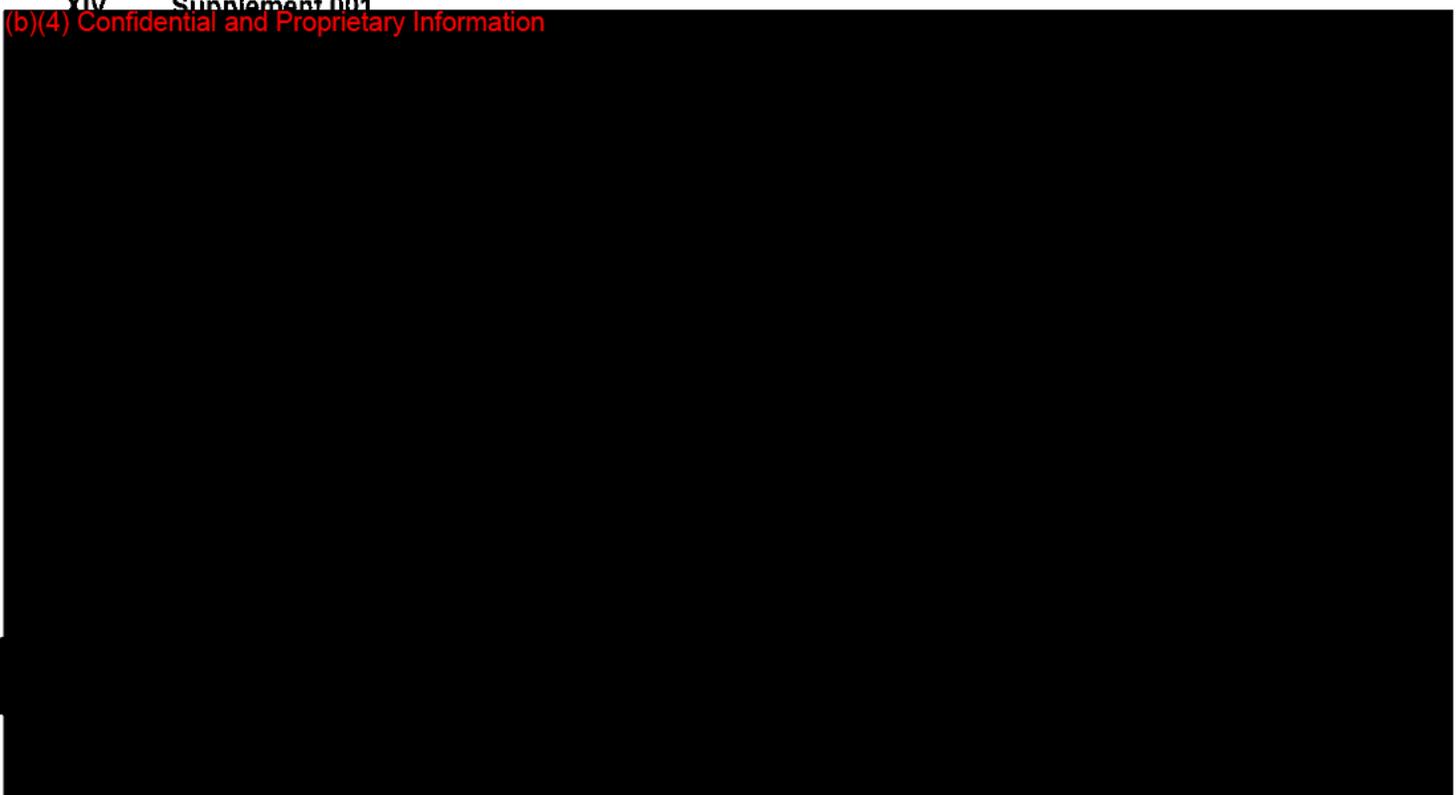


(b)(4) Confidential and Proprietary Information

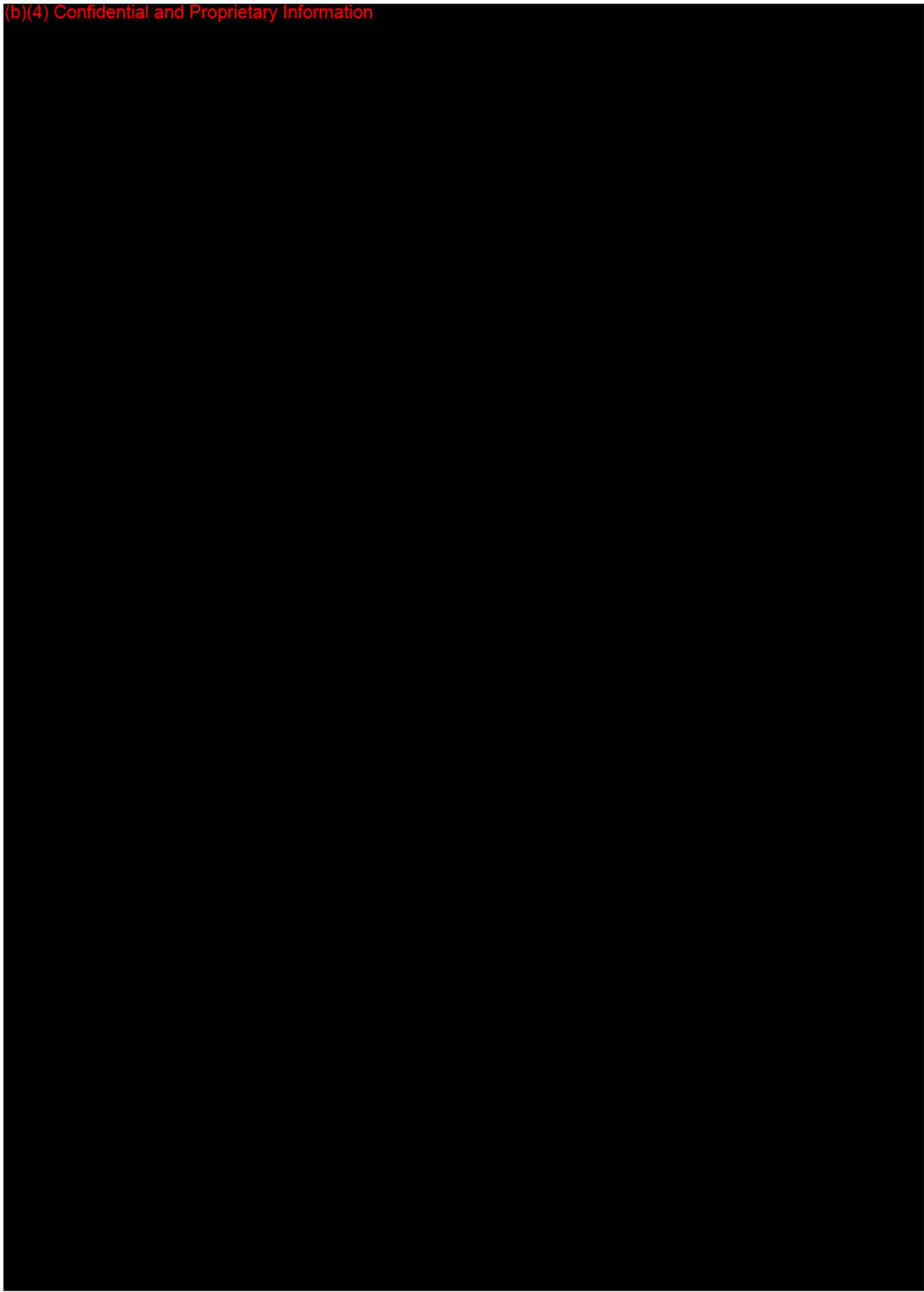


XIV Supplement 001

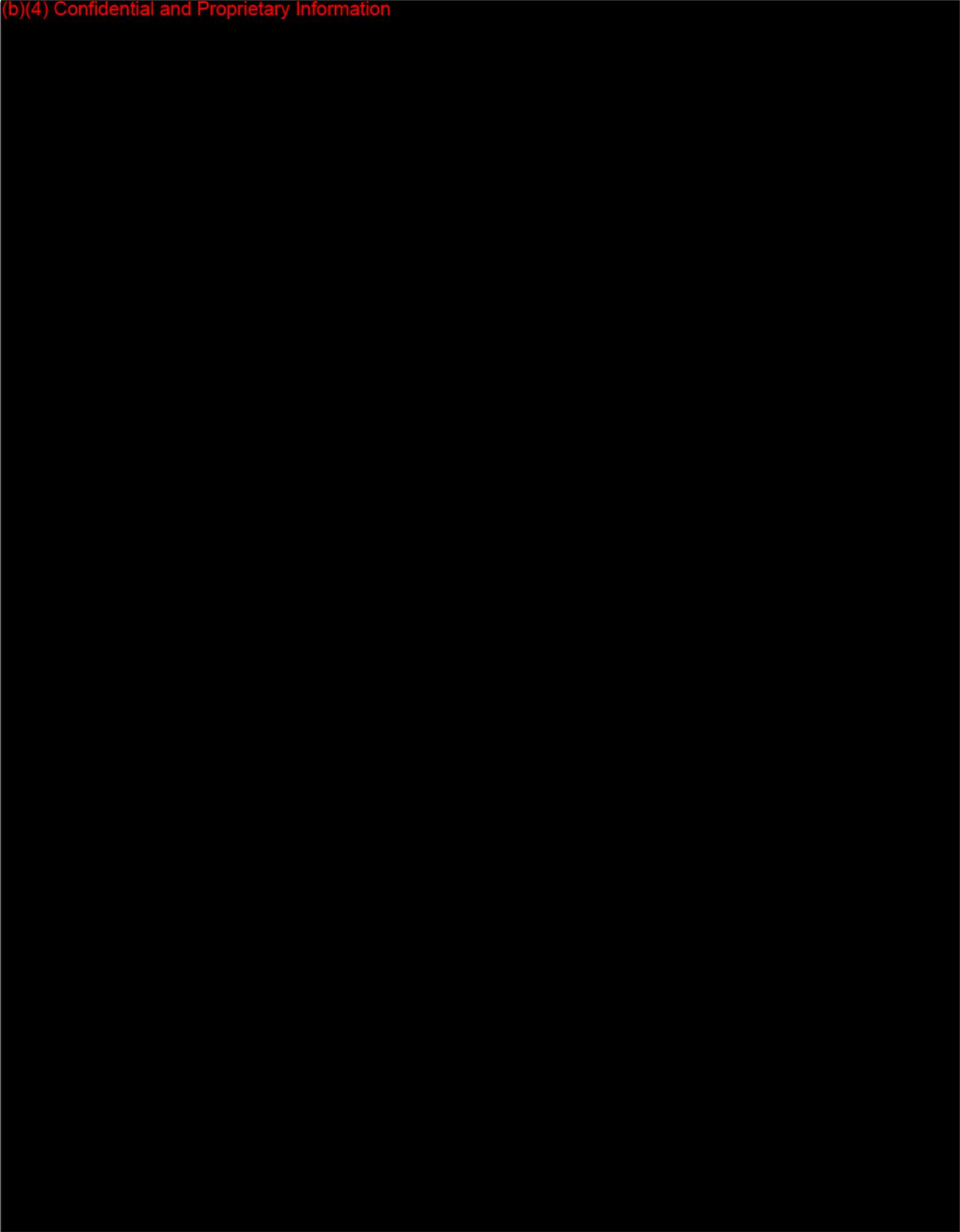
(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



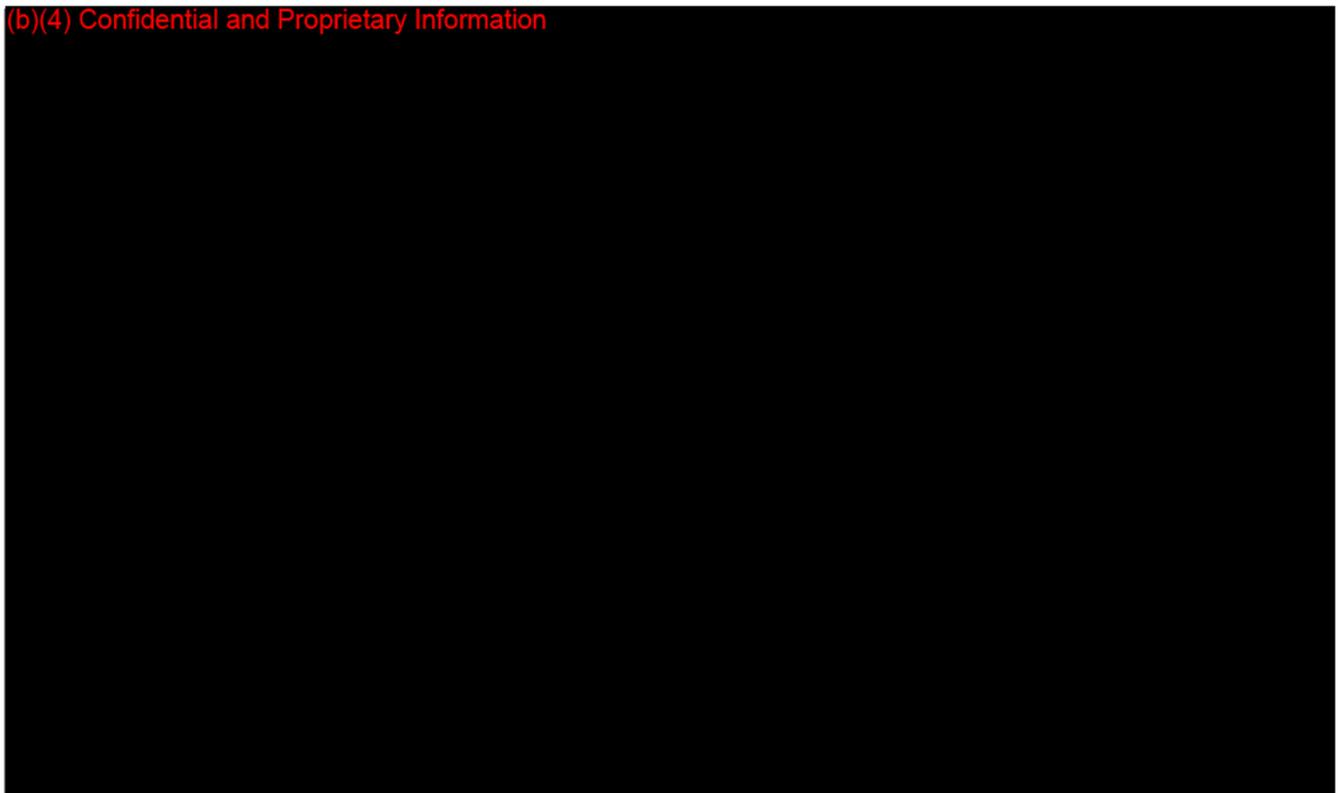
(b)(4) Confidential and Proprietary Information



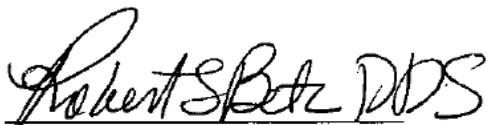
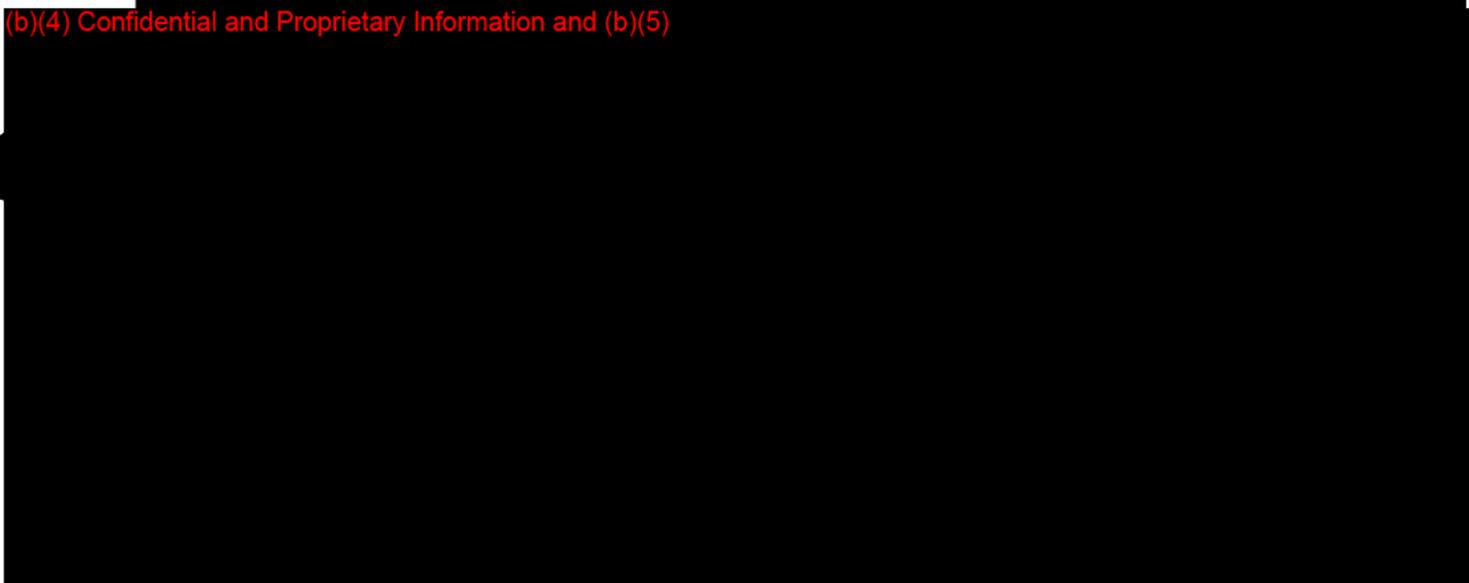
XV. **Deficiencies in Supplement 001**

(b)(4)

(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information and (b)(5)



Robert S. Betz, DDS
DAGID/DEDB

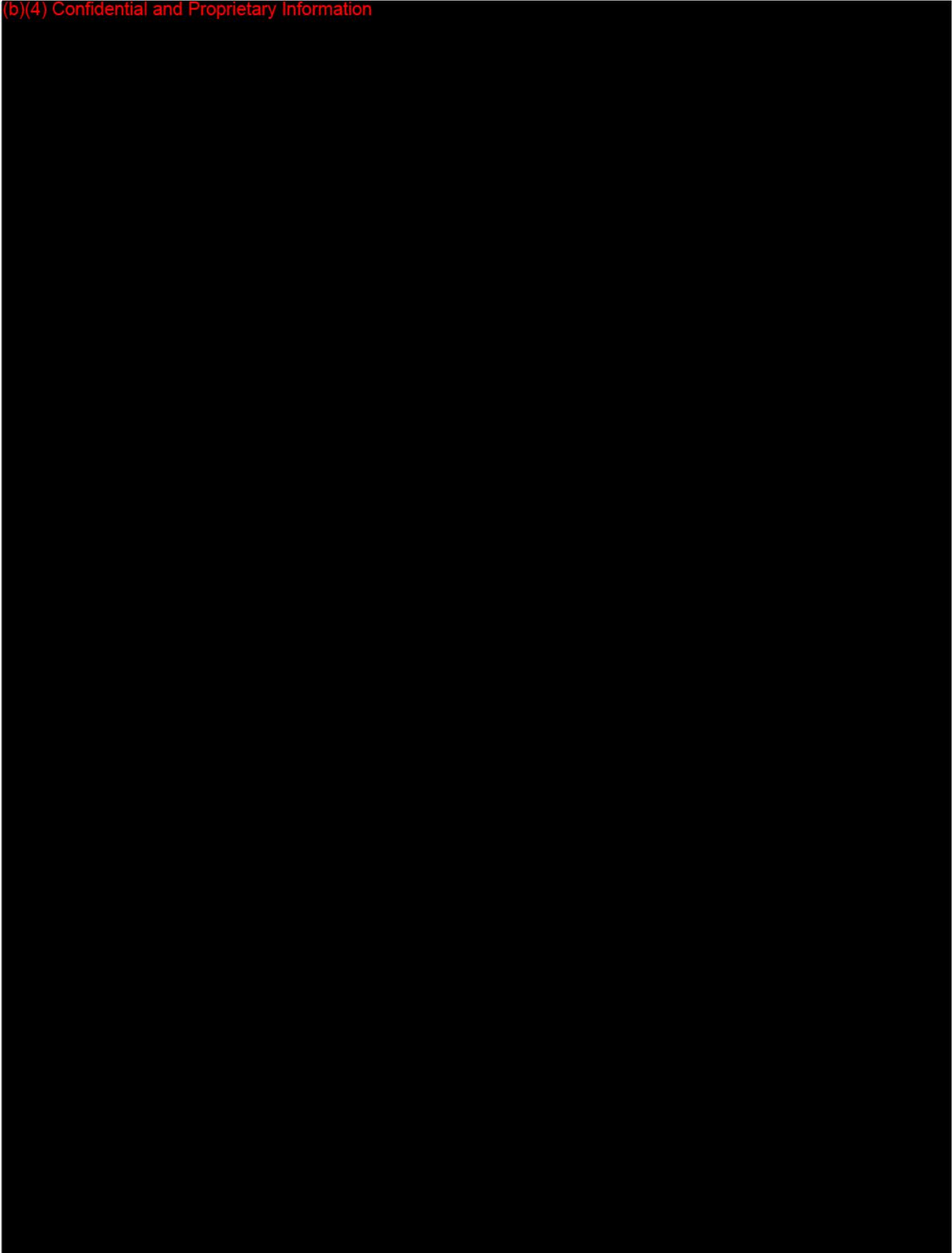
October 12, 2010

Dr. Susan Runner, Branch Chief
DAGID/DEDB

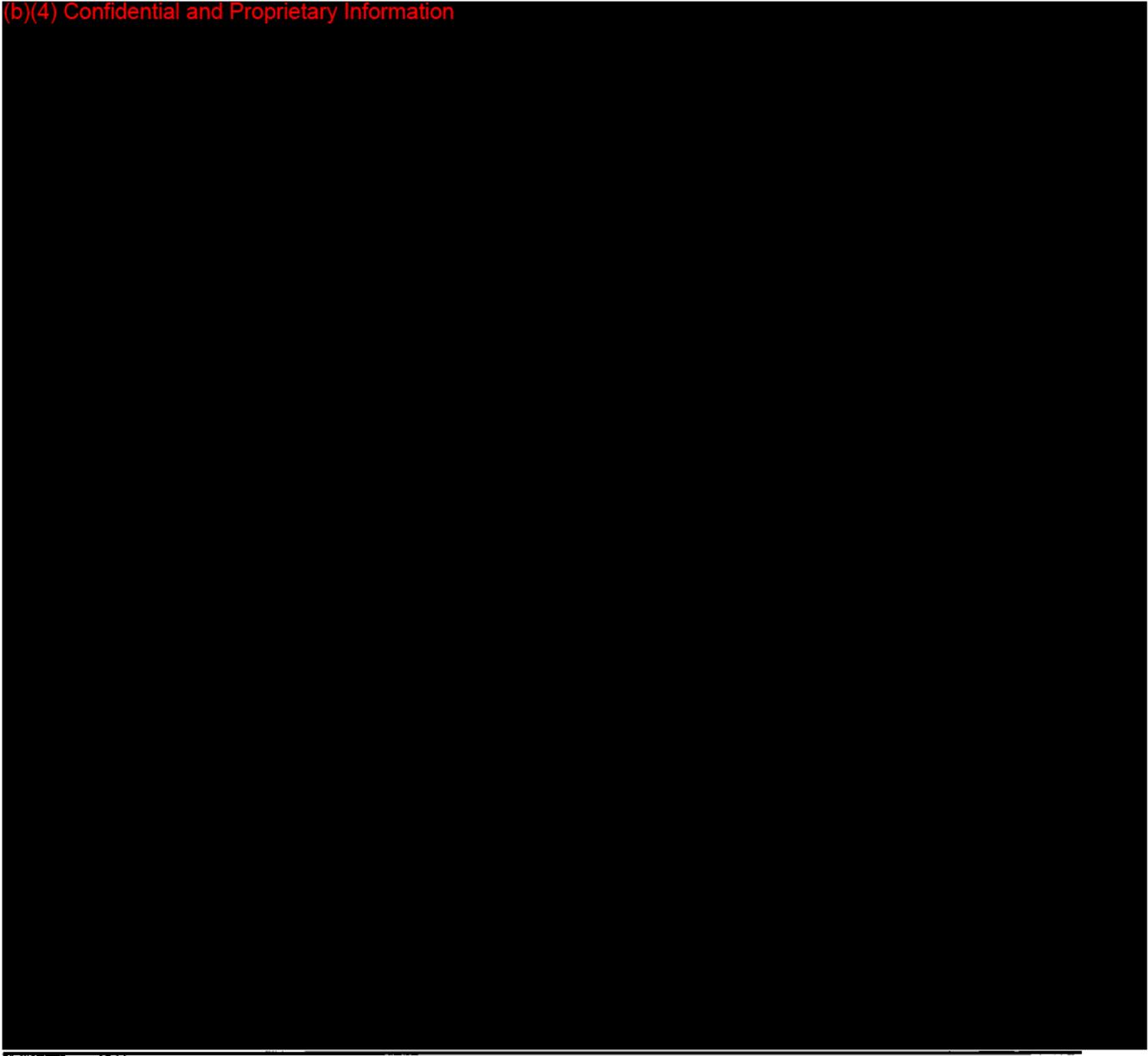
Date

[Text of E-Mail to Sponsor on June 4, 2010]

(b)(4) Confidential and Proprietary Information

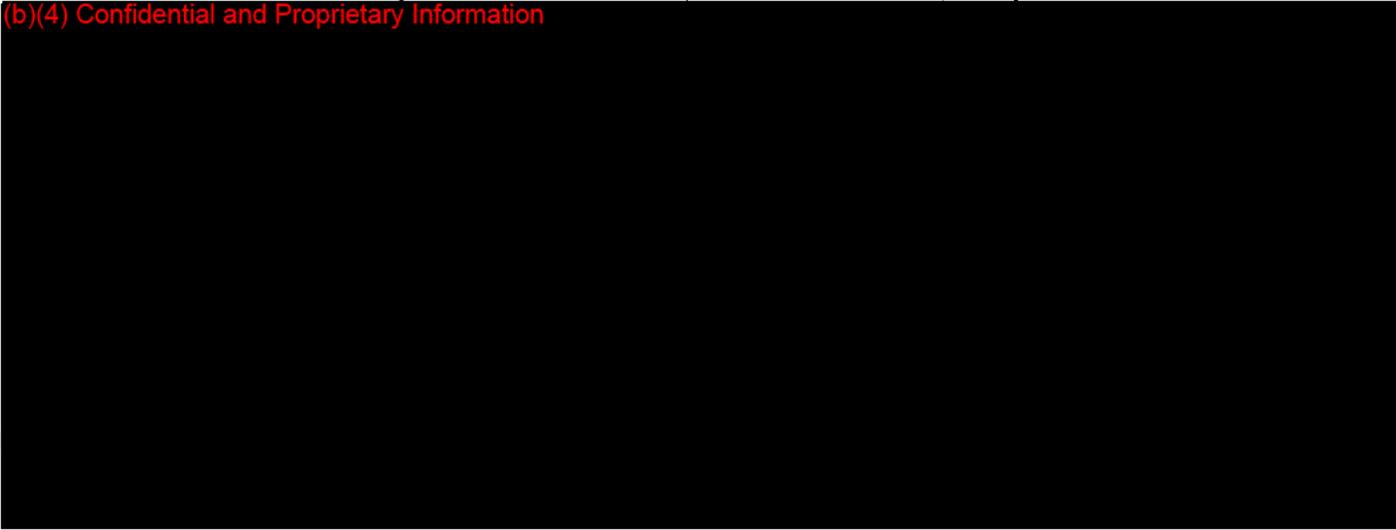


(b)(4) Confidential and Proprietary Information



[Text of E-Mail Sent to Sponsor on October 12, 2010]

(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



Your submission will be placed on hold for up to 30 days to give you time to respond. If you have questions, please feel free to contact me.

Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: November 20, 2012

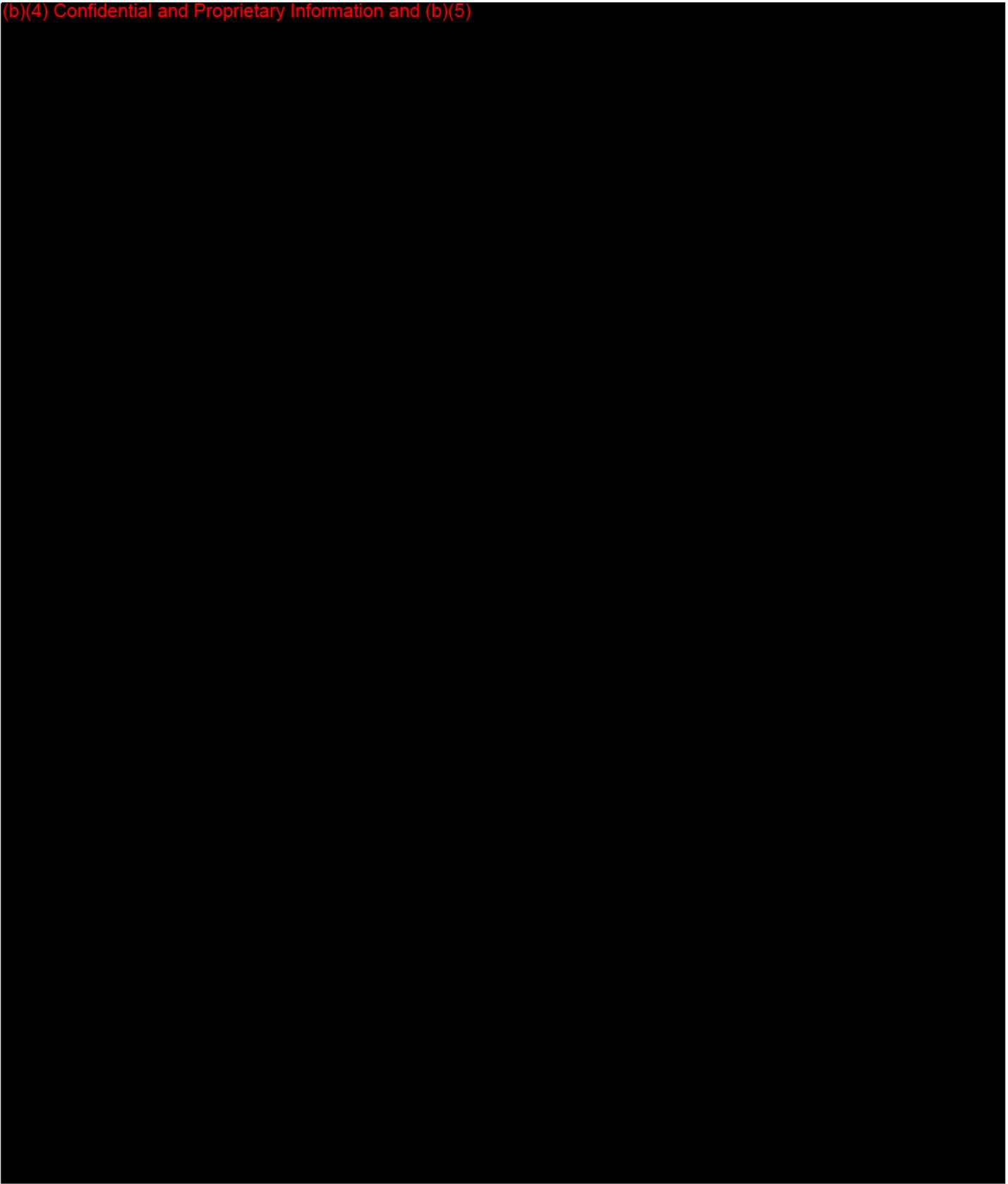
To: The Record

From: Bob Gatling *Bob Gatling*
Director, Program Operations Staff, Office of Device Evaluation

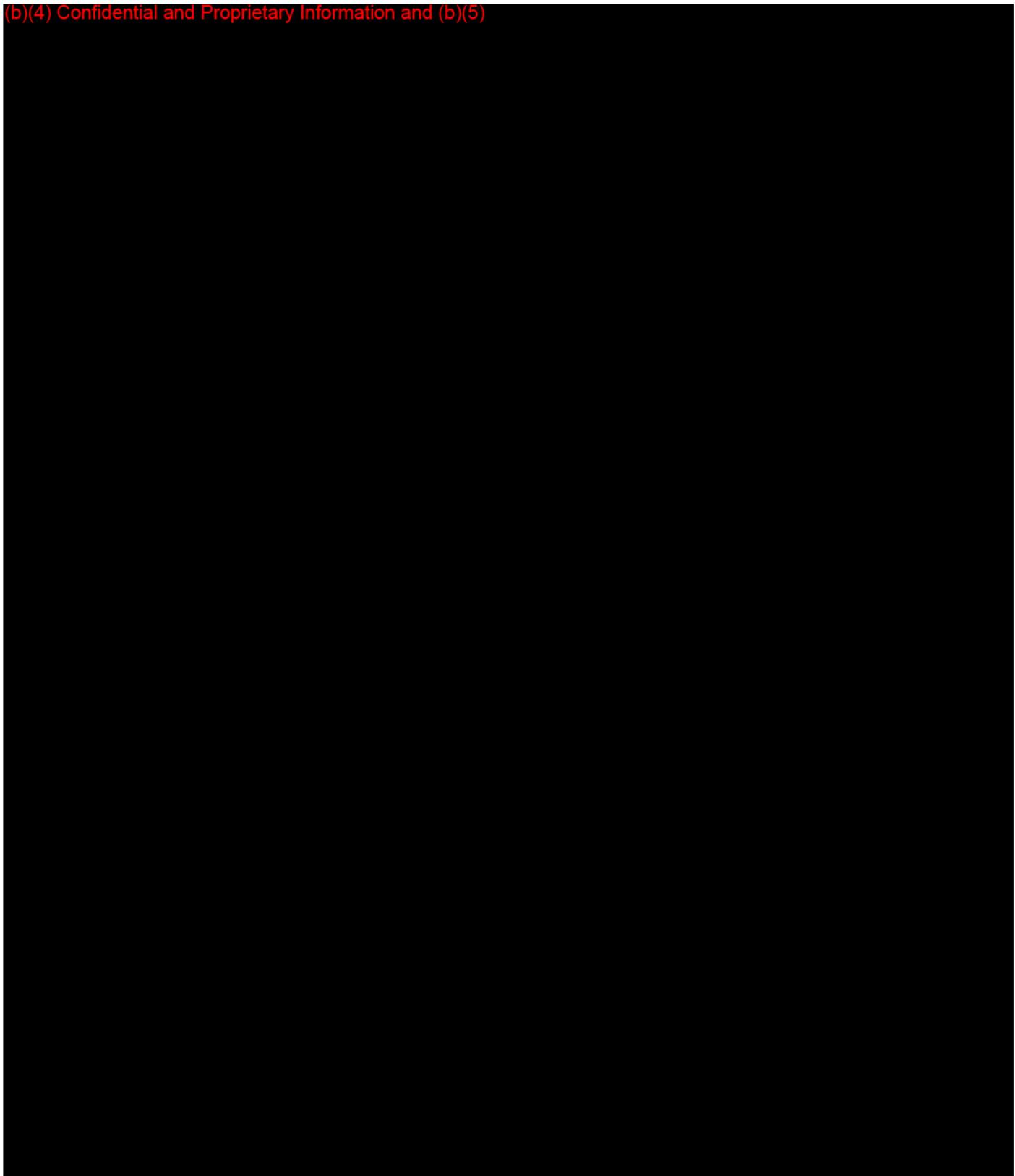
Re: Appeal of 510(k) Withdrawal for:
K100581, CollaDental Matrix
K100695, CollaDental Barrier
K100914, CollaDental Graft

(b)(4) Confidential and Proprietary Information and (b)(5)

(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)





DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room - W066-G609
Silver Spring, MD 20993-0002

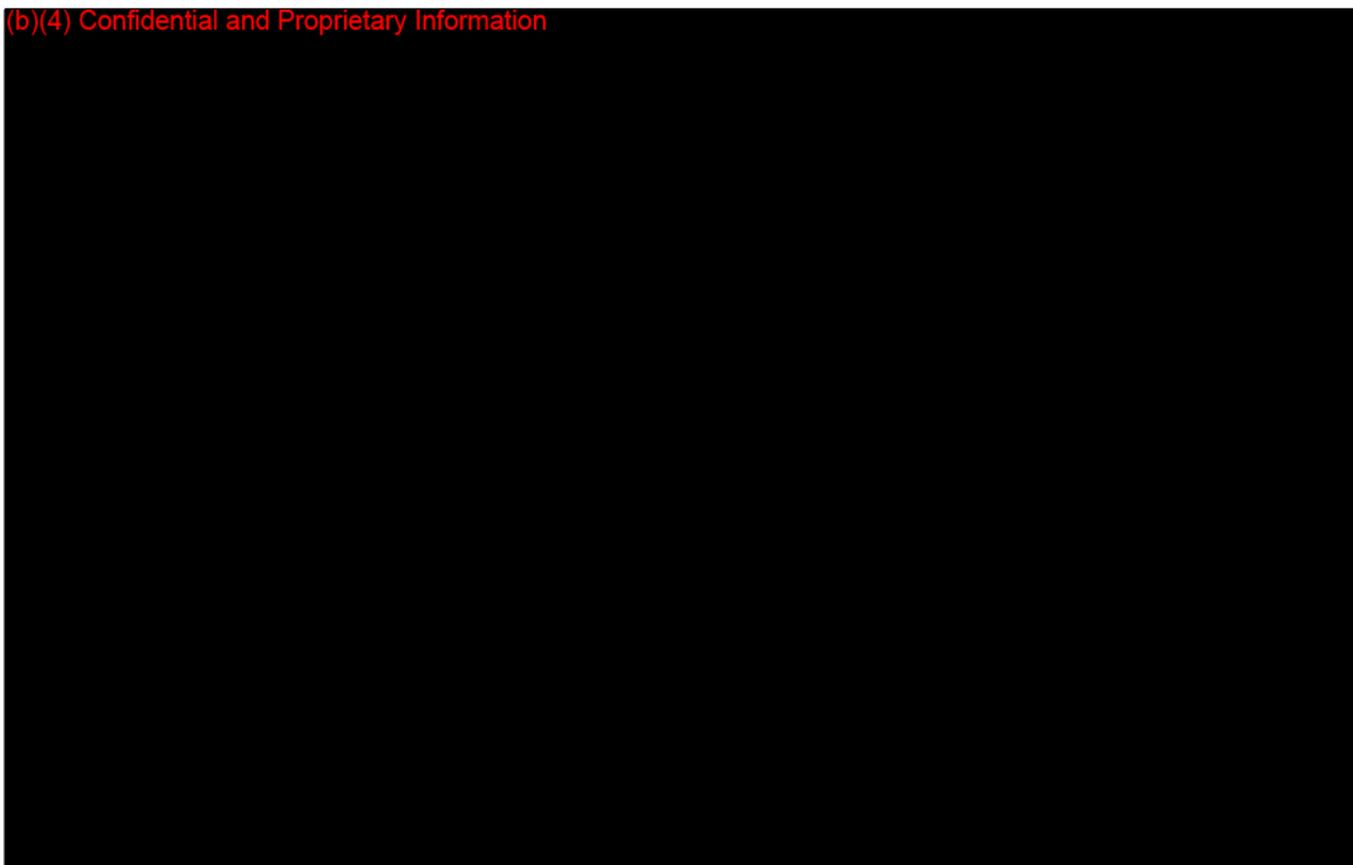
Collamatrix Inc
Quality Assurance
26F, No. 105, Section 2 Dunhua South Road, Da-an District
Taipei
China (Taiwan) 106
Attn: Dennis J.N. Seah

DEC 03 2012

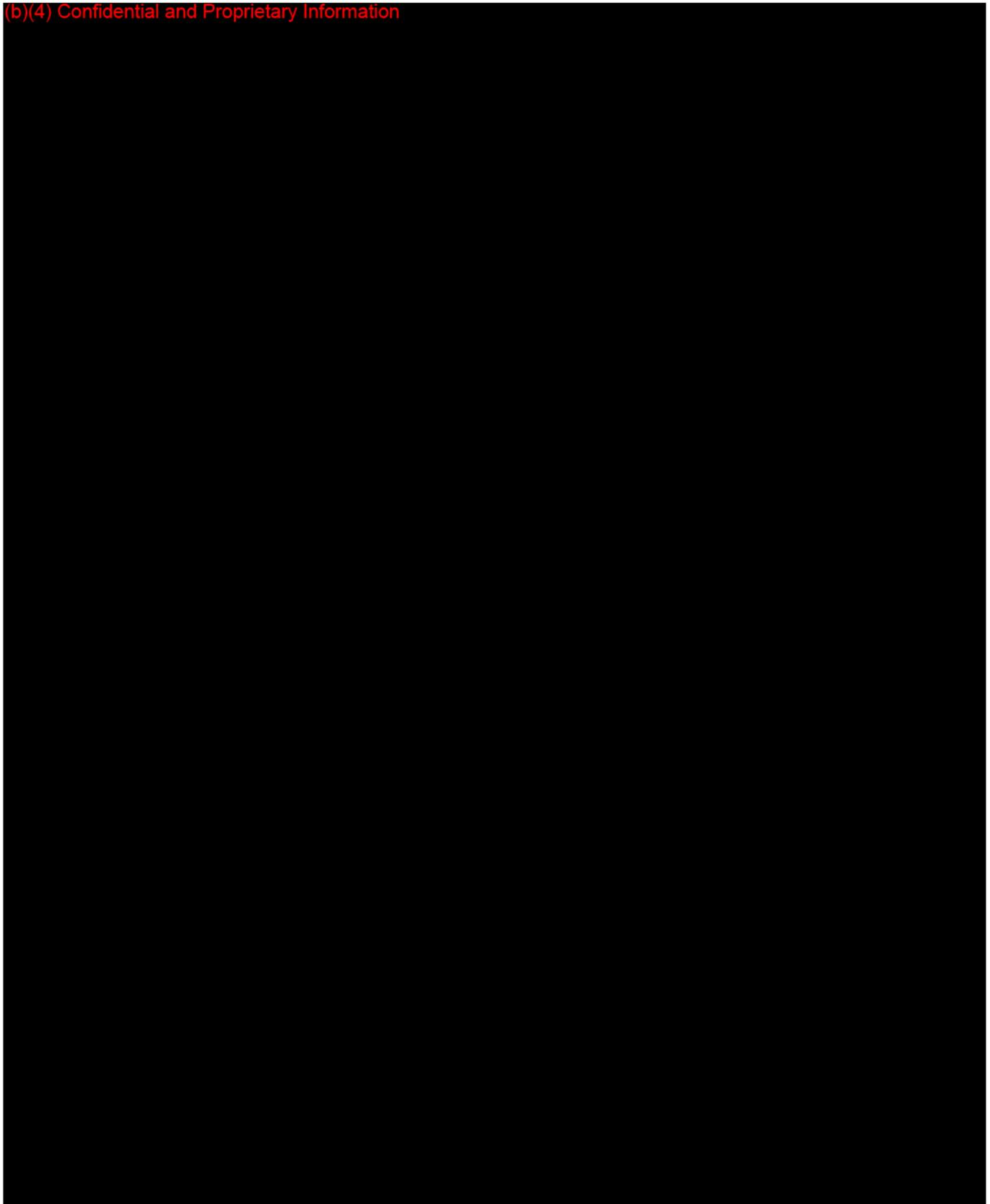
Re: K100581, K100695, K100914
CollaDental Matrix, CollaDental Barrier, and CollaDental Graft
Request to reconsider 510(k) withdrawals
Dated: March 28, 2012

Dear Mr. Seah:

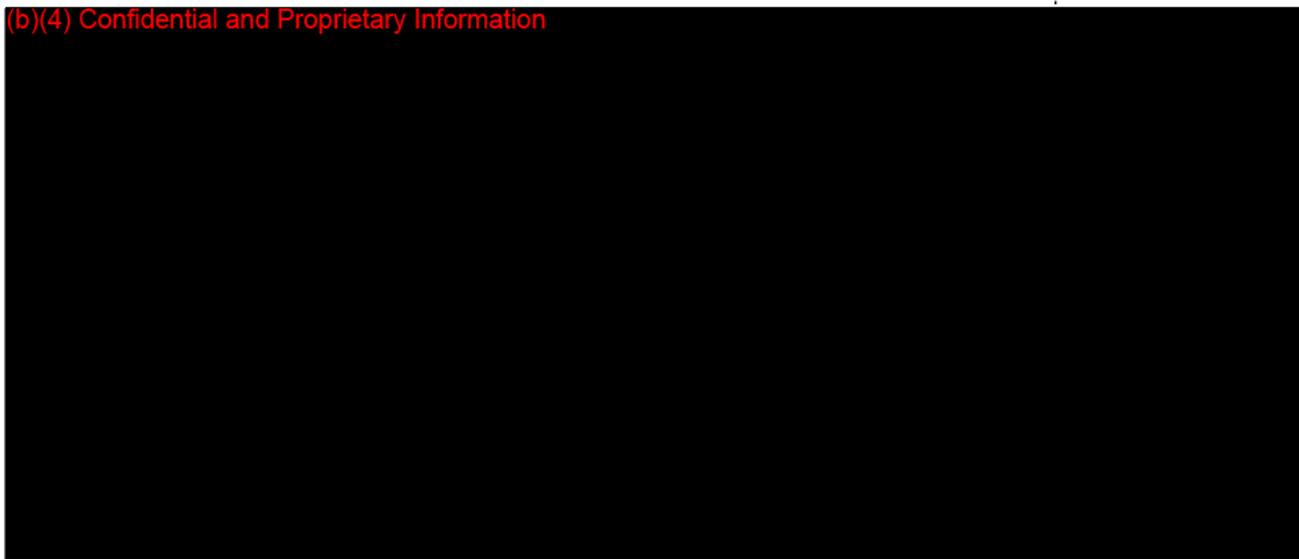
(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information

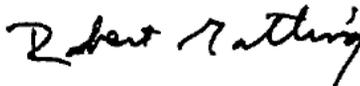


(b)(4) Confidential and Proprietary Information



If you have any questions regarding this letter, please contact Michael Ryan, ODE Regulatory Advisor, at michael.ryan@fda.hhs.gov or 301-796-6283.

Sincerely yours,



Robert Gatling
Associate Director
Office of Device Evaluation
Center for Devices and Radiological Health

K100914

FDA CDRH DMC

MAR 30 2012

Received

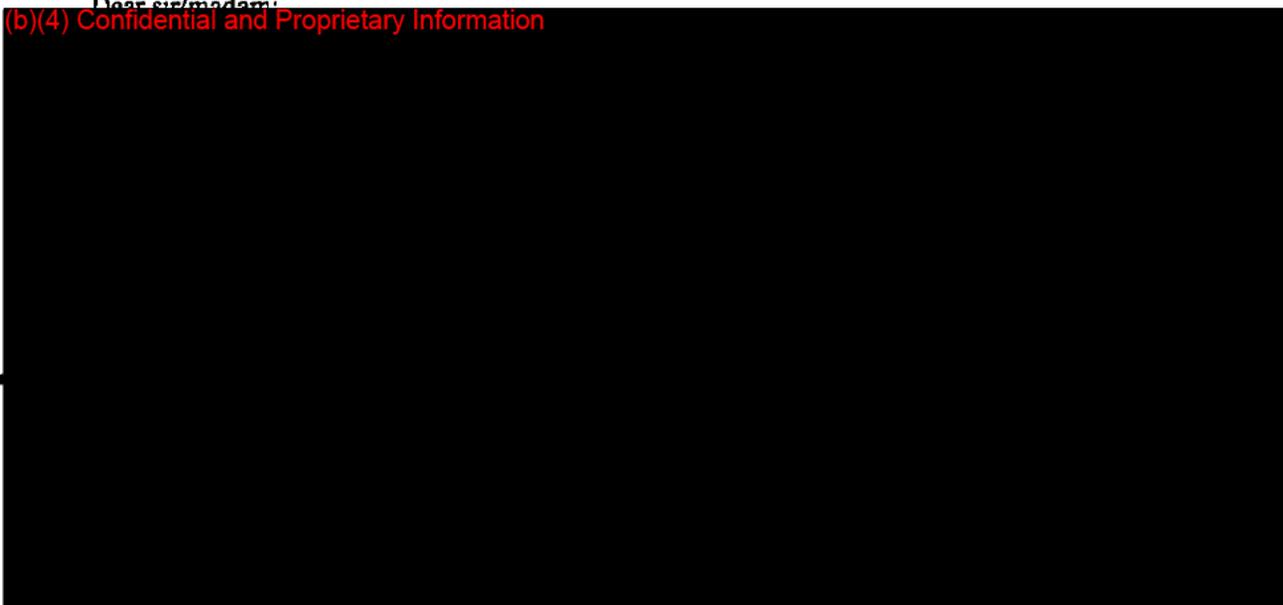
Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

March 28, 2012

Re: Requesting an appeal

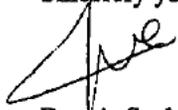
Dear sir/modam:

(b)(4) Confidential and Proprietary Information



Thank you.

Sincerely yours,



Dennis Seah
Collamatrix Inc

Tel: +886 2 7711 3299 Ext 222

Fax: +886 2 7711 3599

Email: jnseah@collamatrix.com

寄件者: 余俊男 寄件日期: 2010/6/17 [星期四] 下午 03:59
收件者: Betz, Bob
副本:
主旨: RE: K100581 CollaDental Matrix
附件: IFU REVISED.doc(40KB)
以網頁檢視

The statement "Complete hemostasis must be achieved prior to placement of CollaDental Matrix in or on alveolar bone." is added to "PRECAUTIONS" section of the Instruction For Use. Please refer to attached document entitled "IFU REVISED". Thank you.

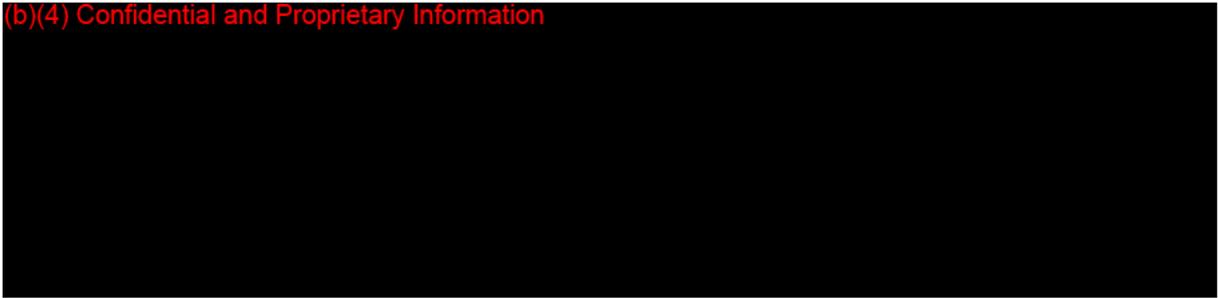
Best regards,
Dennis

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

From: Betz, Bob [mailto:Robert.Betz@fda.hhs.gov]
Sent: 2010/6/15 [星期二] 下午 07:26
To: 余俊男
Subject: RE: K100581 CollaDental Matrix

Thank you for the information.

(b)(4) Confidential and Proprietary Information



Robert S, Betz, DDS, Captain (Ret.) USPHS

Diplomate, American Board of Periodontology
U. S. Food and Drug Administration
Office of Device Evaluation
301-796-6277
robert.betz@fda.hhs.gov <mailto:robert.betz@fda.hhs.gov>

From: 余俊男 [mailto:jnseah@collamatrix.com]

Sent: Monday, June 14, 2010 11:11 PM

To: Betz, Bob

Subject: RE: K100581 CollaDental Matrix

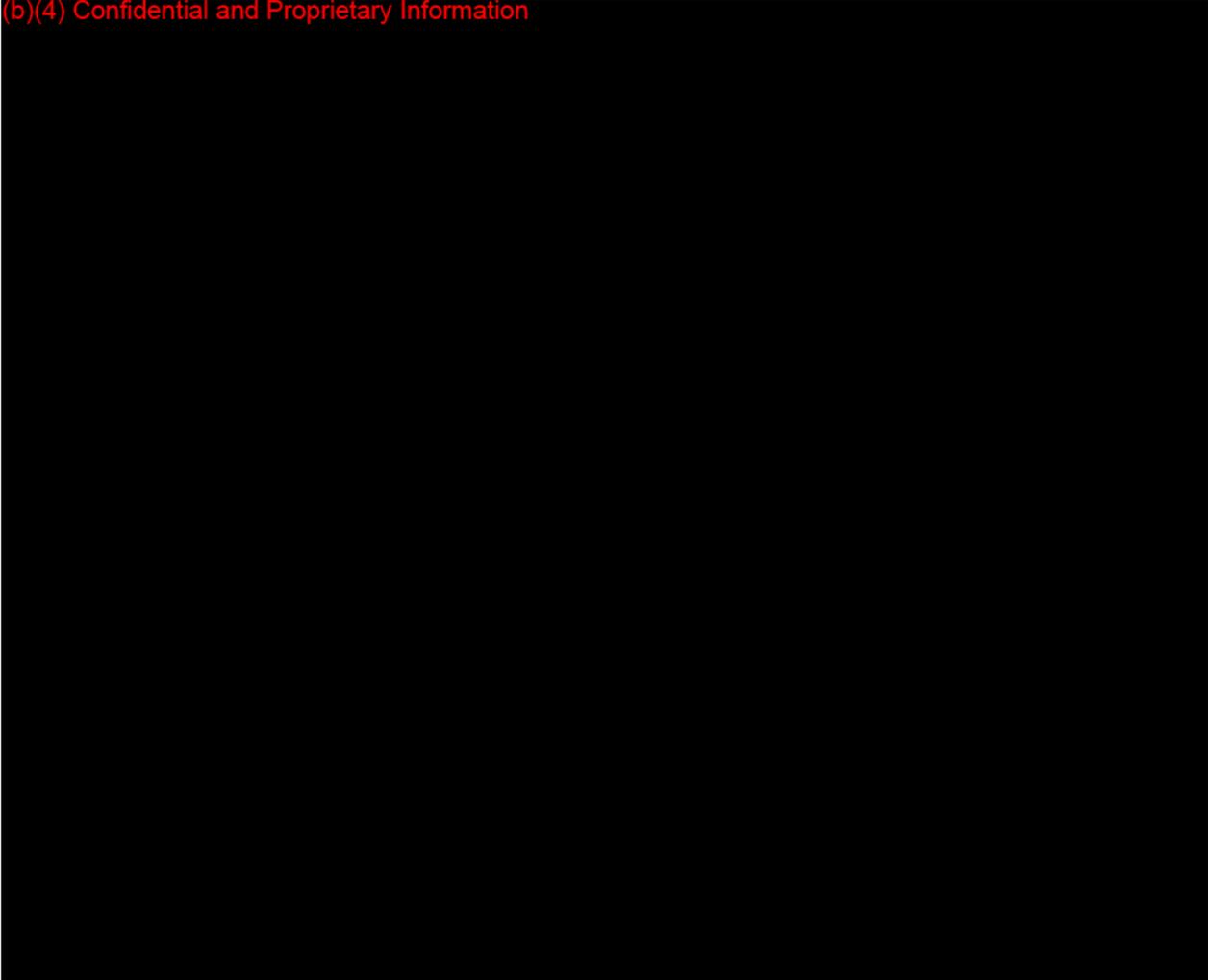
Hi Robert,

I have prepared the responses to the deficiencies with regard to the 510k application of CollaDental Matrix. The corresponding documents are attached herewith for your review. Please let me know should you have any question. I look forward to your favorable reply. Thank you.

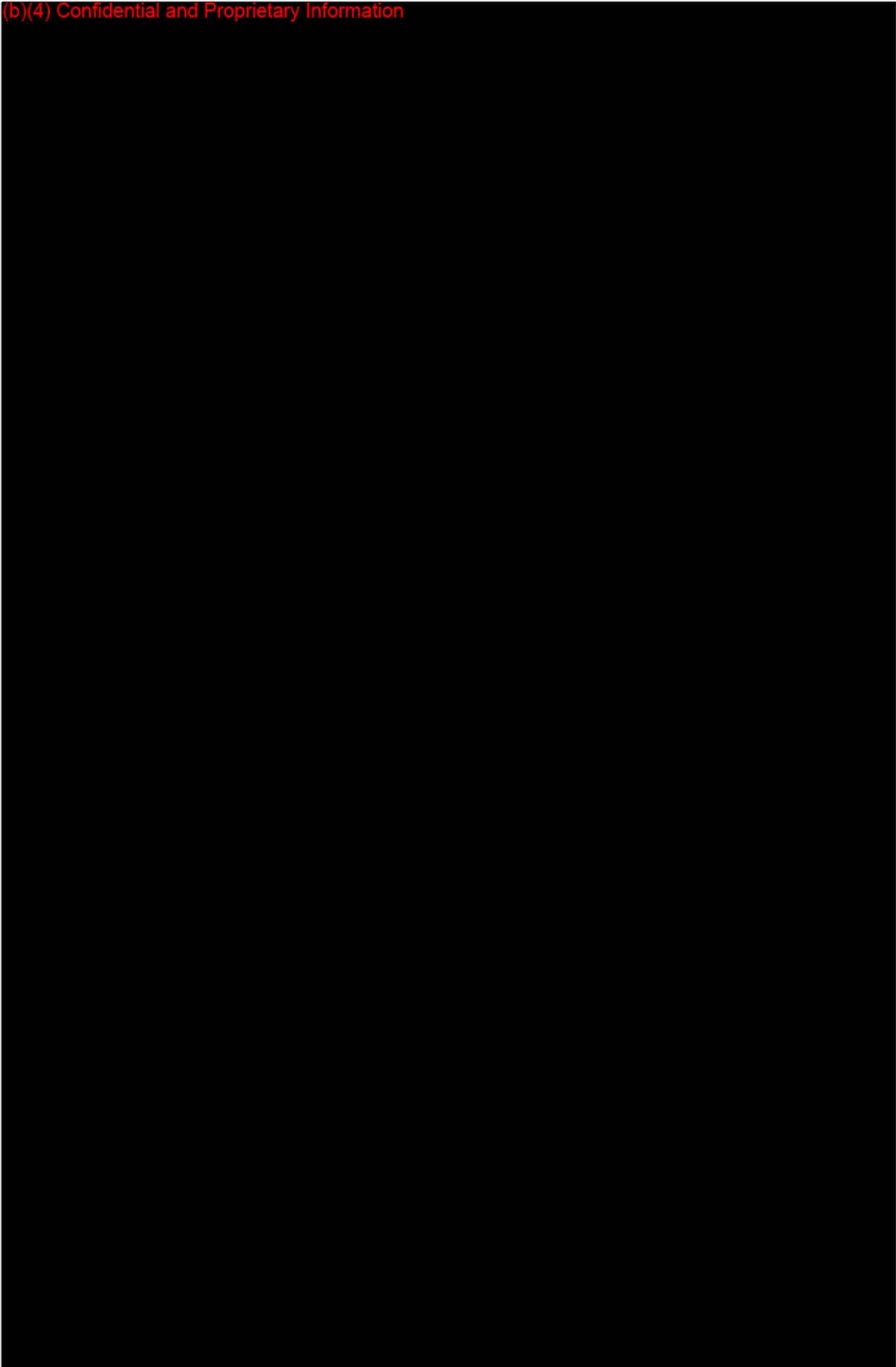
Best regards,

Dennis

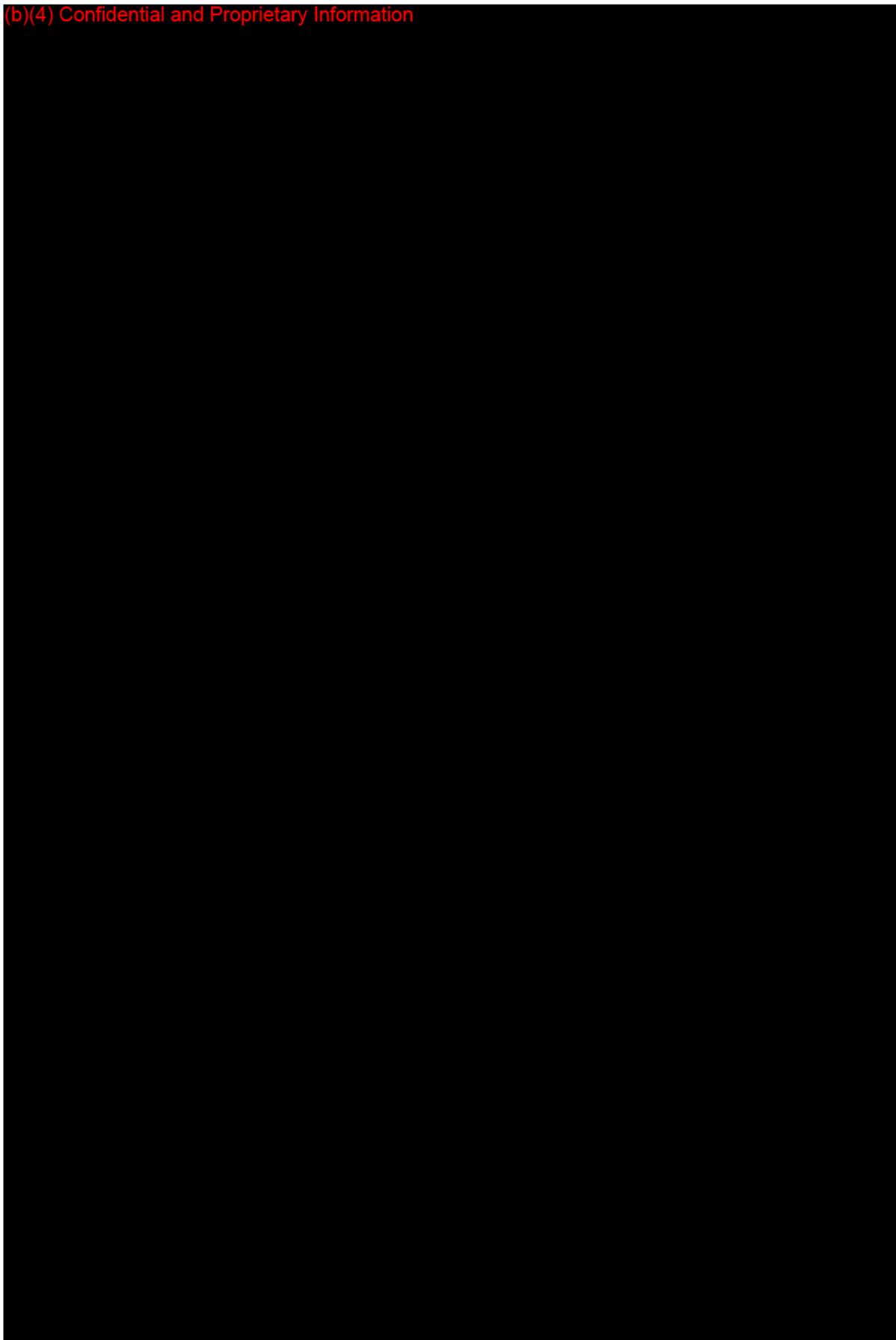
(b)(4) Confidential and Proprietary Information



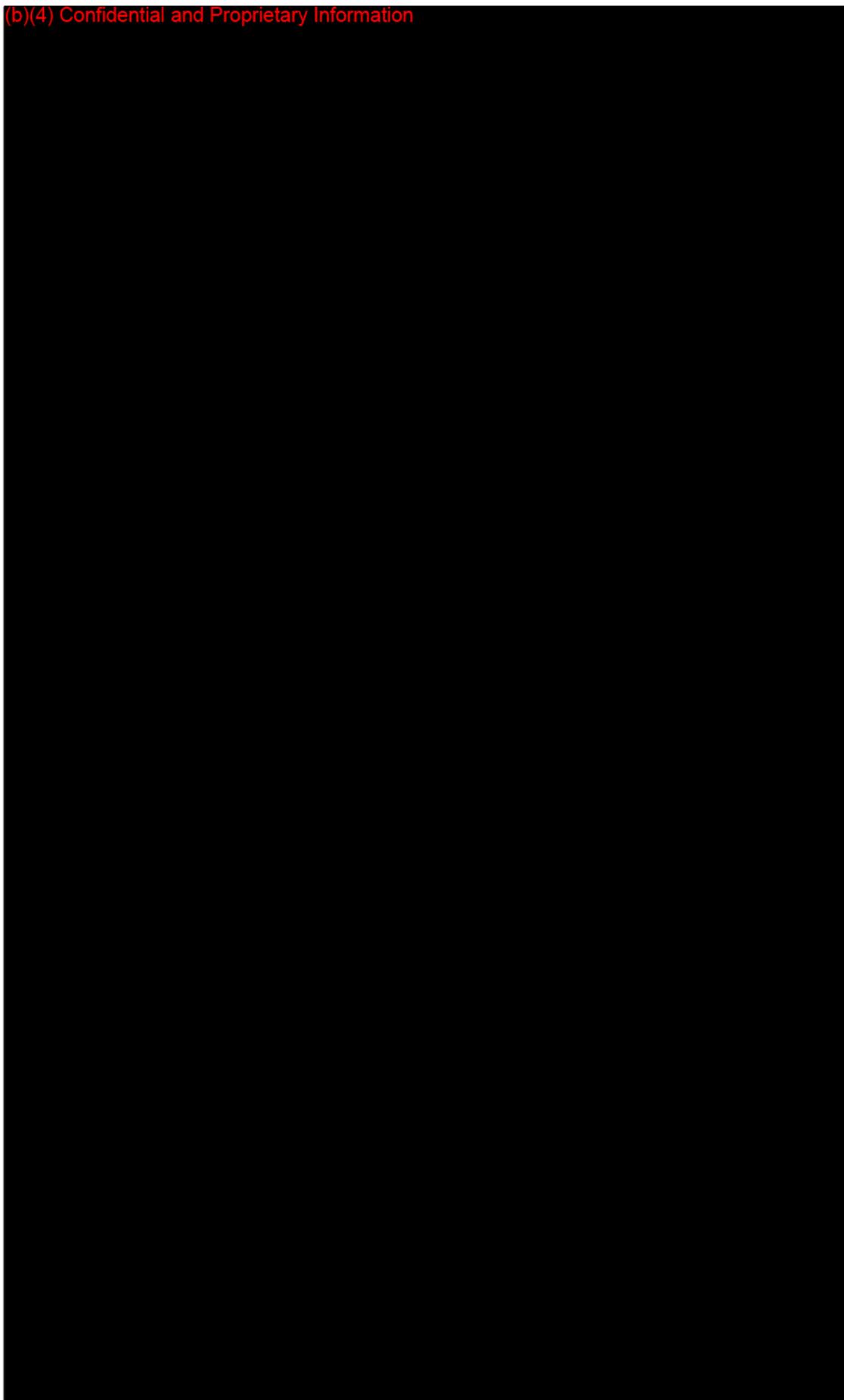
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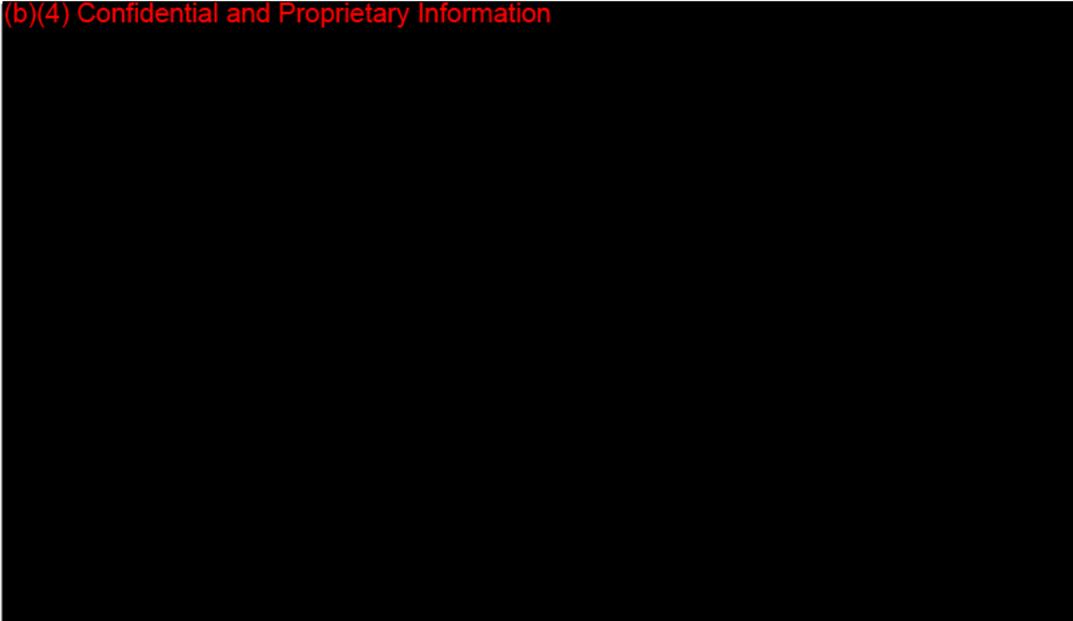
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(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



If you have any questions, please feel free to contact me.

Thank you for your patience and your assistance in the review of this submission,

Robert S. Betz, DDS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

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

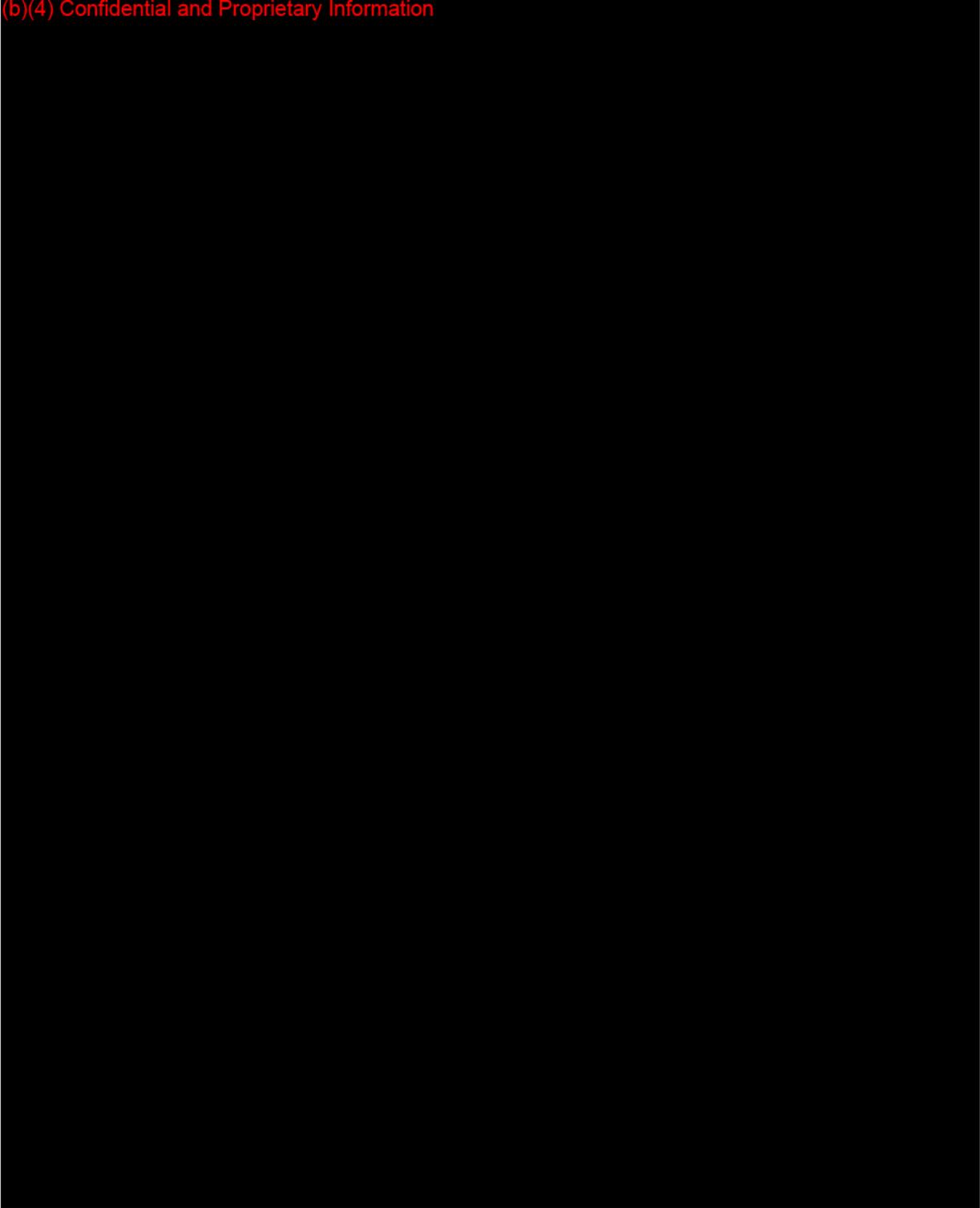
From: Betz, Bob [mailto:Robert.Betz@fda.hhs.gov]

Sent: 2010/12/2 [星期四] 上午 01:03

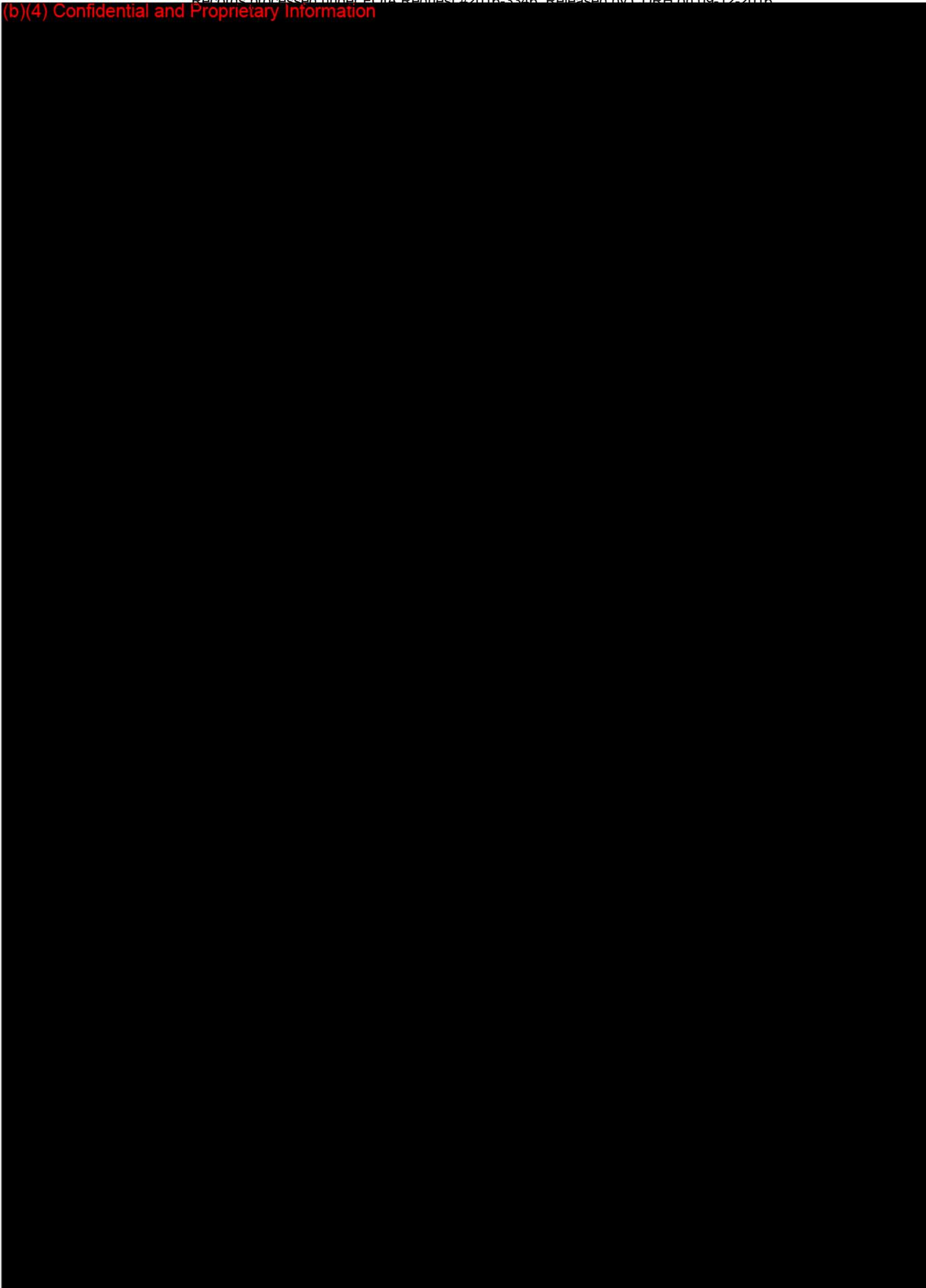
To: 余俊男

Subject: K100695

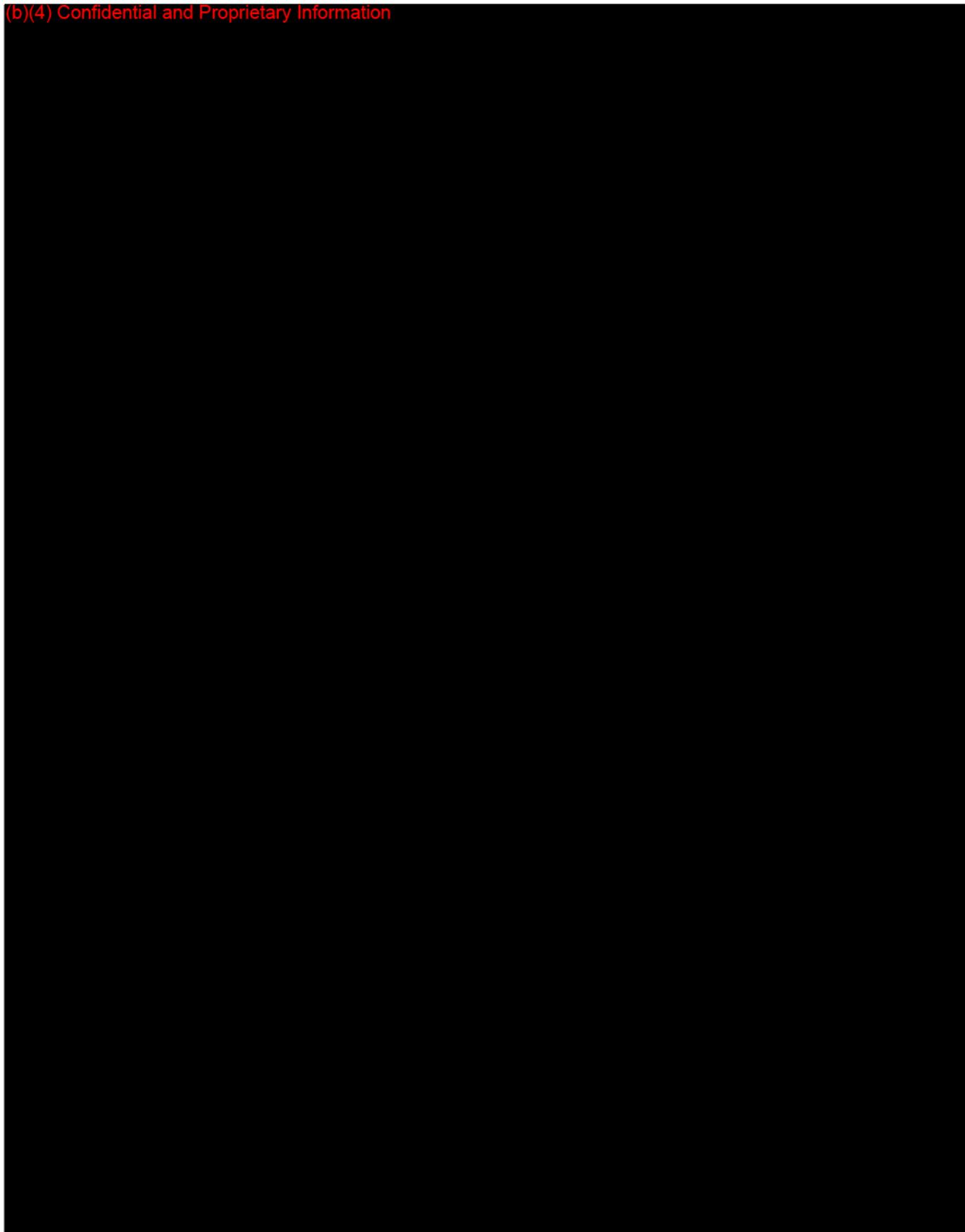
(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



寄件者: 余俊男

寄件日期: 2010/5/2 [星期三] 上午 11:55

收件者: Betz, Bob

副本:

主旨: Re: K100581 CollaDental Matrix

附件:

Dear Bob,

Thank you very much for your mail. I will prepare the requested information and email to you for review as soon as possible. Thank you, once again.

Warm regards,

Dennis

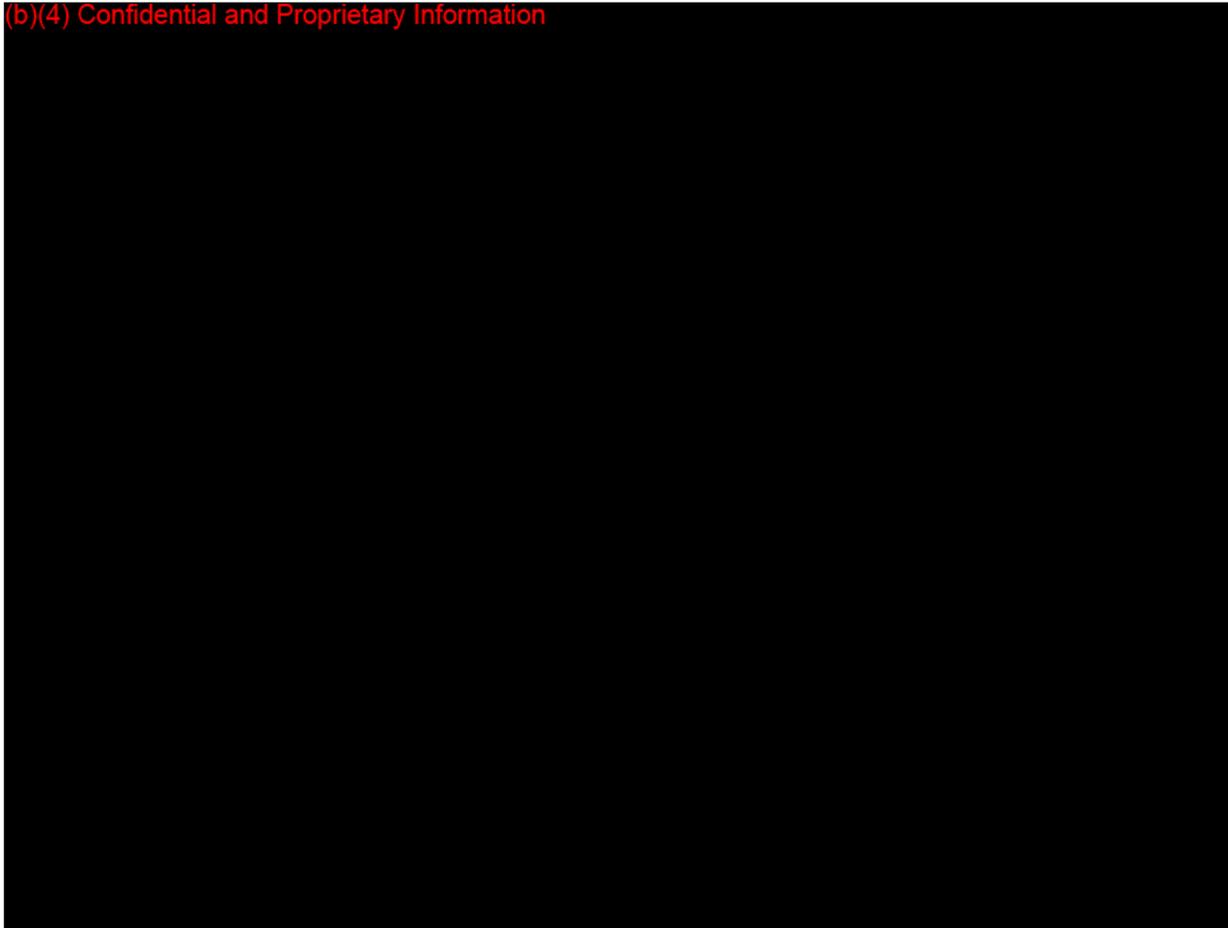
From: "Betz, Bob" <Robert.Betz@fda.hhs.gov>

Date: Fri, 28 May 2010 14:01:28 -0400

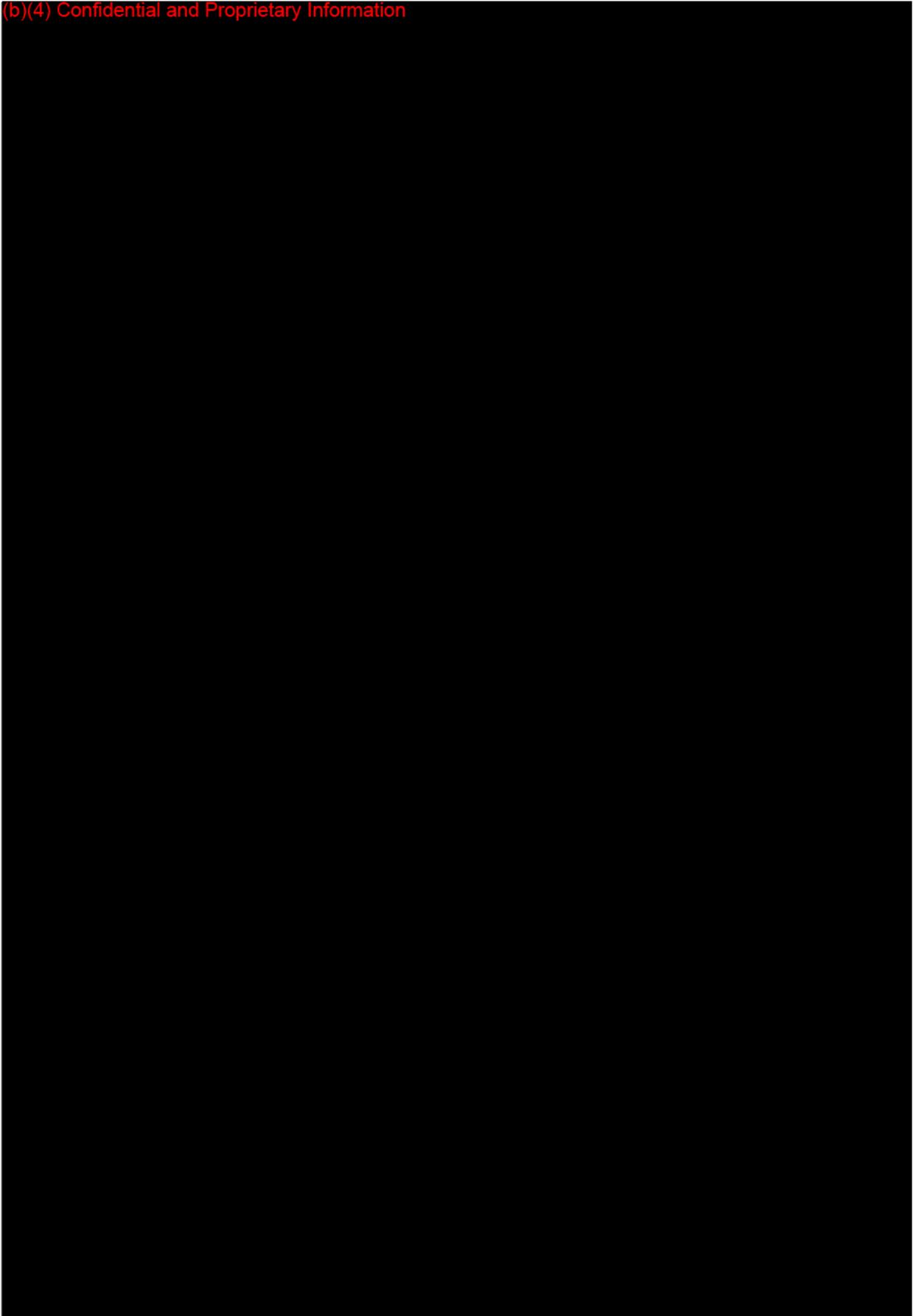
To: <jnseah@collamatrix.com>

Subject: K100581 CollaDental Matrix

(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



If you have any questions, please feel free to contact me.

Thank you for your patience and your assistance in the review of this submission,

Robert S. Betz, DDS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov



Proof of Delivery

[Close Window](#)

Dear Customer,

This notice serves as proof of delivery for the shipment listed below.

Tracking Number:	H8315572997
Service:	UPS Worldwide Express Saver®
Weight:	.50 kg
Shipped/Billed On:	10/01/2010
Delivered On:	10/05/2010 9:30 A.M.
Delivered To:	SILVER SPRING, MD, US
Signed By:	PERRY
Left At:	Receiver

Thank you for giving us this opportunity to serve you.

Sincerely,

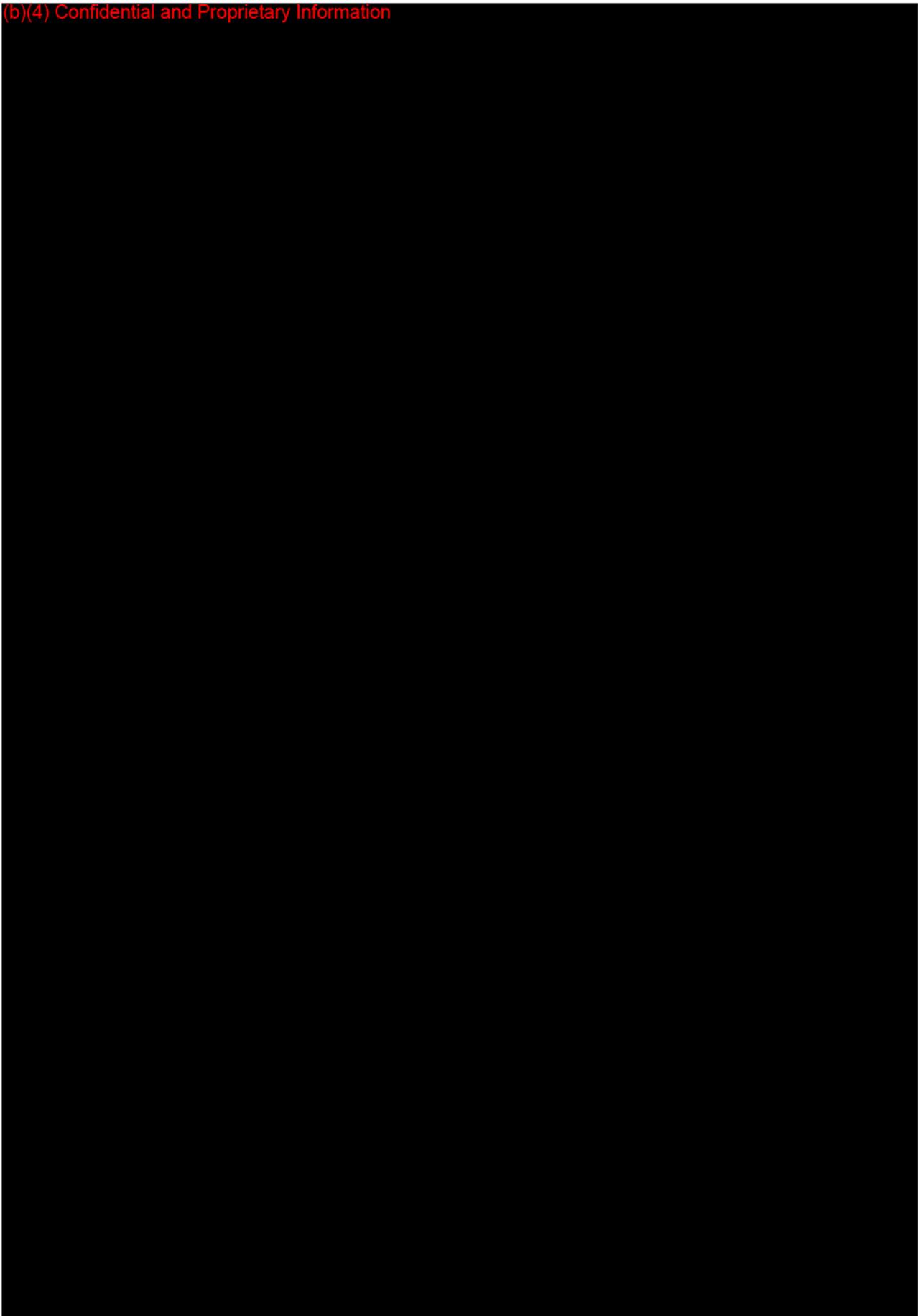
UPS

Tracking results provided by UPS: 02/08/2011 12:19 A.M. ET

[Print This Page](#)

[Close Window](#)

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U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center : WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

December 08, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

This is to notify you that more than 30 days have elapsed since we requested additional information about your Premarket Notification (510(k)) submission. In accordance with our regulations, 21 CFR 807.87(1), we now consider your 510(k) to be withdrawn.

Please note our guidance document entitled, "Guidance for Industry and FDA Staff FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

If you wish to resubmit this 510(k) notification we would be pleased to review this as a new 510(k). A new 510(k) number will be assigned and your submission will be considered a new submission.

You may not market this device until you have received a letter from FDA allowing you to do so. If you market the device without FDA clearance/approval, you will be in violation of the Federal Food, Drug, and Cosmetic Act.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

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



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center, WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

November 30, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

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 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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 in 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.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center 4 WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

November 04, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

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 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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Sincerely,

510(k) Staff



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center 4 WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

October 05, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

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 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center 4 WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

July 08, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

Extended Until: 08/03/2010

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

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

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC

July 05, 2010

JUL 08 2010

Received

Re: K100695

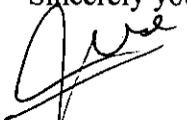
Petition for an extension of time for submission of requested information

Dear sir/madam:

We request for a 30 days extension to prepare the information requested by the agency.

Thank you.

Sincerely yours,


Dennis Seah

169

K-32

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC

JUL 08 2010

July 05, 2010

Received

Re: K100695

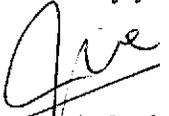
Petition for an extension of time for submission of requested information

Dear sir/madam:

We request for a 30 days extension to prepare the information requested by the agency.

Thank you.

Sincerely yours,


Dennis Seah



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

June 07, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

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 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>.

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/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModerizationAct/ucm136685.htm>.

If after 30 days the additional information (AI), 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 (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm>. 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.

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Records released under FOIA Request # 2019-0046 Released by CDRH on 08-12-2016
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 questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,



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



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

March 16, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695
Received: 3/15/2010
Product: COLLADENTAL BARRIER

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) 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.**

Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center (DMC) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

On September 27, 2007, the President signed an act reauthorizing medical device user fees for fiscal years 2008 - 2012. The legislation - the Medical Device User Fee Amendments of 2007 is part of a larger bill, the Food and Drug Amendments Act of 2007. Please visit our website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm> for more information regarding fees and FDA review goals. In addition, effective January 2, 2008, any firm that chooses to use a standard in the review of ANY new 510(k) needs to fill out the new standards form (Form 3654) and submit it with their 510(k). The form may be found at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm> accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007”

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134034.htm>. According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, “Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements”. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.html>. In addition, the 510(k) Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have questions on the status of your submission, please contact DSMICA at (301)796-7100 or the toll-free number (800)638-2041, or at their internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have procedural questions, please contact the 510(k) Staff at (301)796-5640.

Sincerely,

510(k) Staff



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

March 11, 2010

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA SOUTH ROAD, DA-AN DISTRIC
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695
Received: 3/11/2010
User Fee ID Number: 6048270
Product: COLLADENTAL BARRIER

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), 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 all future correspondence that relates to this submission. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

The Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) and the FDA Amendments Act of 2007 (FDAAA) (Public Law 110-85), authorizes FDA to collect user fees for certain types of 510(k) submissions. The submission cannot be accepted for review until the fee is paid in full ; therefore, the file has been placed on hold. When your user fee payment has been received , review of the 510(k) will resume as of that date. Alternatively, you may request withdrawal of your submission. You now have the option to pay online by credit card. We recommend this form of payment. Credit card payments are directly linked to your user fee cover sheet and are processed the next business day. You may also pay by check. If you choose to mail a check, please send a check to one of the addresses listed below:

By Regular Mail
Food and Drug Administration
P.O. Box 956733
St. Louis, MO 63195-6733.

By Private Courier(e.g., Fed Ex, UPS, etc.)
U.S. Bank
956733
1005 Convention Plaza
St. Louis, MO 63101
(314) 418-4983

The check should be made out to the Food and Drug Administration referencing the payment identification number, and a copy of the User Fee Cover sheet should be included with the check. A copy of the Medical Device User Fee Cover Sheet should be faxed to CDRH at (301)847-8120 referencing the 510(k) number if you have not already sent it in with your 510(k) submission. After the FDA has been notified of the receipt of your user fee payment, your 510(k) will be filed and the review will begin. If payment has not been received within 30 days, your 510(k) will be deleted from the system. Additional information on user fees and how to submit your user fee payment may be found at www.fda.gov/cdrh/mdufma/fy09userfee.html. In addition, the 510k Program Video is now available for viewing on line at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, or

HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>. Records processed under FOIA Request #2016-3346; Released by CDRH on 09-12-2016.

Please note that since your 510(k) has not been reviewed, additional information may be required during the review process and the file may be placed on hold once again. If you are unsure as to whether or not you need to file a 510k Submission with FDA or what type of submission to submit, you should first telephone the Division of Small Manufacturers, International and Consumer Assistance (DSMICA), for guidance at (301)796-7100 or its toll-free number (800)638-2041, or contact them at their Internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>, or you may submit a 513(g) request for information regarding classification to the Document Mail Center at the address above. If you have any questions concerning receipt of your payment, please contact Diane Garcia at Diane.Garcia@fda.hhs.gov or directly at (301)796-6559. If you have questions regarding the status of your 510(k) Submission, please contact DSMICA at the numbers or address above.

Sincerely yours,

Diane Garcia
Public Affairs Specialist
Premarket Notification Section
Office of Device Evaluation
Center for Devices and Radiological Health

K100695

March 6, 2010

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center, WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC

MAR 11 2010

Received

Product: CollaDental Barrier

To whom it may concern:

We are pleased to submit the attached CD-ROM for Product CollaDental Barrier. The contents include

1. Medical Device User Fee form
2. Premarket Review Submission Cover Sheet
3. Truthful and Accurate Statement
4. General information and standard
5. Device Description
6. Characterization of the product
7. Statement of indications for use
8. Labeling
9. 510k summary

This submission is also being submitted as an electronic copy (eCopy) and we attest to the fact that the electronic copy is an exact duplicate of the paper submission.

Please let me know if you have any questions or concerns, please feel free to contact me at +886 2 7711 3299 ext 222.

Sincerely,



Dennis Seah

March 6, 2010

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center, WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Product: CollaDental Barrier

To whom it may concern:

We are pleased to submit the attached CD-ROM for Product CollaDental Barrier. The contents include

1. Medical Device User Fee form
2. Premarket Review Submission Cover Sheet
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8. Labeling
9. 510k summary

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Please let me know if you have any questions or concerns, please feel free to contact me at +886 2 7711 3299 ext 222.

Sincerely,

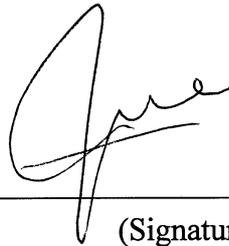


Dennis Seah

1 Truthful and Accurate Statement

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT
[As required by 21 CFR 807.87(k)]

I certify that, in my capacity as Manager of Quality Assurance of Collamatrix Inc., I believe 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 omitted.



(Signature)

DENNIS SEAM

(Typed Name)

MARCH 6 2010

(Dated)

*(Premarket Notification [510(k)] Number)

2 General Information

1. Device name

- 1.1. Propriety name: CollaDental Barrier
- 1.2. Common name: Barrier, animal source, intraoral
- 1.3. Classification name: Bone grafting material

2. Registration number

- 2.1 Registration number: 3005841971
- 2.2 Address of manufacturing establishment

Collamatrix Inc.
1st floor, No. 50-1, Keyan Road, Jhunan Science Park,
Miaoli County, 350, Taiwan

3. Classification

Unclassified

4. Panel

Dental

5. Product code

NPL

6. Guidance and performance standards

- 6.1. ISO 10993 Biological Evaluation of Medical Devices.
- 6.2. ISO 11137:2006 Sterilization of health care products – Radiation.

3 Statement of indications for use

510(k) Number (if known): _____

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

4 Substantial Equivalence Comparison

A. Predicate devices

CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices including:

- (1) BioMend Extend absorbable collagen membrane (K992216) manufactured by Integra LifeSciences corp.
- (2) BIO-GIDE® (K042197) manufactured by Ed. Geistlich Söhne AG für chemische Industrie.

B. Basis for Substantial Equivalence

1. Indications for use

- 1.1 CollaDental Barrier is intended for augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided tissue regeneration procedures in periodontal defects.
- 1.2 BioMend Extend absorbable collagen membrane is indicated for guided tissue regeneration procedures in periodontal defects to enhance regeneration of periodontal apparatus.
- 1.3 BIO-GIDE is indicated for simultaneous use of GBR-membrane and implants; augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects; guided tissue regeneration procedures in periodontal defects.

1.4 Therefore, indications for use of CollaDental Barrier is comparable to predicate device.

2. Technological characteristics

2.1 CollaDental Barrier is a monolayer, conformable, resorbable, non-friable, glutaldehyde-crosslinked membrane.

2.2 BioMend Extend absorbable collagen membrane is a resorbable, non-friable, monolayer, glutaldehyde-crosslinked membrane.

2.3 BIO-GIDE is a bilayer, resorbable non-crosslink membrane.

2.4 Therefore, CollaDental Barrier is similar in technological characteristics to predicate device.

3. Material

3.1 CollaDental Barrier comprises type I collagen obtained from porcine dermis.

3.2 BioMend Extend absorbable collagen membrane contains type I collagen obtained from bovine Achilles tendon.

3.3 BIO-GIDE contains type I and type III collagen obtained from porcine dermis.

3.4 Therefore, CollaDental Barrier is similar to predicate device with respect to materials of construction.

In summary, CollaDental Barrier is substantially equivalent to the predicate devices in terms of indication of use, technological characteristics and material used in manufacturing the device.

A table comparing the characteristics of CollaDental Barrier and predicate devices is provided in Table 1 (Attachment 4.1).

Comparison summary of CollaDental Barrier with predicate devices, BioMend Extend absorbable collagen membrane and BIO-GIDE Resorbable Bilayer Membrane

Device name	CollaDental Barrier	BioMend Extend absorbable collagen membrane	BIO-GIDE® resorbable bilayer membrane
Intended use	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus	Used for guide tissue regeneration procedures in periodontal defects to enhance regeneration of the periodontal apparatus
Incorporate same basic design	Yes	Yes	Yes
Utilizes the same operating principle	Cell occlusive Implantable Resorbable	Cell occlusive Implantable Resorbable Hemostatic	Cell occlusive Implantable Resorbable Hemostatic
Incorporate same material	Yes. Type I Collagen	Yes. Type I collagen	Yes. Type I and type III Collagen
Biocompatibility	Yes	Yes	Yes
Sterilization process	Gamma irradiation	ETO	Gamma irradiation
Compatible sizes	Yes	Yes	Yes
Shelf life	36 months	24 months	36 months

5 Product Description

Description

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. Such a method of preventing epithelial migration into a specific area is known as guided tissue regeneration (GTR).

CollaDental barrier is a resorbable membrane made of type I collagen derived from pig. It is glutaraldehyde crosslinked and takes about eighteen weeks to fully resorb. It can inhibit migration of epithelial cells, promote the attachment of new connective tissue, are not antigenic. Compared to non-resorbable membrane such as ePTFE membranes, resorbable CollaDental barrier allow for fewer exposures and therefore reduce the effects of infection.

CollaDental Barrier is a white to off white, nonfriable, conformable, resorbable, membrane consisting of primarily purified type I collagen derived from porcine dermis. CollaDental Barrier is (b)(4) thick and has a dense impermeable surface with a multi-laminated structure (Figure 1). The average (b)(4) (Figure 2). Device appears white to off white in dry state and translucent and non-slippery when wet. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the material is flexible and conforms to the contours of the defect site.

Degradation of CollaDental Barrier was evaluated in rat subcutaneous implantation. As shown in Figure 3, the membrane remained stable for (b)(4) Confidential was fully absorbed in about (b)(4) Confidential (Attachment 5.1). CollaDental Barrier is an odorless, hydrophilic product. It is water insoluble but lightly soluble in hot water and completely soluble in either acidic solution ($\text{pH} \leq 3$) or basic solution ($\text{pH} \geq 10$). The porcine collagen is extracted from veterinary certified pigs and is carefully purified to avoid antigenic reactions. The collagen extraction process has been demonstrated to have the ability to substantially inactivate potential virus contaminant could be transmitted in the starting collagen-containing materials and to meet the requirement of sterility assurance level (SAL) equal to 10^{-6} . CollaDental Barrier is supplied sterile and for single use.

This device is available in three sizes 15mm x 20mm, 20mm x 30mm and 30mm x 40mm, respectively. CollaDental Barrier can be cut to any size or shape with scissors or scalpel in the wet and dry state, without tearing or fragmenting to meet the needs of the surgeon. CollaDental Barrier is individually housed in PET blister and sterilized by gamma irradiation.

(b)(4) Confidential and Proprietary Information

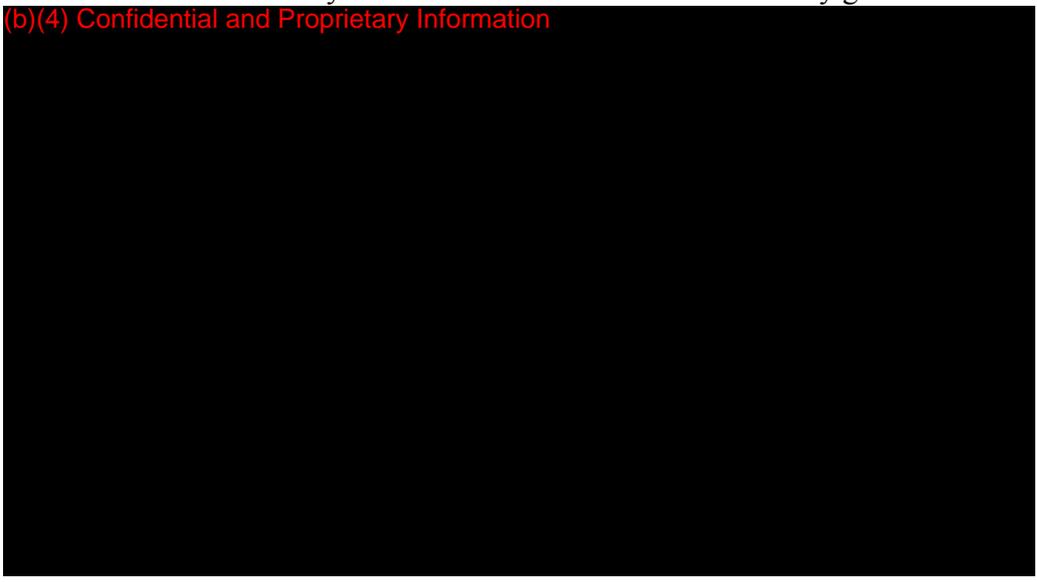


Figure 1 Scanning electron micrography image of CollaDental Barrier. The device has a dense surface and a multi-layer structure with thickness (b)(4) Confidential and Proprietary Information

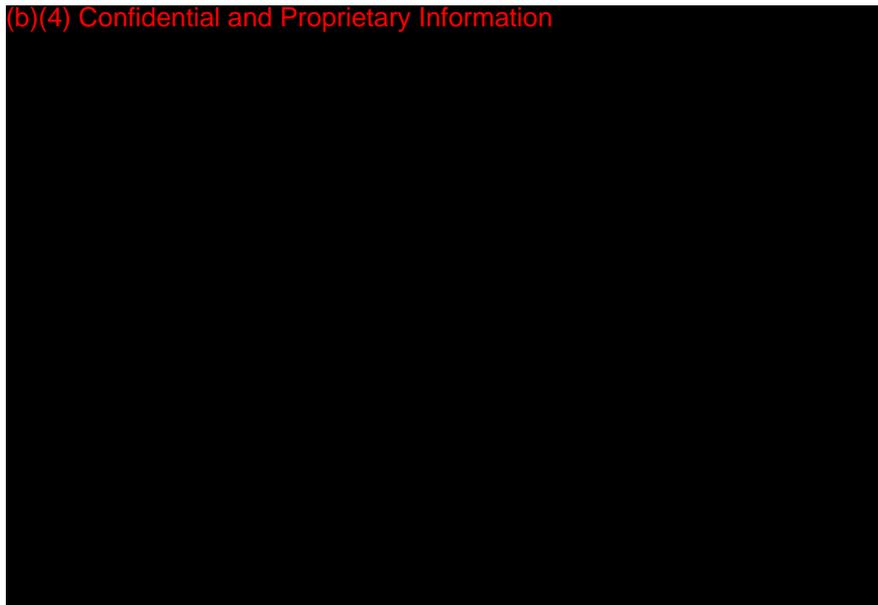


Figure 2 Scanning electron micrography image of CollaDental Barrier. The device has average pore size (b)(4) Confidential and Proprietary Information

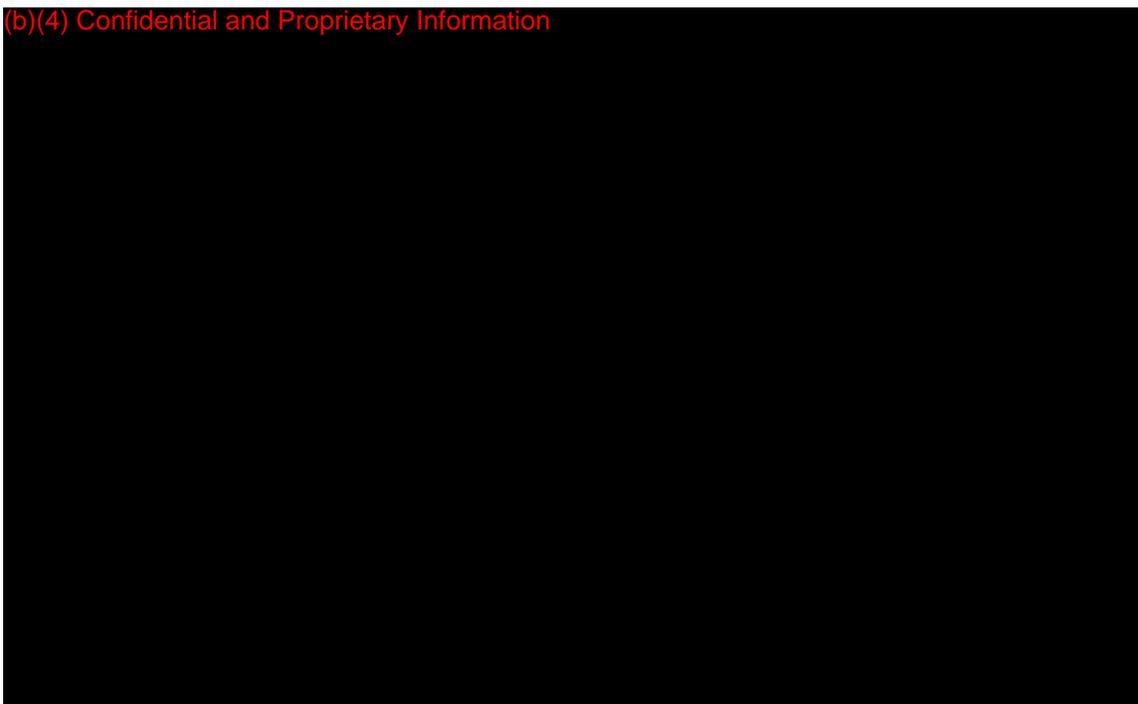


Figure 3 Change in surface area versus implantation time. CollaDental Barrier degradation profile, evaluated in rat subcutaneous implantation, demonstrated the device is degraded in (b)(4) Confidential and

6 Manufacturing information

A. Materials

1. Collagen-containing tissues

Porcine hides are the principle material used in the manufacturing of CollaDental Barrier.

This material is harvested from pigs maintained under the appropriate (b)(4) Confidential veterinary/animal welfare schemes. Extensive veterinary checks are made to the animals on a regular basis throughout their life and both pre- and post-mortem to ensure they are healthy and suitable for use. The animals are slaughtered by (b)(4) Confidential and Proprietary Information slaughterhouse and are qualified for human consumption. Slaughtering of pigs and packing of porcine hides are all provided by (b)(4) Confidential and Proprietary Information slaughterhouse (b)(4) Confidential and Proprietary Information

(b)(4) Confidential whereas packing and distribution of frozen porcine hides are handled by a (b)(4) Confidential (b)(4) Confidential and Proprietary old storage (b)(4) Confidential and Proprietary Information

2. (b)(4) Confidential and Proprietary Information are the three hog species used. The type I collagen used in the device is prepared from the pig hides. No other animal tissues have been used.

3 How the health of herd is maintained and monitored.

3.1.1 Yes, the herd is closed.

3.1.2 Vaccination for (b)(4) Confidential and Proprietary Information standard. The type of vaccine used is (b)(4) Confidential .

3.1.3 Veterinarian inspections are performed with the frequency of once a month.

3.1.4 Composition of the animal feed is composed of corn, barley, grain sorghum, oats, and wheat.

3.1.5 (b)(4) Confidential and Proprietary Information

3.1.6 No bovine origin or other animal derived material has been used in the preparation of CollaDental Barrier.

4 How the health of each animal is maintained and monitored.

4.1 The animal is sacrificed at the age of (b)(4) Confidential and Proprietary Information

4.2 Yes. Pre and post mortem are performed.

4.3 Animal material subjects to several tests as shown in the table. When the test results meet the acceptance criteria, the animal material is then qualified for further processing.

4.4 The following tests are performed (Table 1) to qualify porcine hides for further processing:

Table 1: Acceptance criteria for porcine hide's inspection

Tests	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

5. Validation of virus inactivation study

Study was performed to provide evidence that (a) the virus inactivation steps in the manufacturing process have the capability to substantially inactivate potential virus contaminant could be transmitted in the starting collagen-containing materials; (b) the virus inactivation steps in the manufacturing process has the capacity to inactivate and remove novel or yet undetermined virus contamination in the product. The results of inactivation meet the requirement of sterility assurance level (SAL) equal to 10^{-6} (Attachment 6.1).

6. Upon receipt, goods are inspected for proper documents and undergo visual inspection for any non-conformity. After which, porcine hides are (b)(4) Confidential and Proprietary Information or proceed to decontamination according to steps listed in Table 2 shown below.

Table 2: Cleaning SOP

Treatments
(b)(4) Confidential and Proprietary Information

7. Chemicals

- 7.1 Chemicals used in manufacturing CollaDental Barrier are tabulated in Table 3.

Table 3: Chemicals and specification

Items	Specification
(b)(4) Confidential and Proprietary Information	

7.2 Packaging of CollaDental Barrier

- 7.2.1 CollaDental Barrier is individually packaged in a polyethylene terephthalate (PET) blister pouch, heat-sealed with an aluminum foil and sterilized by gamma (γ)-irradiation.

B. Manufacture of CollaDental Barrier

1. Incoming inspection of collagen-containing animal tissues and other raw ingredients including (b)(4) Confidential and Proprietary Information

(b)(4) Confidential and are carried out to demonstrate the specification of each ingredient complies with quality requirements (Table 4). Certificate of Analysis and safety data sheet of each ingredient can be found in attachment 6.2

Table 4: Specification of ingredients

Items	Specifications
(b)(4) Confidential and Proprietary Information	

2. Disinfection of porcine collagen-containing tissues is carried out as described in Table 5 shown below.

Table 5: Cleaning steps and parameters for porcine tissues

Treatments	Parameters/conditions
(b)(4) Confidential and Proprietary Information	

3. Suspend disinfected tissues in an aqueous solution containing (b)(4) Confidential and Proprietary and (b)(4) Confidential and Proprietary (v/v). This acid/enzymatic extraction process is carried for at least (b)(4) Confidential and Proprietary with constant agitation (b)(4) Confidential. The extraction utilizes solubility of porcine collagen, which is predominantly found in pigskins, in (b)(4) Confidential solution. Temperature is adjusted to (b)(4) Confidential and this temperature range is maintained throughout the entire manufacturing process. 10mL solution is recovered for (b)(4) Confidential and Proprietary Information.
4. After acid extraction, the acid soluble collagen-containing fraction is filtered (b)(4) Confidential and Proprietary Information and then followed by (b)(4) Confidential to remove debris or large insoluble particulates. The filtered acid soluble solution is further clarified by (b)(4) Confidential and Proprietary Information.
5. After clarification, the acid soluble collagen is precipitated by (b)(4) Confidential and Proprietary Information. A (b)(4) Confidential and Proprietary Information is prepared and gradually added to the collagen-containing acid soluble fraction with its final concentration (b)(4) Confidential (b)(4) Confidential (b)(4) Confidential. The formation of collagen-containing sludge, indicated by the appearance of whitish aggregate, is facilitated by constant stirring (b)(4) Confidential of the solution. The solution is (b)(4) Confidential and Proprietary for additional (b)(4) Confidential to allow the precipitation of collagen.
6. The collagen-containing sludge is harvested by (b)(4) Confidential and Proprietary Information and followed by (b)(4) Confidential and Proprietary Information for (b)(4) Confidential and then transferred to a (b)(4) Confidential. (b)(4) Confidential and Proprietary Information After washing, the collagen sludge can be stored at (b)(4) Confidential. (b)(4) Confidential One gram of the collagen sludge is collected from each lot for in-process analysis including (b)(4) Confidential and Proprietary Information (b)(4) Confidential and Proprietary Information.

7. Preparation of collagen membrane Dissolve collagen sludge in (b)(4) Confidential and Proprietary Information by gently (b)(4) Confidential and Proprietary Information to generate a homogeneous solution with collagen concentration about (b)(4) Confidential and Proprietary Information. Pour the solution into a (b)(4) Confidential and Proprietary Information and (b)(4) Confidential and Proprietary Information with collagen solution to a (b)(4) Confidential and Proprietary Information. The (b)(4) Confidential and Proprietary Information is then transferred to a (b)(4) Confidential and Proprietary Information for (b)(4) Confidential and Proprietary Information. The (b)(4) Confidential and Proprietary Information process continues for (b)(4) Confidential and Proprietary Information until the solution is completely (b)(4) Confidential and Proprietary Information. The collagen membrane appears to be opaque, non-friable, off white and conformable.

8. Immerse (b)(4) Confidential and Proprietary Information in a solution containing (b)(4) Confidential and Proprietary Information solution and keep at (b)(4) Confidential and Proprietary Information with constant agitation (b)(4) Confidential and Proprietary Information, followed by (b)(4) Confidential and Proprietary Information to remove unused glutaraldehyde. The collagen membrane is then (b)(4) Confidential and Proprietary Information before transferred to a refrigerated lyophilizer. Vacuum is applied and, the vacuum is maintained at (b)(4) Confidential and Proprietary Information the process. Lyophilization continues for (b)(4) Confidential and Proprietary Information. The resultant lyophilized membrane has a thickness of (b)(4) Confidential and Proprietary Information. The membrane is further processed to give different dimensions including 15mm x 20mm, 20mm x 30mm and 30mm x 40mm, respectively. Five pieces of air-dried product are collected for (b)(4) Confidential and Proprietary Information

9. Filling and packaging of CollaDental Barrier are carried out in a class 10k clean room environment. CollaDental Barrier CollaDental Barrier is individually packaged in a polyethylene terephthalate (PET) blister, heat-sealed with a lidding material and sterilized by gamma (γ)-irradiation.

10. Five pieces of finished product are collected for sterility test and physical appearance inspection after γ -irradiation. Finished product release test is performed on every product lot. Semi-quantitative analysis of (b)(4) Confidential and Proprietary Information is also carried out. The acceptance criterion for γ -irradiation products is sterile, validated by (b)(4) Confidential and Proprietary Information. The release/acceptance criteria for finished product are listed in table 6 shown below.

Table 6: Release/acceptance criteria for finished product inspection

Description	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

C. Environmental control

The clean room is equipped with an air shower room and with environmental temperature maintained at (b)(4) (b)(4) and the relative humidity (b)(4) Particle count is performed (acceptance criterion: (b)(4) Confidential and Proprietary Information (b)(4) (b)(4) monitor environmental cleanliness of the clean room as well as any leakage in HEPA filters. A positive pressure condition (acceptance criterion (b)(4) Confidential) which monitors through a pressure gauge, is established and maintained to expel the back-flow of air from other compartments. Operators are required to wear appropriate clean room attire.

The Class 100 safety hood is equipped with UV light and HEPA filter that help to control airborne contaminants. Air quality monitoring is carried out by particle count (acceptance criterion (b)(4) (b)(4)) and air-borne microorganisms is detected by culture plate exposure using (b)(4) Confidential and Proprietary (acceptance criterion (b)(4) Confidential and Proprietary

D. Final testing

Final product release tests of CollaDental barrier include bioburden and physical appearance inspection. Table 7 summarizes the acceptance criteria for release tests.

Table 7: Release/acceptance criteria

Description	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

E. Cleaning

Cleaning/disinfection of the production line is carried out by a cleaning procedure comprises (b)(4) Confidential and Proprietary Information. Rinsing with (b)(4) Confidential is carried out in between each washing session. The washing conditions are tabulated in Table 8 shown below.

Table 8: Clean-in-Place parameters

Steps	Description/parameters
(b)(4) Confidential and Proprietary Information	

7 Labeling

All labeling information for CollaDental Barrier is supplied together with this application including

1. Pouch label (Attachment 7.1)
2. Package box label (Attachment 7.2)
3. Instruction for use (Attachment 7.3)

The content of the labeling information of CollaDental Barrier specifies the intended use, product claims, direction for use, contraindications, precautions and storage conditions that meet the requirements as defined in 21 CFR § 807.87

8 Controls

A. Quality assurance

1. Quality management system

The establishment is Good Manufacturing Practice certified as required by the regulatory agency of Taiwan. In addition, the establishment also implements a quality management system complies with the requirements of BS EN ISO 13485:2003 and is certified (b)(4) Confidential

(b)(4) Confidential by British Standards Institution management system.

2. Quality assurance program: QA program is implemented to assure that the product quality is consistently met. The entire program can be divided into four parts.

i. Raw materials

Quality of materials used directly or indirectly in the manufacturing of the device must be substantiated by incoming QC inspection according to each inspection SOP. Standard procedure of decontamination is established for source materials used in collagen extraction as described under section “Manufacturing information”. Provisions of veterinary inspection licenses or certificates must be met prior to or accompanied with the delivery of the purchased items.

ii. Process controls

1. In process control at various manufacturing points is implemented to monitor the manufacturing parameters as well as the intermediates. This is to ensure that the quality requirements are consistently met and do not show deviation throughout the manufacturing process.

2. A closed production system is installed in order to reduce exposure to environmental change and minimized air-borne contamination.
3. Vessels and piping lines are made of (b)(4) Confidential and Proprietary that comply with ASTM standard. All surfaces that come in contact with product(s) are mechanically polished to (b)(4) Confide so that residual substances left behind between different or similar production batches can be efficiently removed by a CIP cleaning process.

iii. Personnel training

Personnel working in the production site and QC laboratory received properly training to ensure that tasks are performed per SOPs. All records and test results are documented, filed to create a Device History Record of each product lot.

iv. Environment management

A well-maintained clean environment is important in controlling bioburden level in the product. In order to meet the standard of clean environment, Collamatrix manufacturing site divides into two zones. The first zone is a class 10K clean room where the production facilities are located. The second zone is a class 10K clean room where a class 100 Biosafety hood is housed. The handling and filling of CollaDental Barrier is performed in a class 10K clean room. In addition to routine cleaning procedure, a monitoring program comprising temperature, humidity, air-borne viable count, air-borne particle count and differential pressure between two clean zones are also included to maintain a clean and hygienic working environment.

3. Validation of Systems and Equipments: Utility systems, manufacturing equipments, manufacturing processes and analytical methodologies used in the production of CollaDental Barrier have been validated according to established written procedures. Procedures are in place to ensure the regular maintenance of equipment and the regular monitoring of environmental conditions within the production facilities.

B. Stability studies

The proposed shelf life of CollaDental Barrier is one month. Stability study of the device comprises real time stability at room temperature. The studies evaluate the effectiveness of terminal γ -sterilization by determining the bioburden level in the products. In addition, the color and the physical appearance of the product are also inspected.

Real-time study at room temperature condition (b)(4) Confidential is ongoing. Interim results of bioburden level for 1 month and physical appearance of the product revealed no deviation from the specification (Attachment 8.1).

C. Production batch/lot identification

Each production lot of CollaDental Barrier is assigned with an unique lot number for manufacturing and product traceability control. For example, lot number (b)(4) Confidential (b)(4) Confidential and Proprietary Information which means the CollaDental Barrier lot was manufactured o (b)(4) Confidential and Proprietary Information

9 Performance

A. Biocompatibility tests

CollaDental Barrier was subjected to a battery of tests in accordance with Part-10993 of the International Standard Organization (ISO) Standard (Biological Evaluation of Medical Devices) and the United States Pharmacopeia (USP) methods.

CollaDental Barrier has been designed to meet the following requirements: (1) cytotoxicity study, (2) ISO modified intracutaneous study (irritation), (3) murine local lymph node assay (sensitization), (4) acute systemic toxicity study, (5) *Salmonella typhimurium* reverse mutation (Ames) test, (6) hemolytic study and (7) Endotoxin test.

1. Summary of cytotoxicity study

A single extract of CollaDental Barrier was prepared using single strength supplemented Minimum Essential Medium and tested on L-929 mouse fibroblast cells at standard culture conditions for 48 hours. CollaDental Barrier showed no evidence of causing cell lysis or toxicity. (Attachment 9.1)

2. Summary of ISO modified Intracutaneous study

Two extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution and sesame oil were injected intracutaneously into the dorsal sites of rabbits. Observations for erythema and edema were conducted after injection. CollaDental Barrier showed no evidence of causing any sign of irritation at the injection sites and the primary irritation index of CollaDental Barrier was negligible. (Attachment 9.2)

3. Summary of murine local lymph node assay

The delayed contact sensitization of CollaDental Barrier was tested in mice. Two extracts of CollaDental Barrier, prepared in 0.9% sodium chloride solution and dimethylsulfoxide, were used to dose on the dorsum of ear for 3 consecutive days. The radioactive counts in the lymph nodes draining were measured using scintillation counter. The Stimulatory Index of CollaDental Barrier was insignificant and considered non-sensitizing. (Attachment 9.3)

4. Summary of Acute systemic toxicity study

Two extracts of CollaDental Barrier, prepared in 0.9% sodium chloride solution and sesame oil, were injected either intravenously or intraperitoneally into mice. Sign of mortality or evidence of systemic toxicity from the extracts were not found. Therefore, CollaDental Barrier did not cause systemic toxicity in test animals. (Attachment 9.4)

5. Summary of genotoxicity study

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested for the genotoxicity activity using the *Salmonella typhimurium* reverse mutation (Ames) test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.5)

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution or sesame oil was tested for the genotoxicity activity using micronucleus test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.6)

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride or DMSO was tested for the genotoxicity activity using mouse lymphoma test. Signs of mutagenic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause genetic mutation. (Attachment 9.7)

6. Summary of hemolysis study

Extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested for the hemolytic activity. Signs of hemolytic activity from the extracts were not found. Therefore, CollaDental Barrier did not cause blood incompatibility. (Attachment 9.8)

7. Summary of Endotoxin test

The extracts of CollaDental Barrier prepared in 0.9% sodium chloride solution were tested the pyrogenic activity using Limulus ameocyte lysate (LAL) gelation assay. Sign of LAL reactivity from the extracts was not found. (Attachment 9.9)

B. Sterilization

CollaDental Barrier is sterilized by γ -irradiation. The terminal sterilization service was performed by China Biotech Corporation (FDA establishment registration number: 9681277), an ISO 13485:2003 and ISO 9001:2000 quality management systems certified contract sterilizer.

Sterilization of CollaDental Barrier was validated according to ISO 11137:2006

Sterilization of Health Care Products – Radiation. Dosimetry results revealed that the (b)(4) Confidential

(b)(4) Confidential and Proprietary Information

indicating that devices received

sufficient sterilization dose (Attachment 9.10).

C. Sterility

CollaDental Barrier is sterilized by irradiation according to ISO 11137:2006. Sterility of CollaDental Barrier was verified using fluid thioglycollate medium (for bacteria) and Potato Dextrose agar (for yeasts and molds) per USP <71>. Results have consistently demonstrated that no microorganism was detected in the sterilized CollaDental Barrier. The effectiveness of γ -sterilization is validated and further substantiated by stability study. (Attachment 8.1)

10 510k Summary

A summary of the 510k safety and effectiveness information upon which the substantial equivalence of CollaDental Barrier is based is prepared to meet the requirements as defined in 21 CFR § 807. (Attachment 10.1)

Attachment 4.1 Substantial equivalence of Barrier

Substantial Equivalence comparison chart

Device name	CollaDental Barrier	BioMend Extend absorbable collagen membrane	BIO-GIDE®
Manufacturer	Collamatrix Inc.	Integra LifeSciences corp.	Ed. Geistlich Söhne AG für chemische Industrie.
510(k)	-	K992216	K042197
Product code	NPL	LYC	NPL
Intended use	augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided tissue regeneration procedures in periodontal defects.	Indicated for guided tissue regeneration procedures to enhance regeneration of periodontal apparatus.	Simultaneous use of GBR-membrane and implants; augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects; guided tissue regeneration procedures in periodontal defects.
Contents	Collagen	Collagen	Collagen
Biocompatibility	Yes	Yes	Yes
Sterility	Yes	Yes	Yes
Compatible sizes	Yes	Yes	Yes

Attachment 5.1 Subcutaneous implantation

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Report no:

CMI-2009118B

Study Title:

Subcutaneous implantation study

Test Article:

CollaDental Barrier

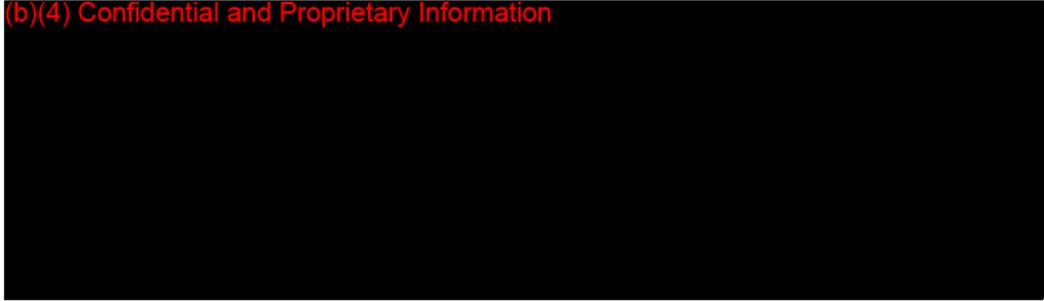
November, 2009

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Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Township

Miaoli County, 350, Taiwan

Study announcement:

1. This report could not be reprinted or adapted without the permission from (b)(4) Confidential and Proprietary Information

(b)(4) Confidential and Proprietary Information and Collamatrix Inc.

Approved by

Date

Jasper Chou

2009.11.30

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The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

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SUMMARY

A subcutaneous implantation study was conducted on CollaDental Barrier to test for its biodegradability. CollaDental Barrier was surgically implanted in the subcutaneous tissue

of rats and the remaining surface area of test article was evaluated periodically at

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Proprietary Information

weeks post-implantation. Under the test condition described here,

(b)(4)
Confidential

the resorption time of CollaDental Barrier was

(b)(4) Confidential
and Proprietary

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OBJECTIVE

The objective of the test is to evaluate the resorption of CollaDental Barrier in surgically created subcutaneous wounds as reference to determine the duration of use of the device.

MATERIALS AND METHODS

Test article

Test article: CollaDental Barrier (Table 1)

Table 1 Information on CollaDental Barrier

Dimension	15mm x 20mm
Feature	Membrane
Sterility	Gamma ray irradiated
Color	White to off white
Component(s)	Porcine collagen
Packaging	Sponge houses in PET blister pouch
Storage condition	23°C ± 3°C, 60% Relative humidity

Experimental Animals

Thirty five male Sprague-Dawley (SD) rats were received from BioLASCO Taiwan Co, Ltd., with body weights in the range of 200g to 220g. The animals were kept for 3~4 days prior to initiating the experiment (for acclimatization), examined, and separated into two groups of three rats on the basis of body weights. All animals were housed in (b)(4) Confidential and Proprietary Information and cared for according to the Animal Welfare Act and Guidelines for the Care and Use of Laboratory Animals.

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Wounding Technique

Experimental animals were clipped with standard animal clippers on the day of the experiment. The skin on the back and both sides of the animal were prepared for wounding by washing with a non-antibiotic soap and sterile water. Antiseptics were not used because of their potential effect on the healing process. Each animal was anesthetized I.M. with ketamine HCl (15mg/kg), xylazine (0.2mg/kg) and atropine (0.05mg/kg), followed by mask inhalation of an isoflurane and oxygen combination.

Pockets were created on the back of the animals. One test article (1cm x 1cm) was implanted subcutaneously into each pocket created by a blunt dissection through 10 mm incision of the skin of each rat. The skin was closed with stainless steel wound clip and was returned to their respective cages and monitored for recovery from the anesthetic. Another dose of buprenorphine was administered a minimum of 4 hours following the first dose.

Rats were observed daily for general health and body weights were recorded prior to implantation and at termination. Rats were sacrificed according to a pre-determined schedule to determine the degree of resorption of CollaDental Barrier. Rats were weighed and euthanized by an intravenous injection of a sodium pentobarbital based drug.

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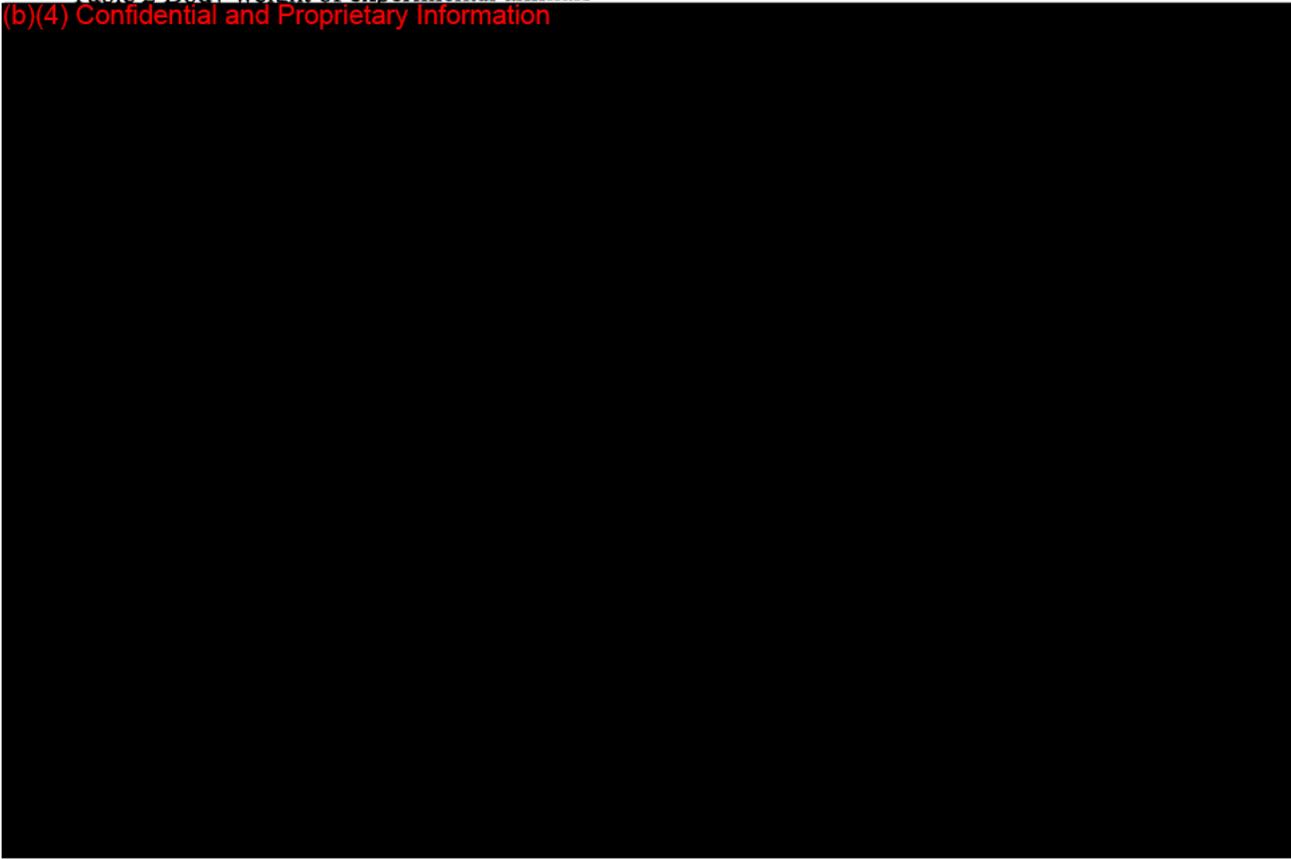
RESULTS

Clinical observations

All animals were clinically normal during this study. Gradual increase in body weight of the animals was observed during the course of experiment as shown in Table 2 below.

Table 2 Body weight of experimental animals

(b)(4) Confidential and Proprietary Information

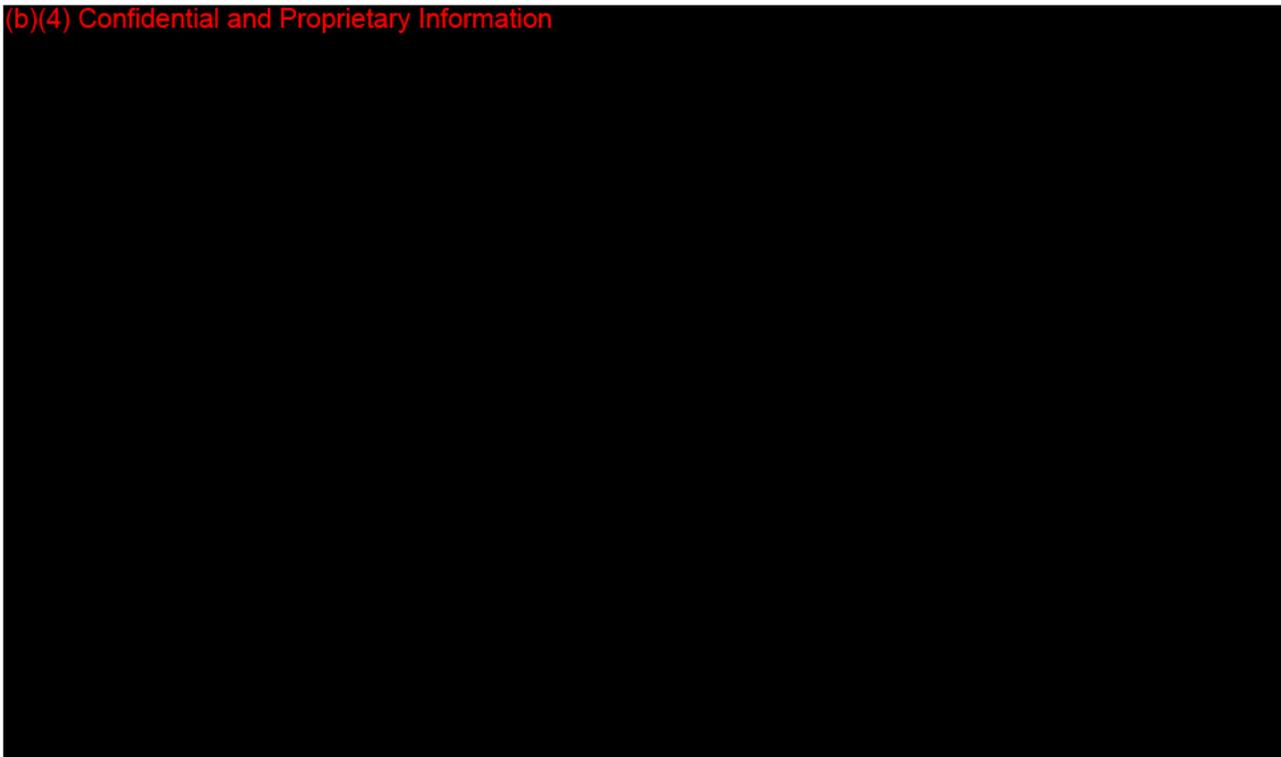


Resorption of CollaDental Barrier

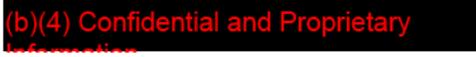
The study duration of CollaDental Barrier resorption (b)(4) Confidential and Five rats were sacrificed according to the pre-determined sampling schedule and the area of each implant was individually measured. The readings of implant area obtained from different time point were shown in Table 3. An average (\pm SD) of area measurements from each time point was determined and plotted against implantation duration (Figure 1).

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(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



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CONCLUSION

CollaDental Barrier is a biodegradable collagen-based device. The biodegradability of CollaDental Barrier was evaluated in a subcutaneous implantation in rats to substantiate its claims for biodegradability and time required to achieve resorption. During this study, all animals appeared clinically normal including grooming behavior and sweating, and the gradual change in body weight have been observed (Table 2). Under the test condition described above, results shown in Figure 1 revealed that CollaDental Barrier began to degrade (b)(4) Confidential and Proprietary Information. Degradation continued for (b)(4) Confidential and Proprietary Information weeks until two of the implants were not detected (Table 3). Results indicated CollaDental Barrier was resorbed within (b)(4) Confidential and Proprietary Information.

Attachment 6.1 Virus inactivation report

COLLAMATRIX

Virus inactivation study	Date	20081103
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Introduction

The primary concern of using animal-derived materials was the cross-species transfer of transmissible agents such as virus. The goal of this study was to evaluate the virus inactivation steps for the production of non-bovine derived extracellular matrix biomaterials for manufacturing medical devices and implantation applications. Avian feet and porcine hides were used as the source for biomaterial preparation. This aim of this study was to demonstrate the inactivation processes (1) could effectively inactivate transmissible pathogens that could potentially be transmitted by the product; (2) had the capacity to inactivate novel or yet undetermined pathogens contamination in the product; (3) could ensure that product quality was consistently maintained and met customers or regulatory requirements.

The inactivation steps comprised a disinfection step (b)(4) Confidential and Proprietary Information
 (b)(4) Confidential and Proprietary Information

The virus inactivation achieved by the disinfection step and the (b)(4) Confidential and Proprietary Information was validated using (b)(4) Confidential and Proprietary Information. Their molecular characteristics were summarized in Table 1. These viruses are the representatives of different genomic types and composition, envelope or sizes of viral contaminant that could present in animal tissues.

Table 1. Model viruses used for inactivation study

Virus	Genome type	Envelope	Size (nm)
(b)(4) Confidential and Proprietary Information			

COLLAMATRIX

Virus inactivation report	Date	20081103
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Materials and methods

Viruses and cells

The following virus-cell systems were used for viral propagation and titration: (b)(4) Confidential

(b)(4) Confidential and Proprietary Information

(b)(4) Confidential and Proprietary Information

was used as a model virus for any endogenous uncharacterized retroviruses found in animals. These combinations were chosen because plaque formation and focus formation assays performed using these systems are commonly accepted as valid assays to evaluate viral inactivation for medical device regulatory approval.

(b)(4) Confidential were cultured in DMEM supplemented with 10% fetal bovine serum and 2 mM L-Glutamine. (b)(4) Confidential and Proprietary were maintained in RPMI 1640 supplemented with 10% fetal bovine serum and 2 mM L-Glutamine. (b)(4) Confidential were maintained in RPMI 1640 supplemented with 10% fetal bovine serum. All cells were maintained in a humidified chamber at 37°C, with 5% CO₂.

Samples preparation and spiking

Frozen porcine hide prepared from the market weight pigs with hair and fat had been removed was thawed at room temperature before use. Hides were washed thoroughly in sterile water to remove debris or blood. 10 grams of tissues were randomly injected with (b)(4) Confidential and Proprietary Information suspended in culture medium to a concentration approximately (b)(4) Confidential plaque-forming unit (PFU).

Disinfection steps

After spiking with virus-containing medium, hides were thoroughly rinsed with sterile water and then followed by the treatment with (b)(4) Confidential and Proprietary Information in a sequential order at room temperature. Treatment parameters were summarized in Table 2. Three samples of tissue for each virus were tested.

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Virus inactivation report	Date	20081103
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After air-dried, the disinfected tissues were homogenized and the residual virus activity was measured by plaque-formation assays.

Table 2. Procedures and details of the disinfection treatment

Steps	Final concentration	Duration (min)
(b)(4) Confidential and Proprietary Information		

(b)(4) Confidential and Proprietary Information

Homogenized spiked samples were suspended (b)(4) Confidential in an aqueous solution containing (b)(4) Confidential and Proprietary Information. The suspension was incubated at (b)(4) Confidential with constant stirring for (b)(4) Confidential.

Viral plaque assay

(b)(4) Confidential and Proprietary Information cultured in triplicate in six-well plate to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were ten fold serially diluted in MEM cell culture medium. Plates were incubated at 37°C, 5% CO₂ for 1 hr with gentle rocking at 20 min interval to facilitate absorption. Following absorption, plates were overlaid with 0.5% Sea Plaque agarose containing dissolved in MEM medium and continua to grow until plaque formation was observed in positive control (4~5 days post-infection). Infected cells were fixed in formaldehyde solution for 12 hrs. Fixative and agarose were gently removed before the addition of plaque-staining dye, crystal violet blue. The 0.1% staining dye was prepared by dissolving the dye in ethanol. The lightly stained plaque against the densely stained dark background was calculated and expressed as plaque-forming unit.

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Virus inactivation report	Date	20081103
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(b)(4) Confidential and Proprietary Information cultured in triplicate in six-well plates to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were ten fold serially diluted in RPMI culture medium. After infection, the plaques were counted by eye under the microscope after 2 days post-infection.

(b)(4) Confidential and Proprietary Information cultured in triplicate in six-well plates to 80% confluency were incubated with 0.1mL of homogenized tissue samples, which were tenfold serially diluted in RPMI 1640 cell culture medium. Plates were incubated at 37°C, 5% CO₂ for 1 hr with gentle rocking at 20 min interval to facilitate absorption. Following absorption, culture medium was replaced with fresh RPMI 1640 containing (b)(4) Confidential and Proprietary Information. The culture medium was replaced with fresh medium after 72 hours post-infection and continued to grow for another 5 days. After 8 days, foci observed as clustered and remained attached to the culture plate were counted and expressed as viral titer.

Results

Spike recovery of virus following injection into tissue samples before the inactivation steps was performed to show that virus remained viable after injection into the tissues. Virus titers were not significantly affected in the culture system (Table 3. *Spike recovery*). After confirming the stability of the virus in the culture system, these value readings were used as the basis for inactivation studies.

Inactivation studies utilizing spiking experiments with (b)(4) Confidential and Proprietary Information were performed to give a quantitative estimate of viral inactivation.

COLLAMATRIX

Virus inactivation report	Date	20081103
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Table 3. Validation of viral inactivation

	Reduction log ₁₀
	(b)(4) Confidential and Proprietary Information
Treatments	
Spike recovery	
Disinfection step	
Total clearance	

	* Reduction log ₁₀
	(b)(4) Confidential and Proprietary Information
Treatments	
Spike recovery	
(b)(4) Confidential and Proprietary Information	
Total clearance	

Overall total clearance	(b)(4) Confidential and Proprietary Information
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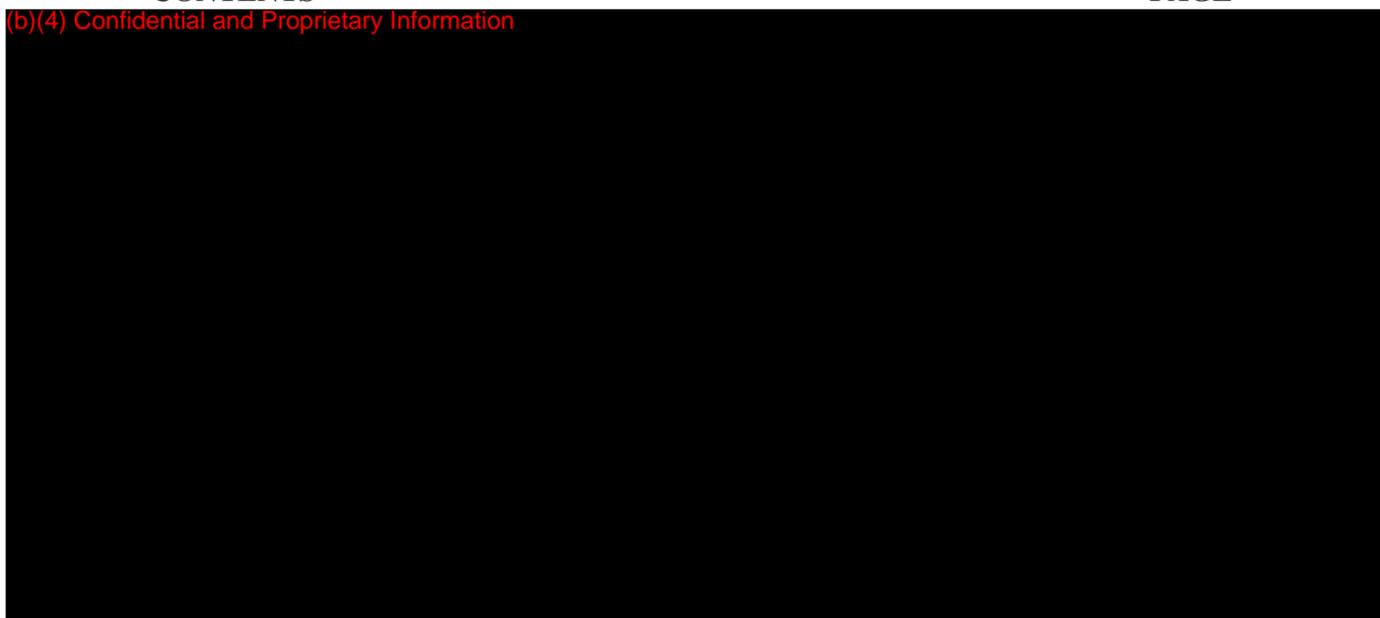
* Calculation of log reduction value = $[(C1 \times V1) / (C2 \times V2)]$, *C1*, *V1* initial viral concentration and volume, *C2*, *V2* postprocessing viral concentration and volume.

MSDS and COA of Manufacturing Materials

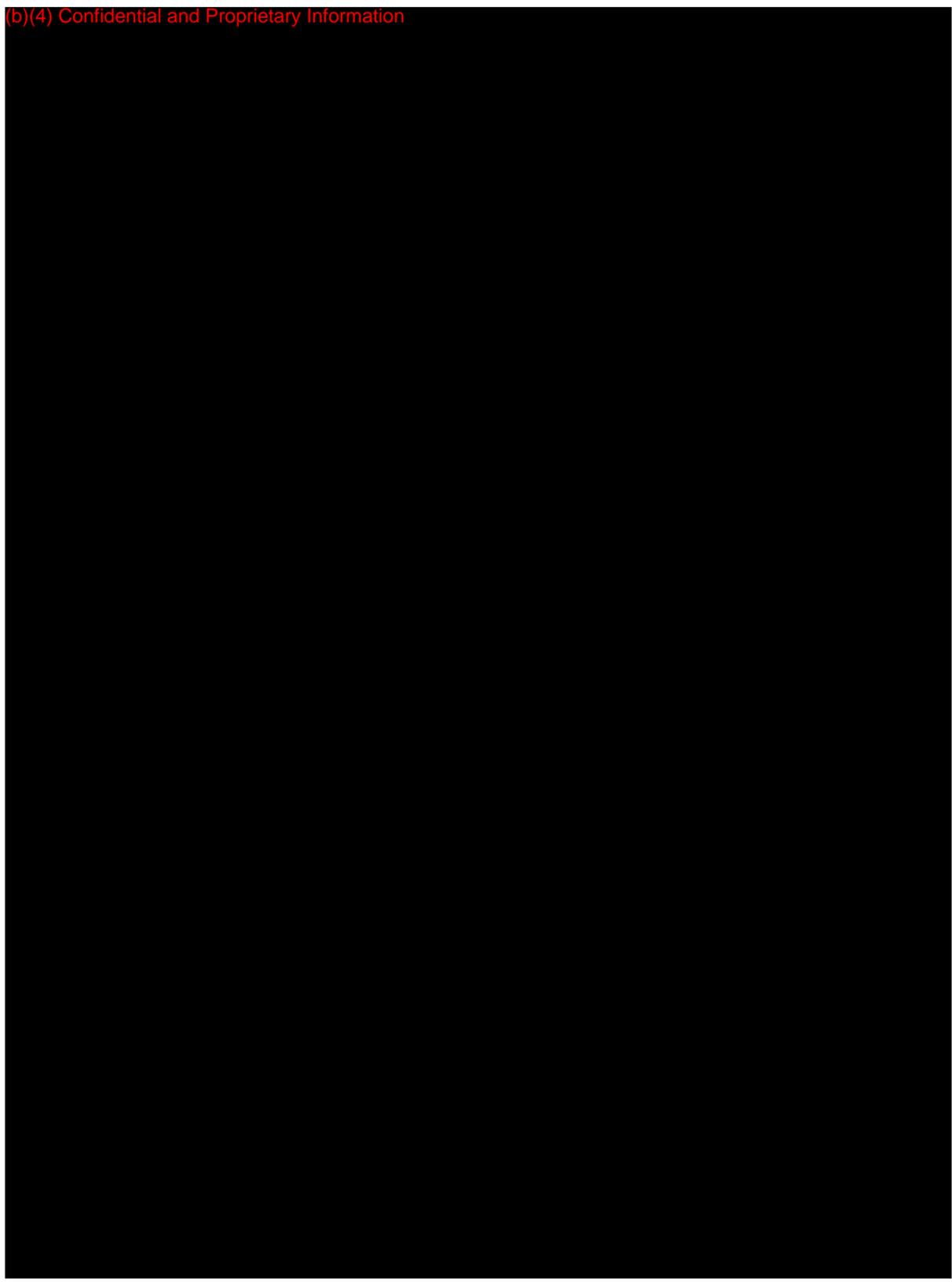
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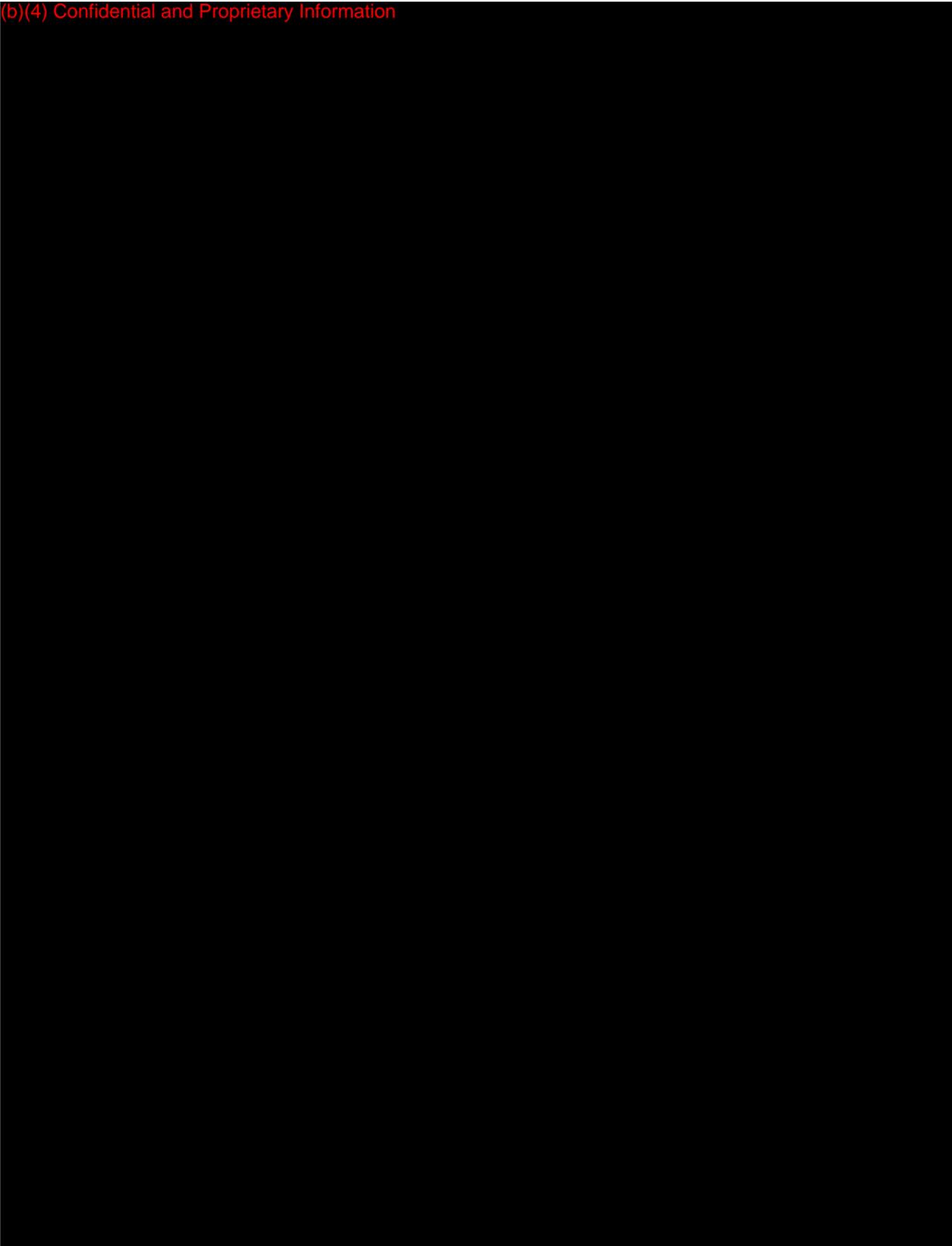
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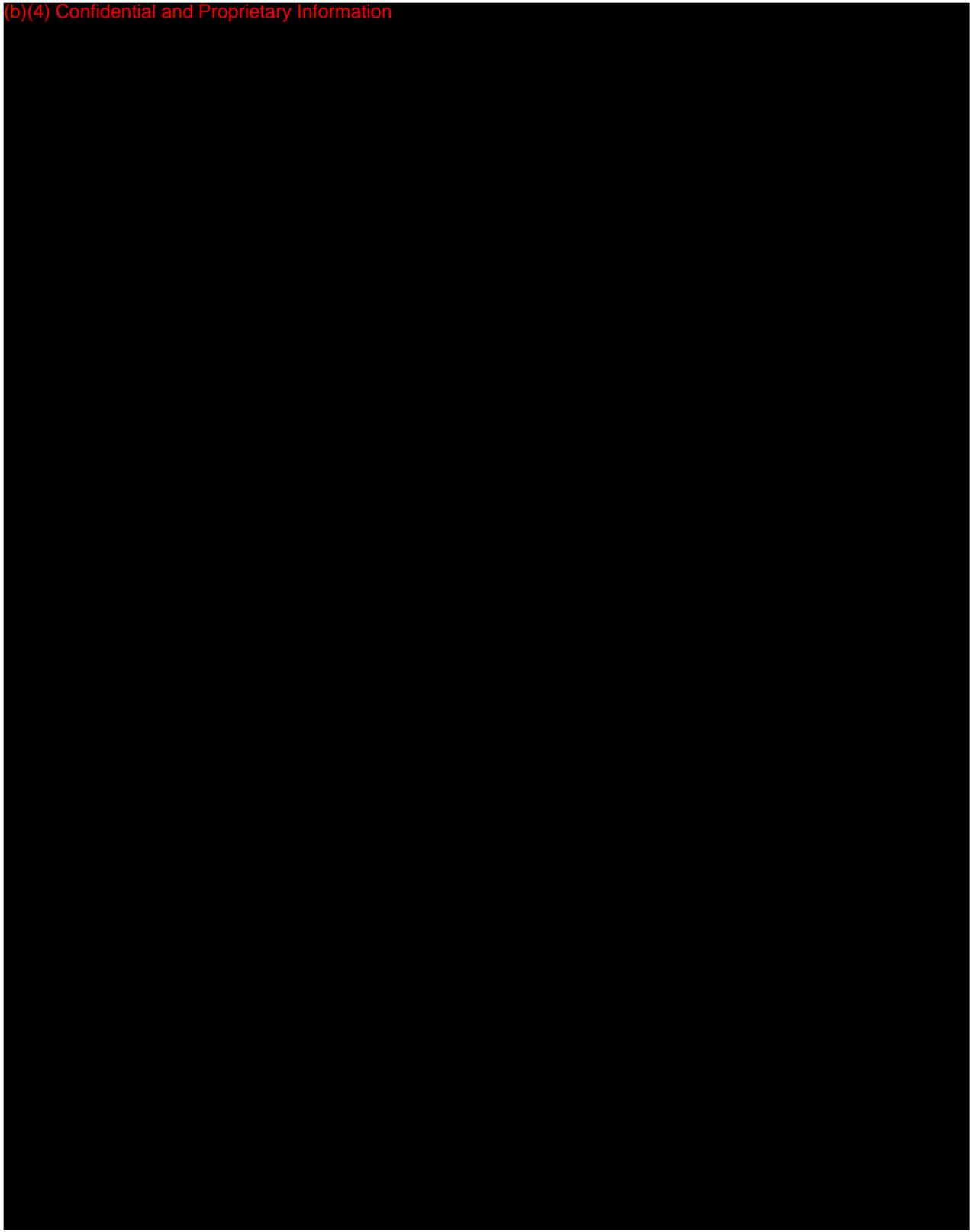
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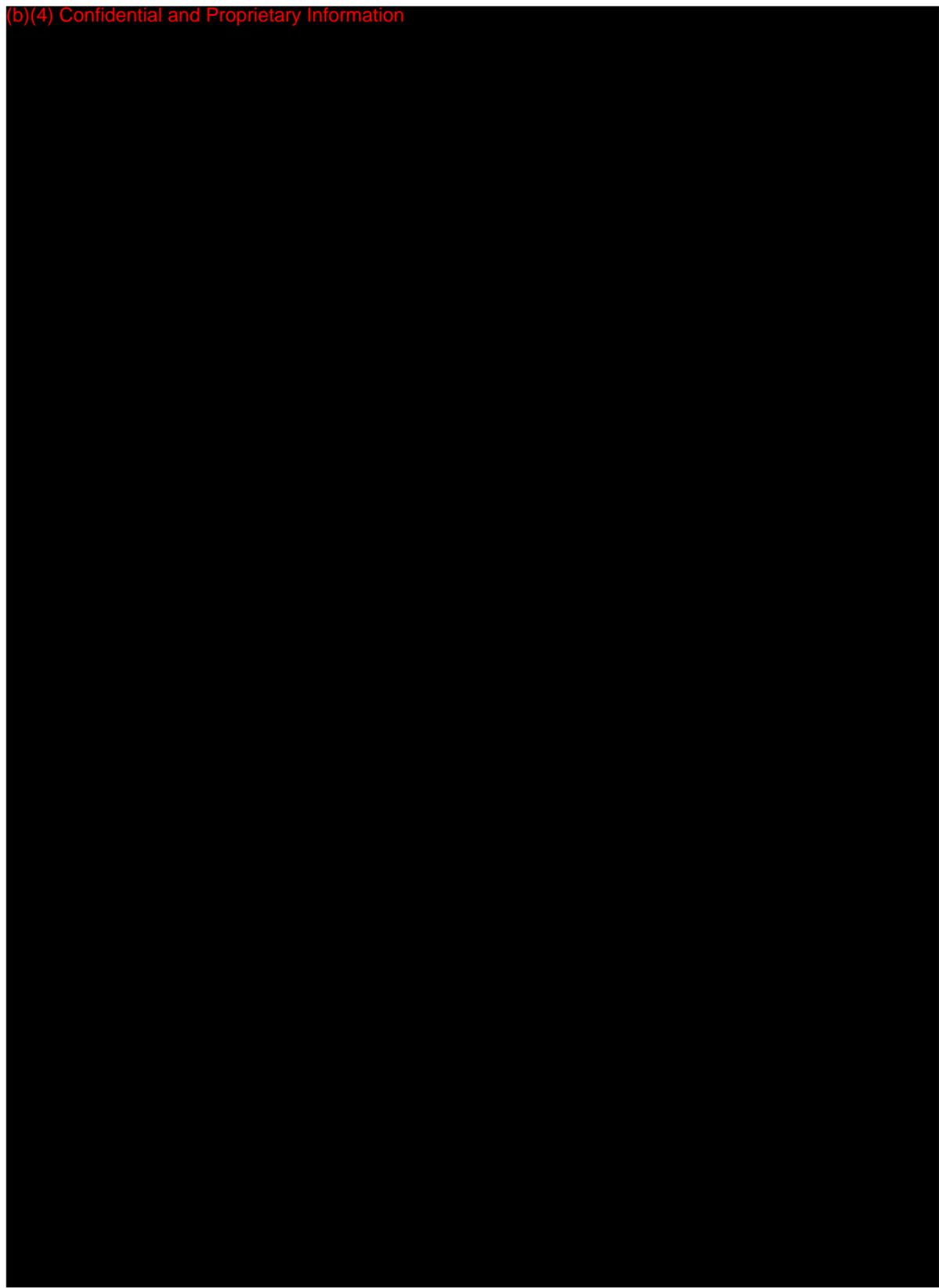
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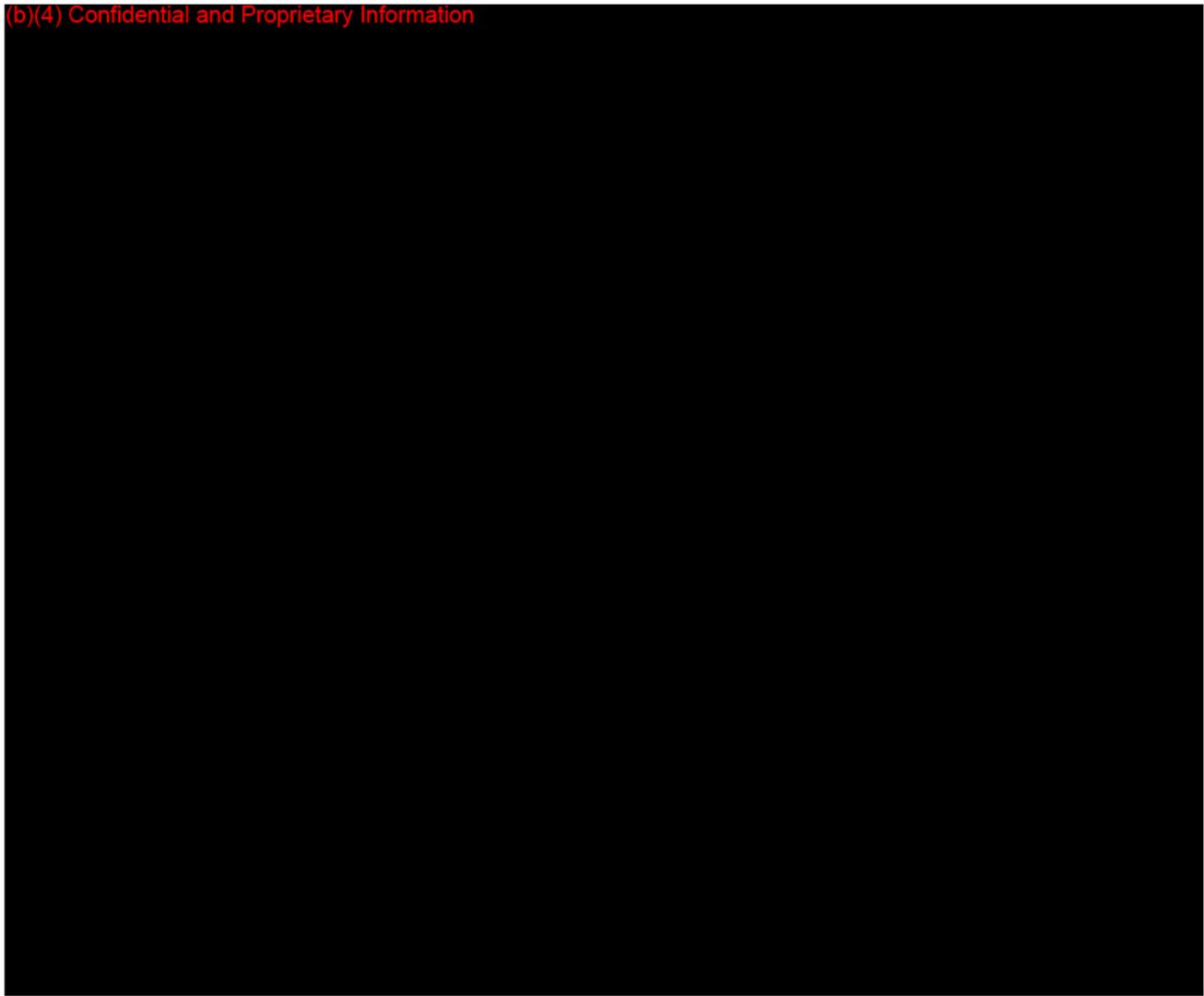
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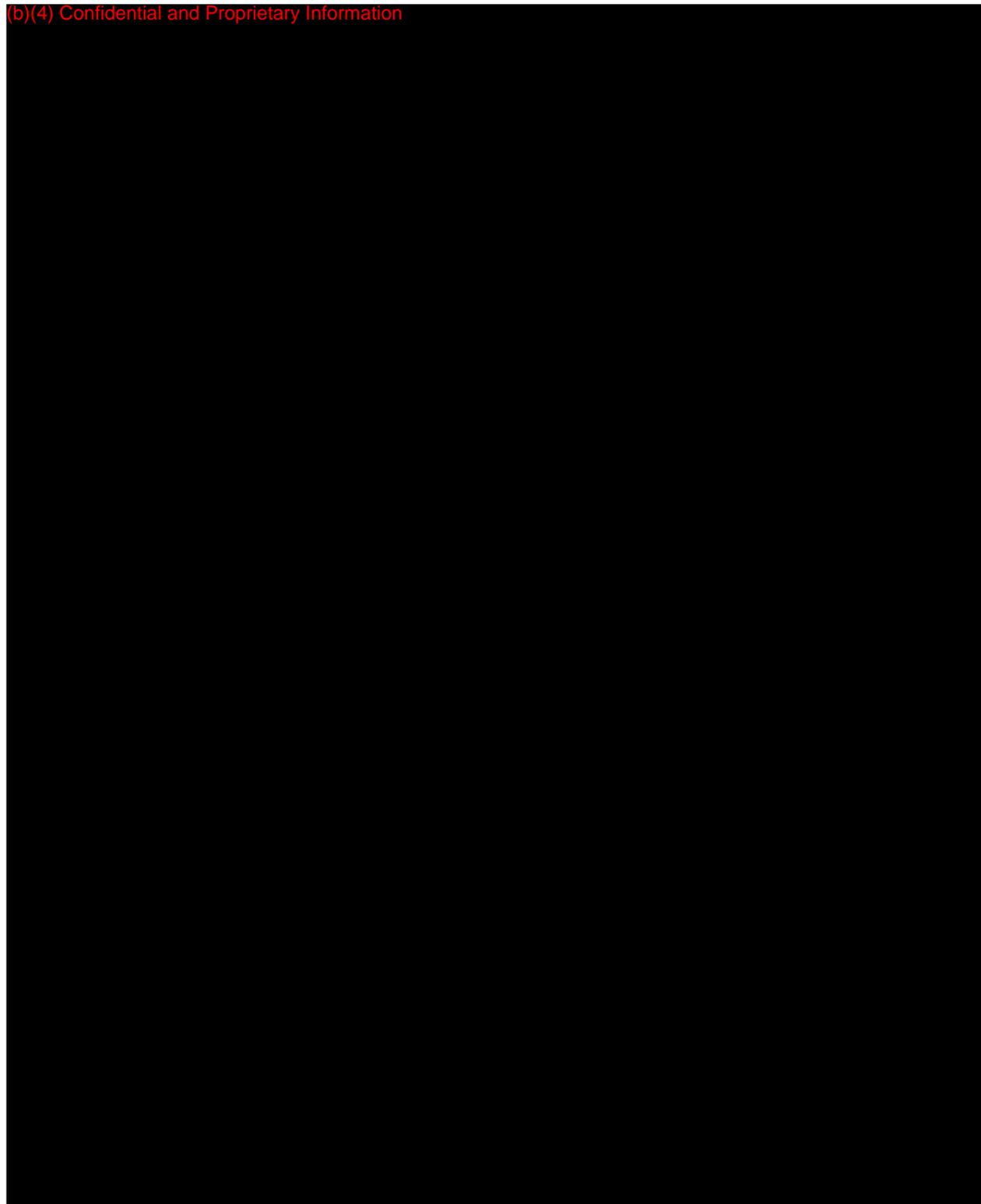
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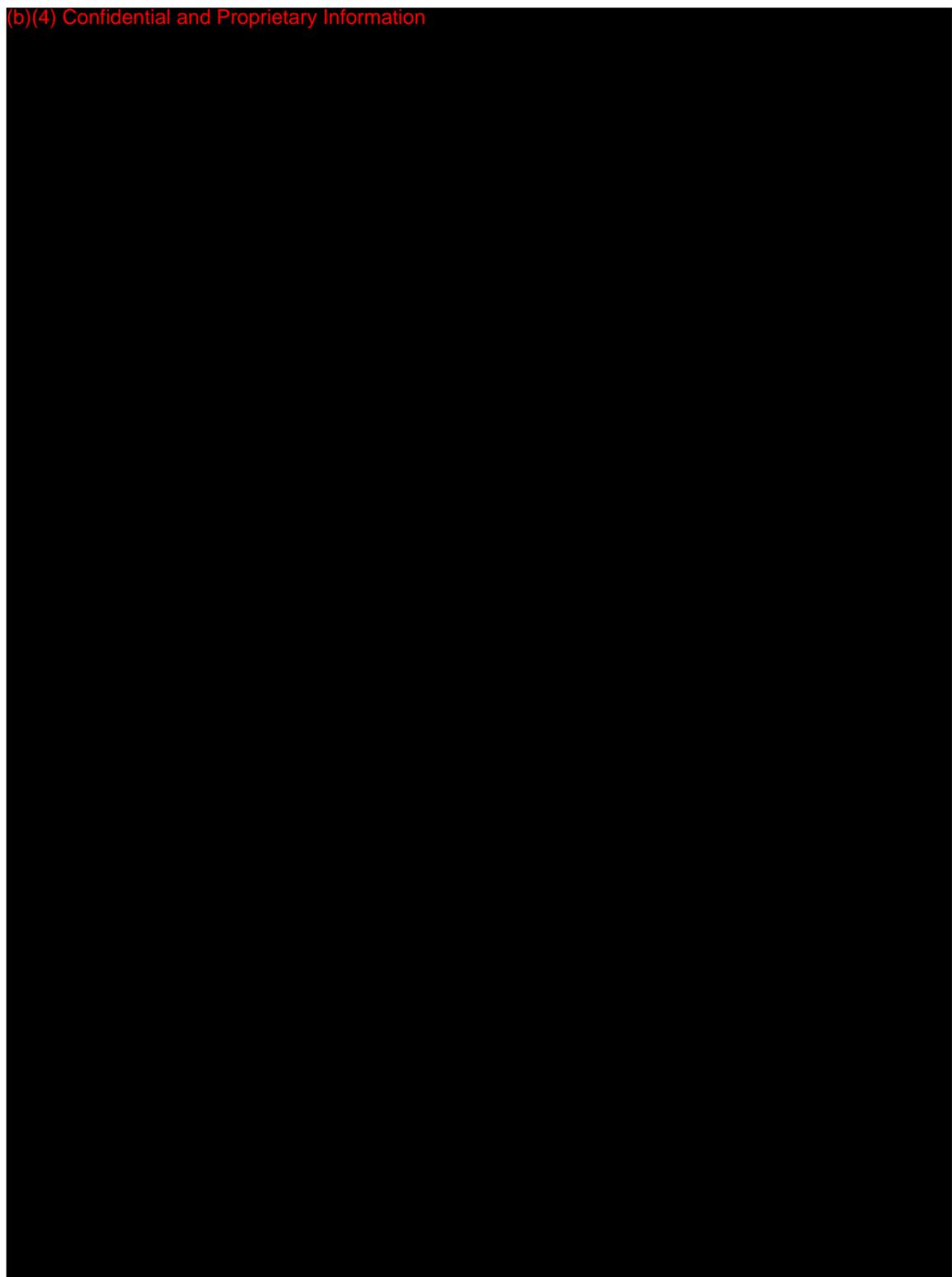
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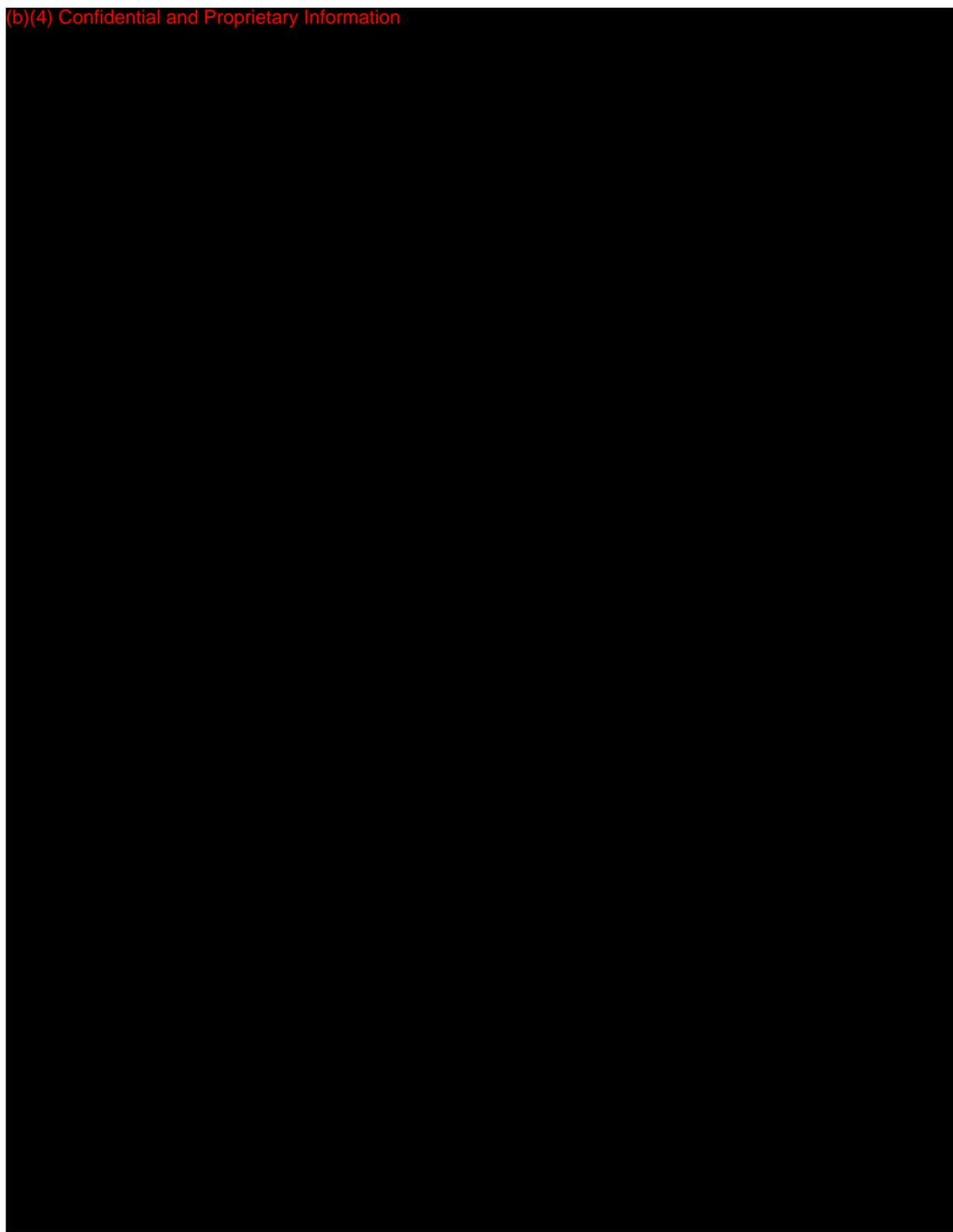
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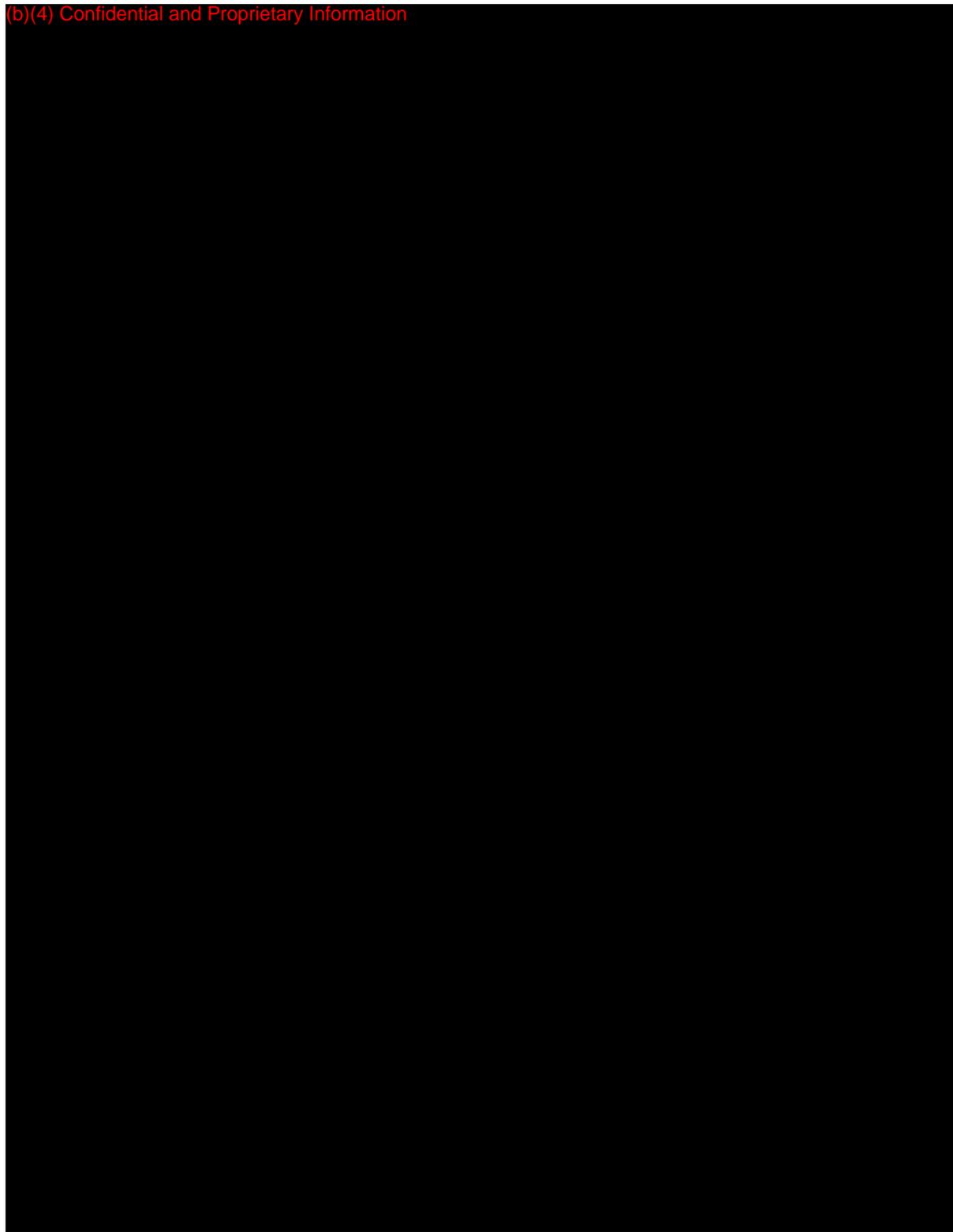
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(b)(4) Confidential and Proprietary Information



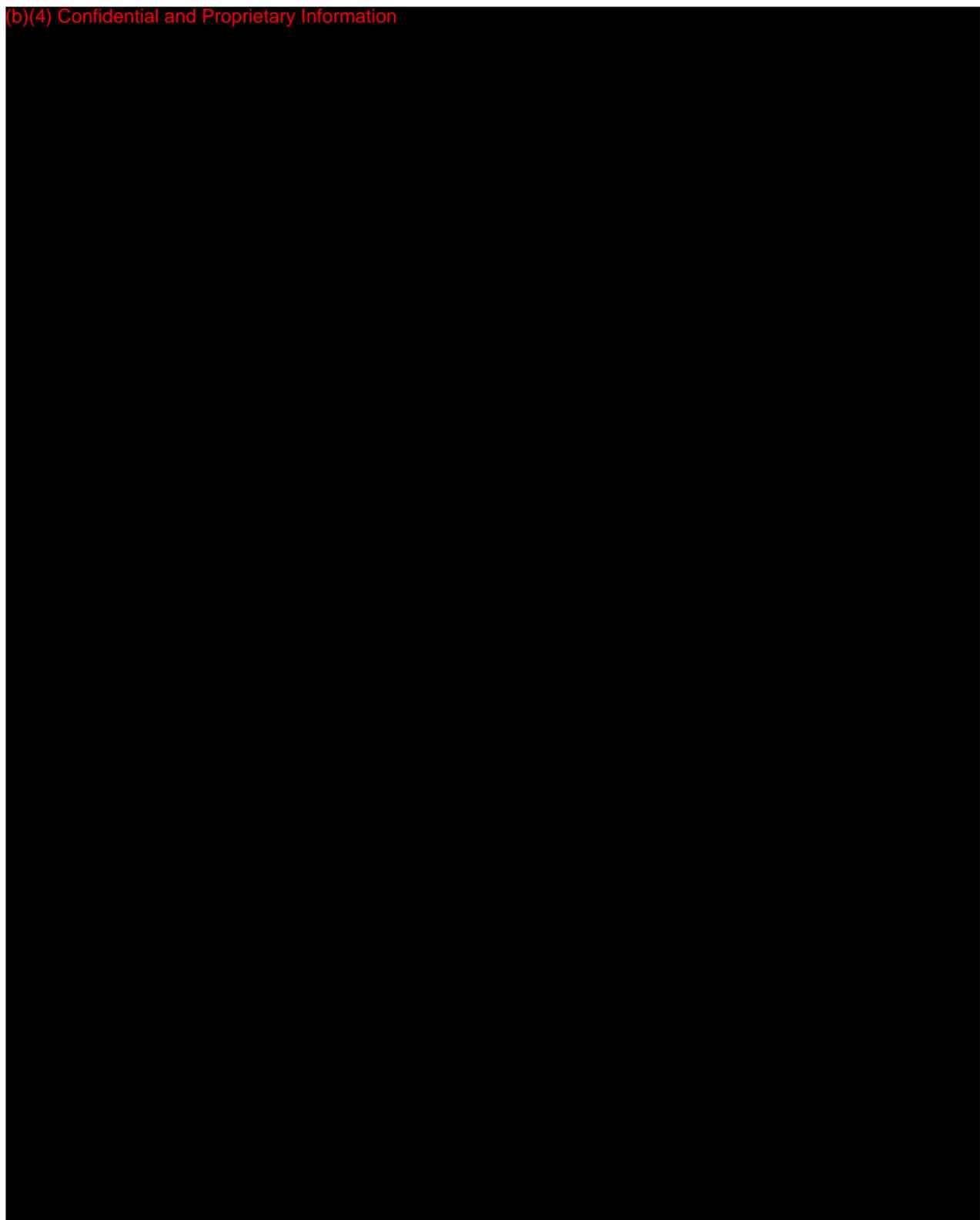
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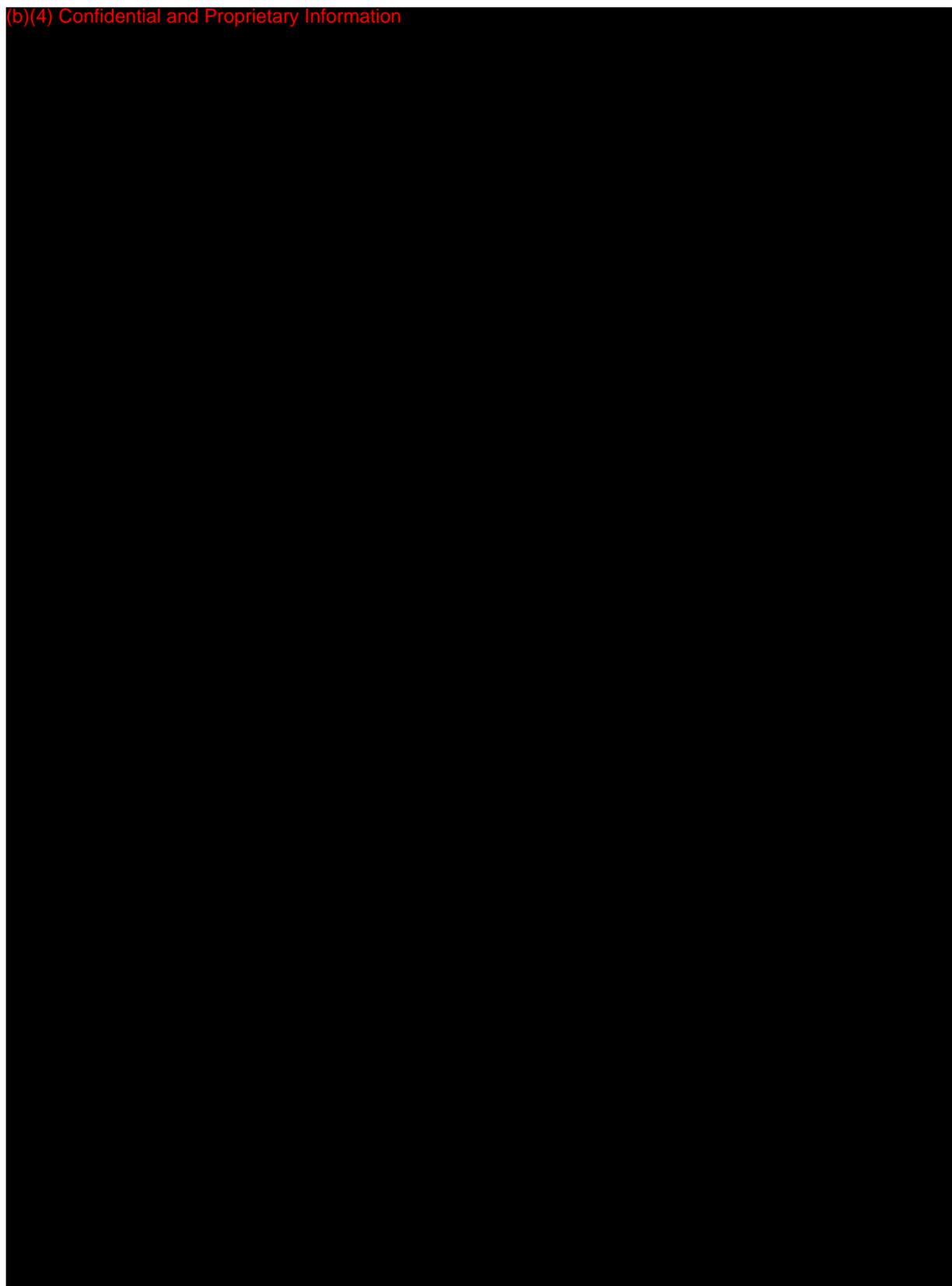
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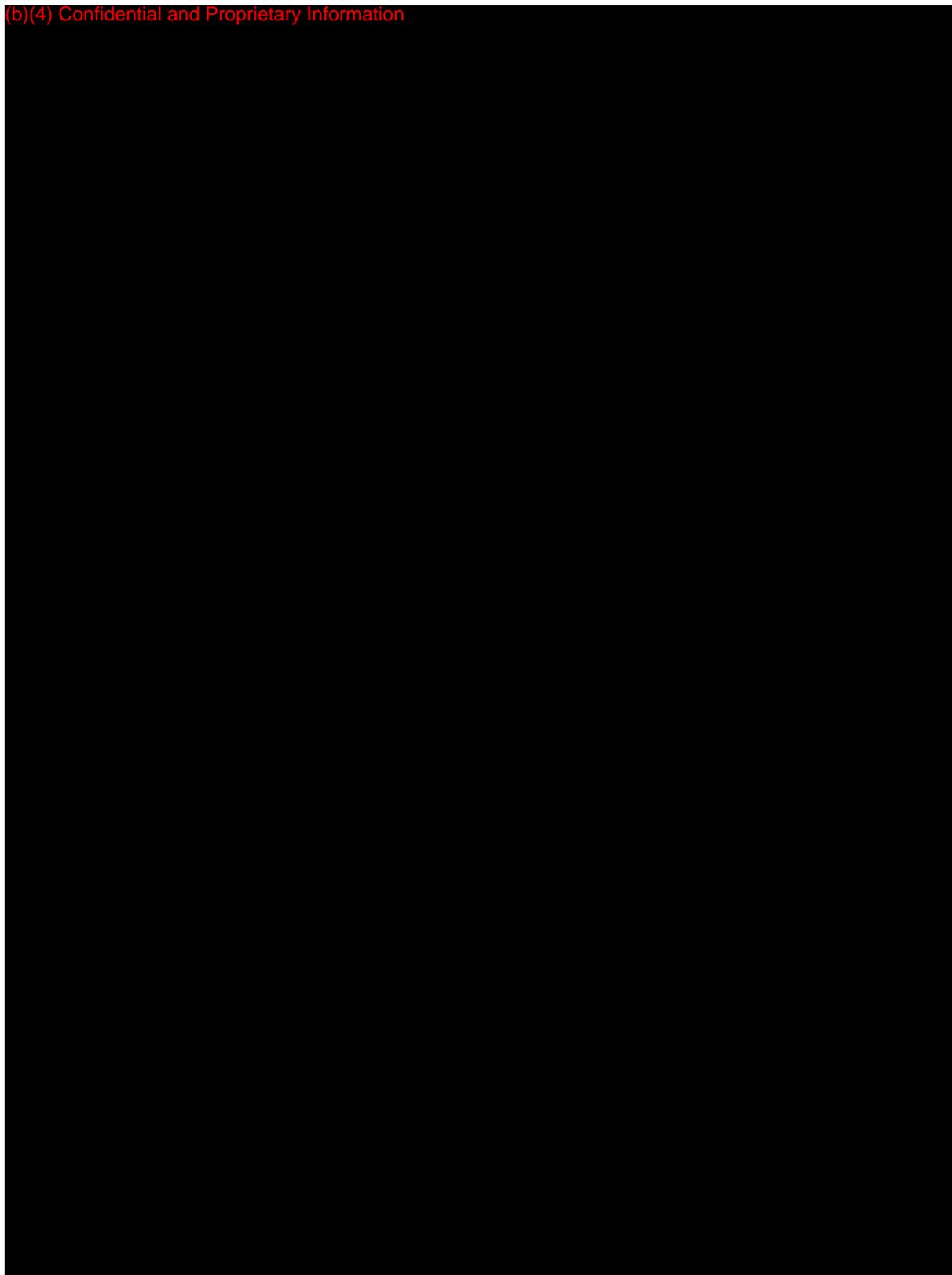
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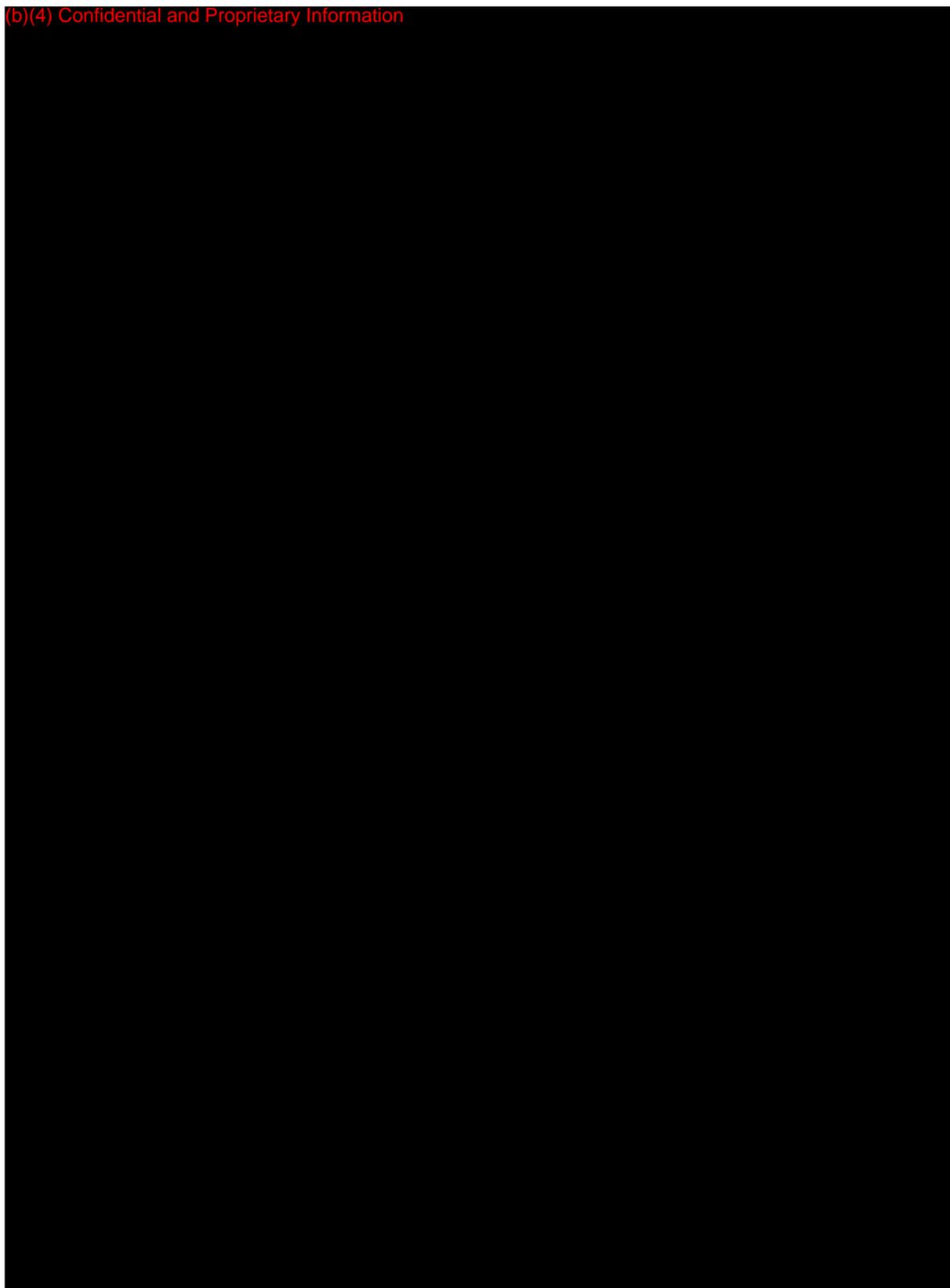
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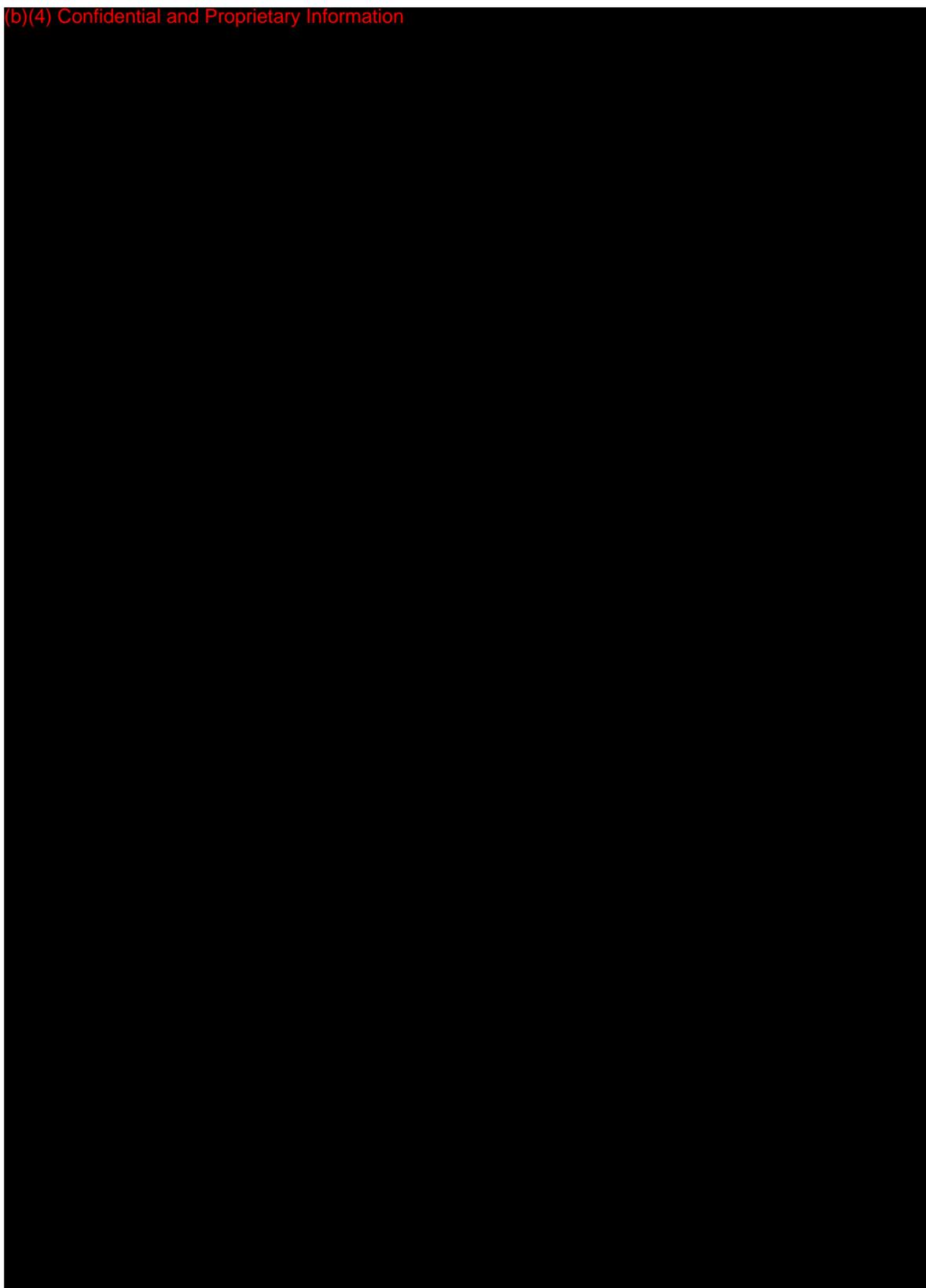
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(b)(4) Confidential and Proprietary Information



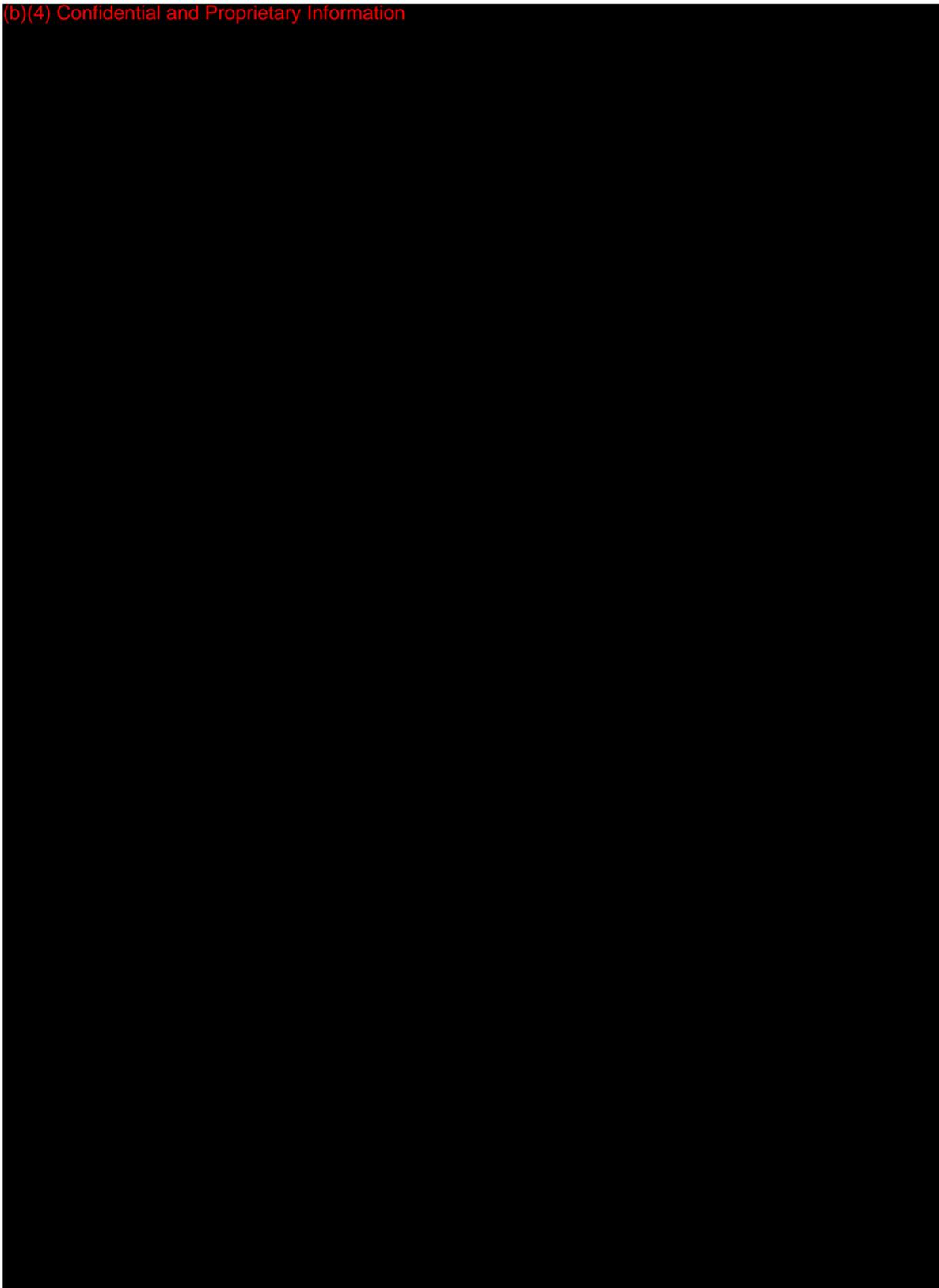
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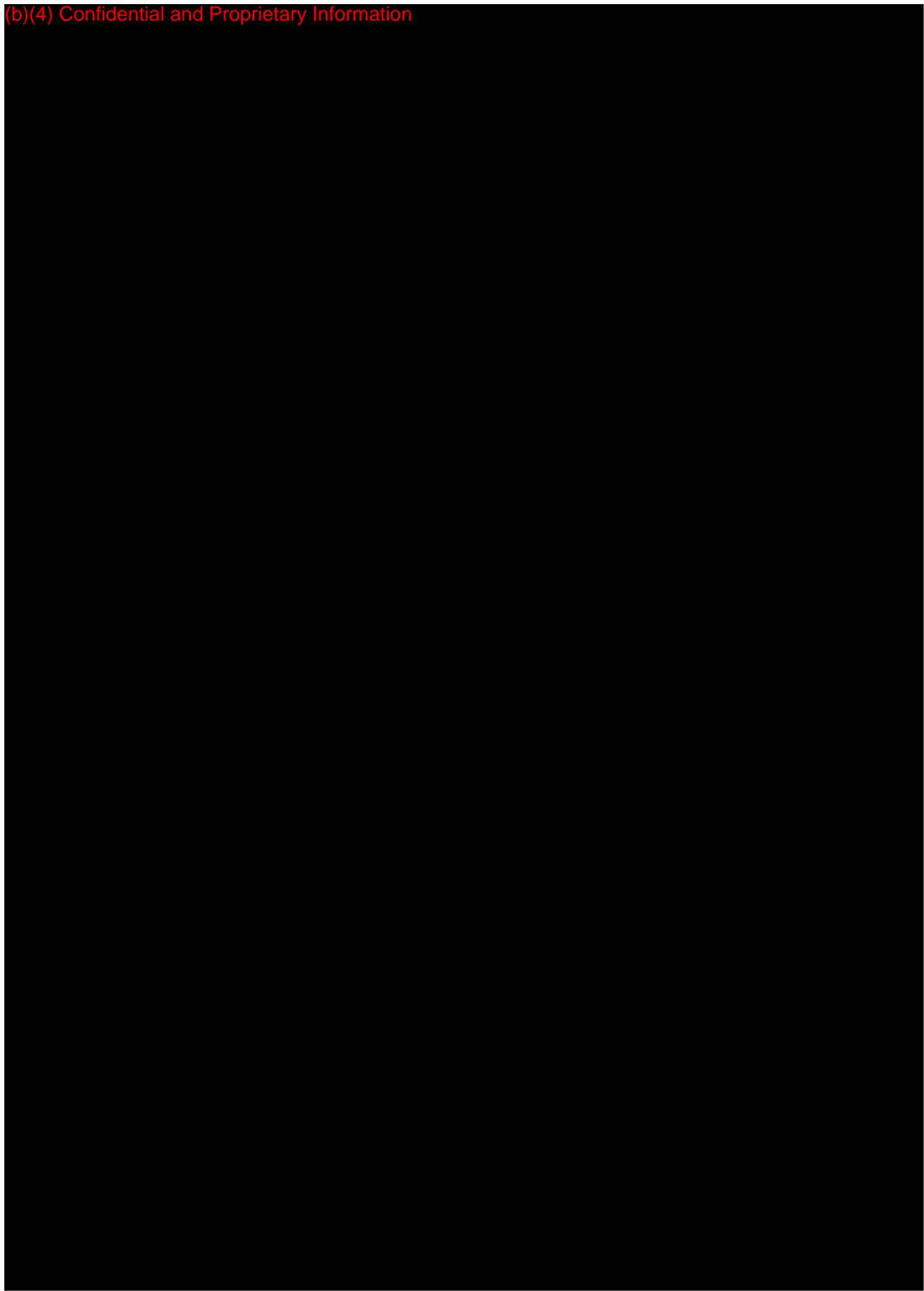
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(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



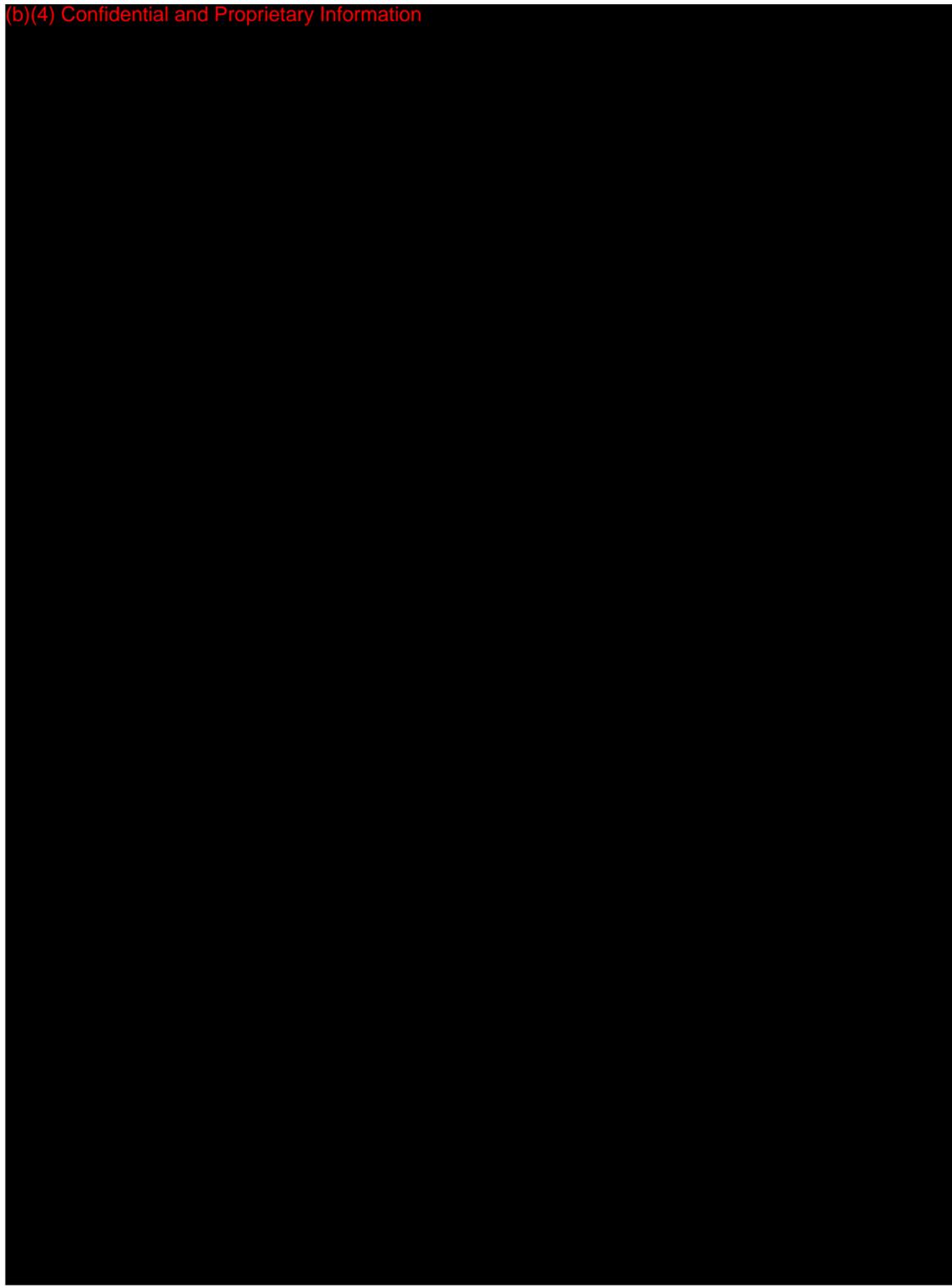
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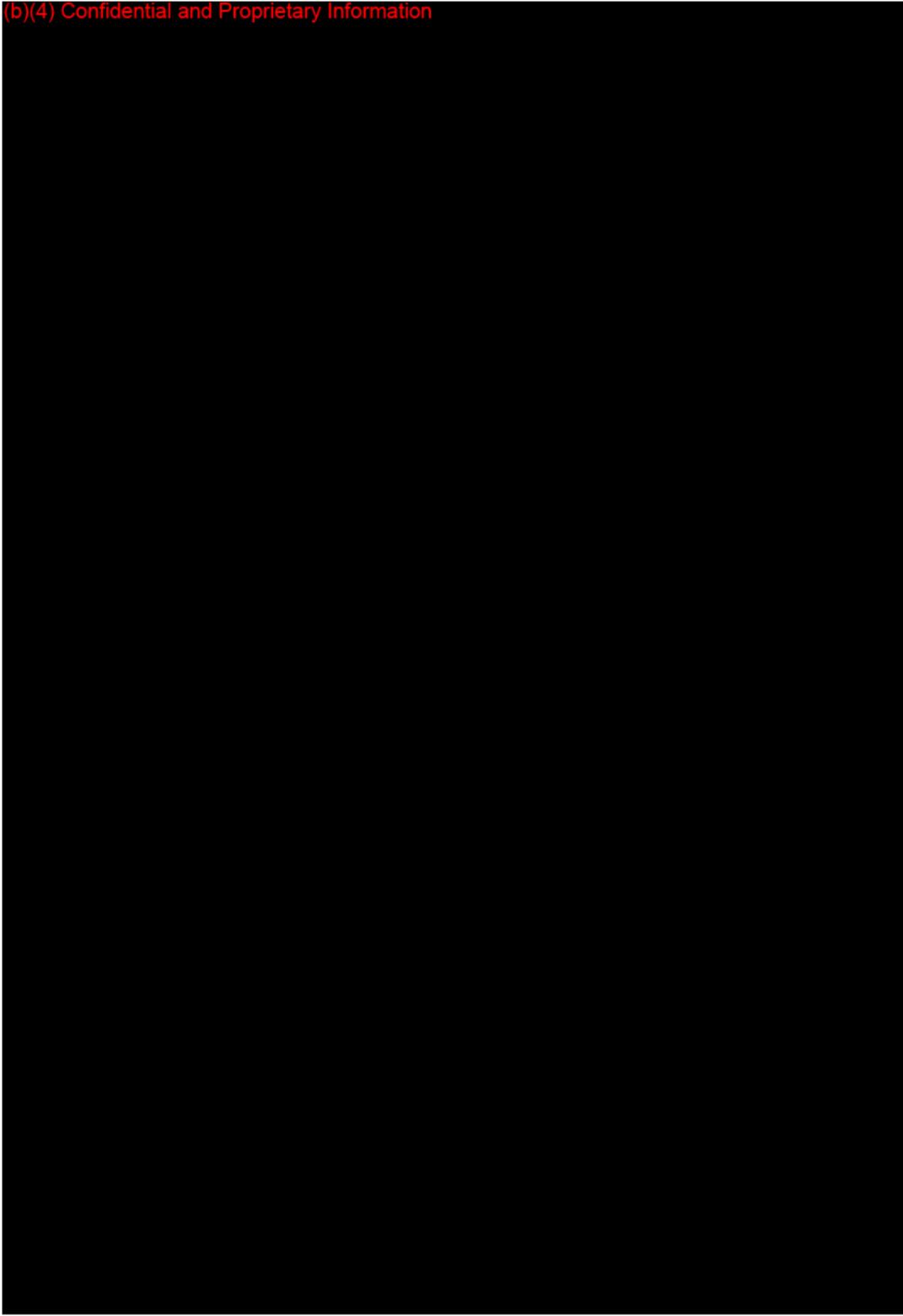
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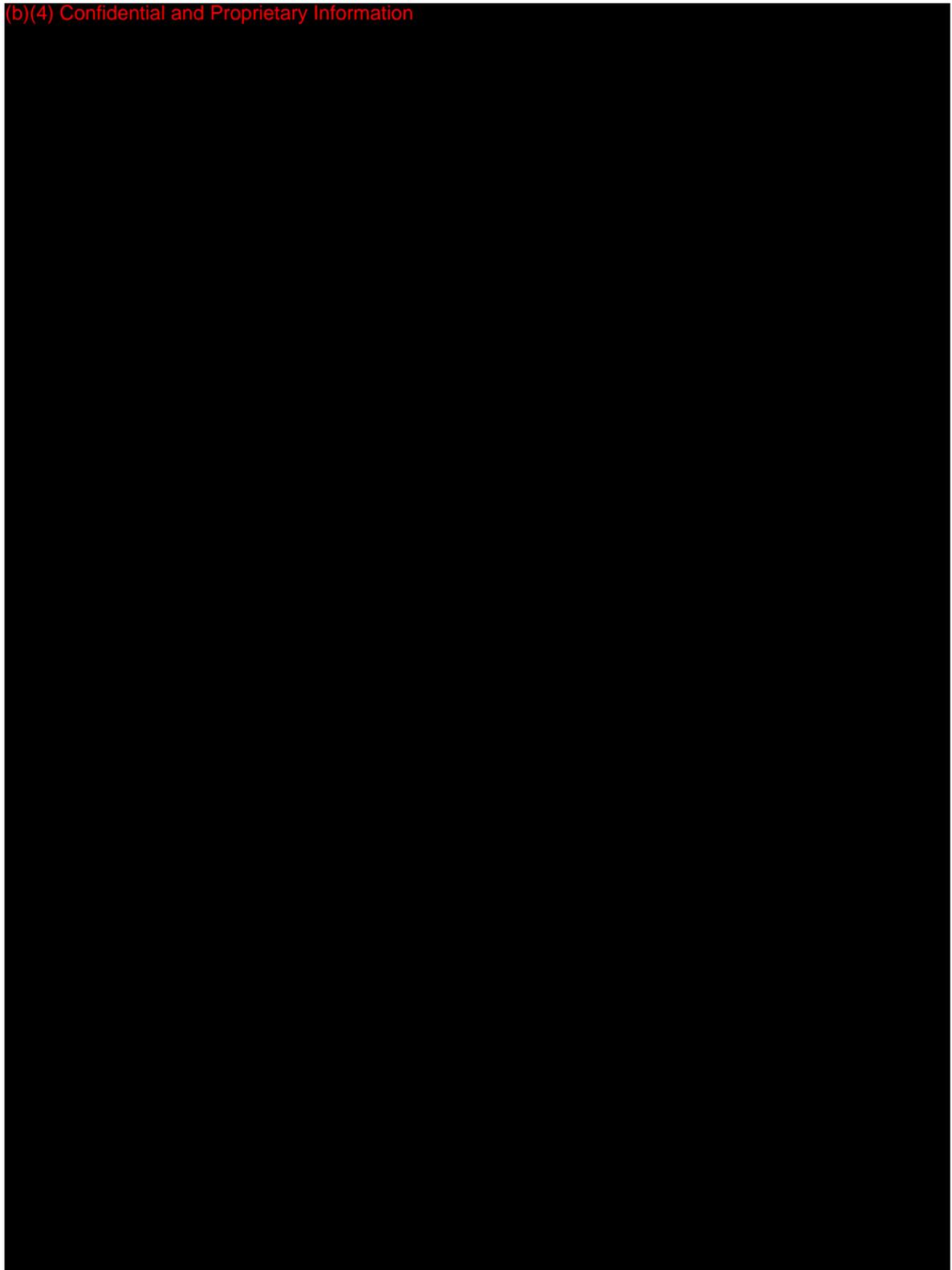
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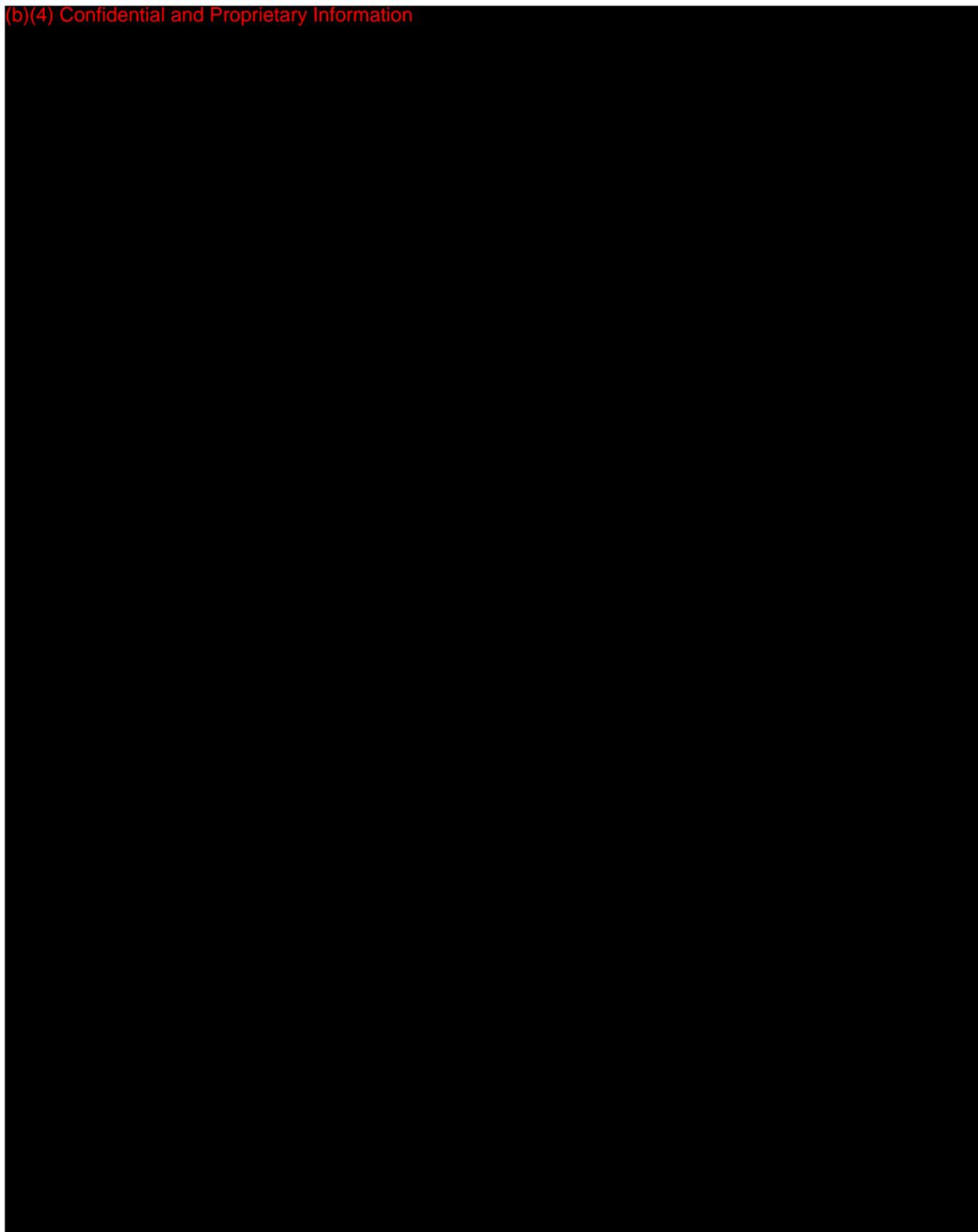
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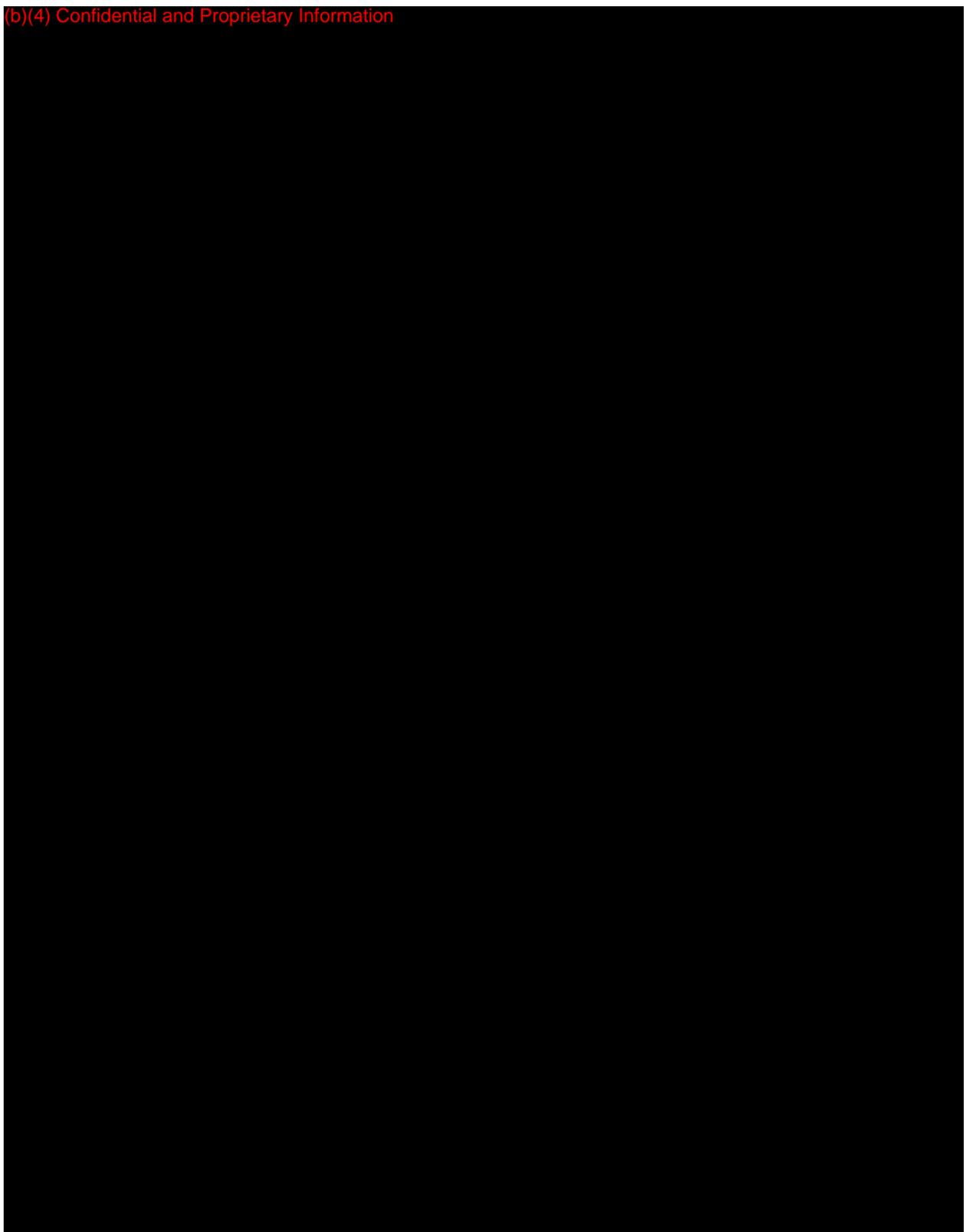
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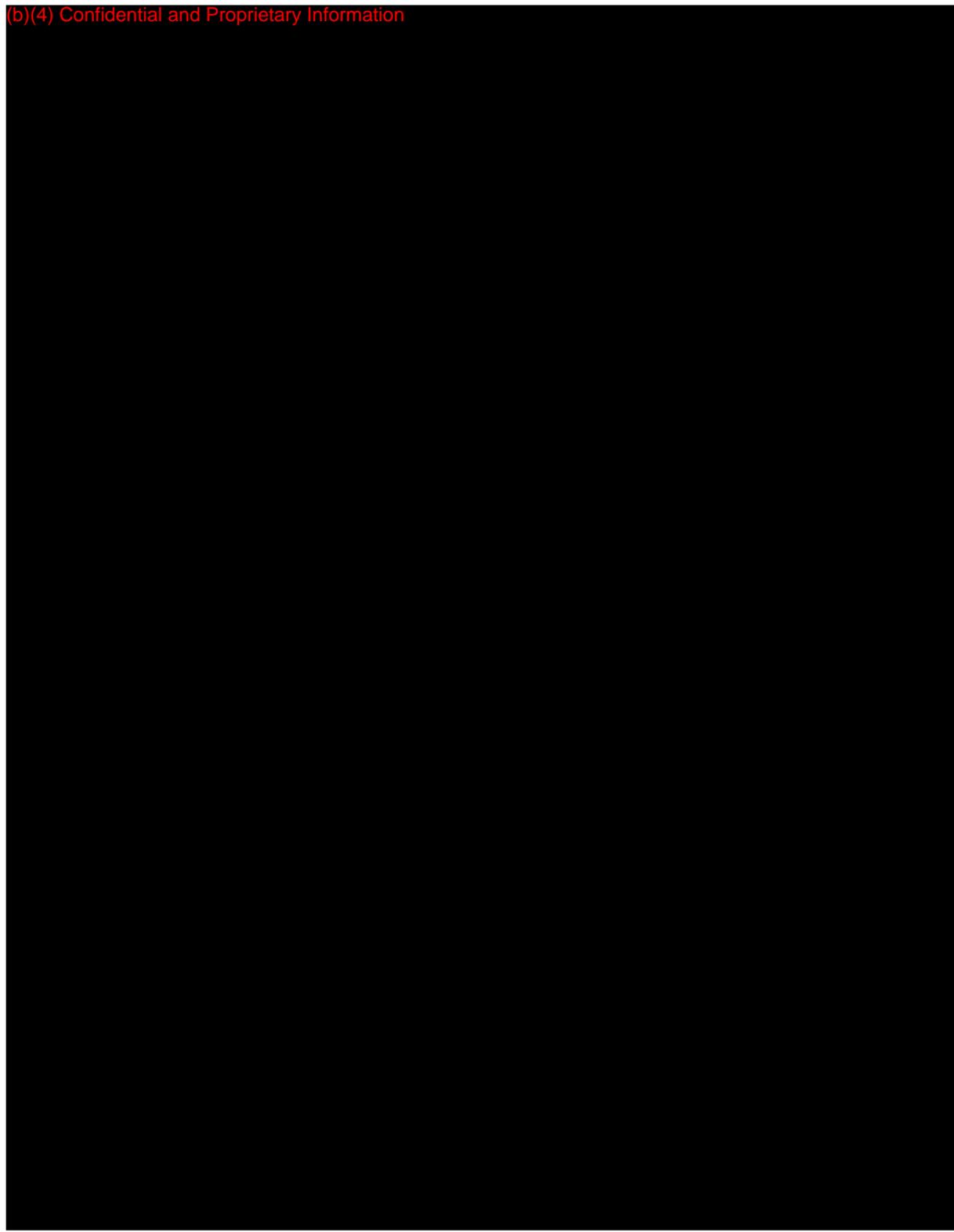
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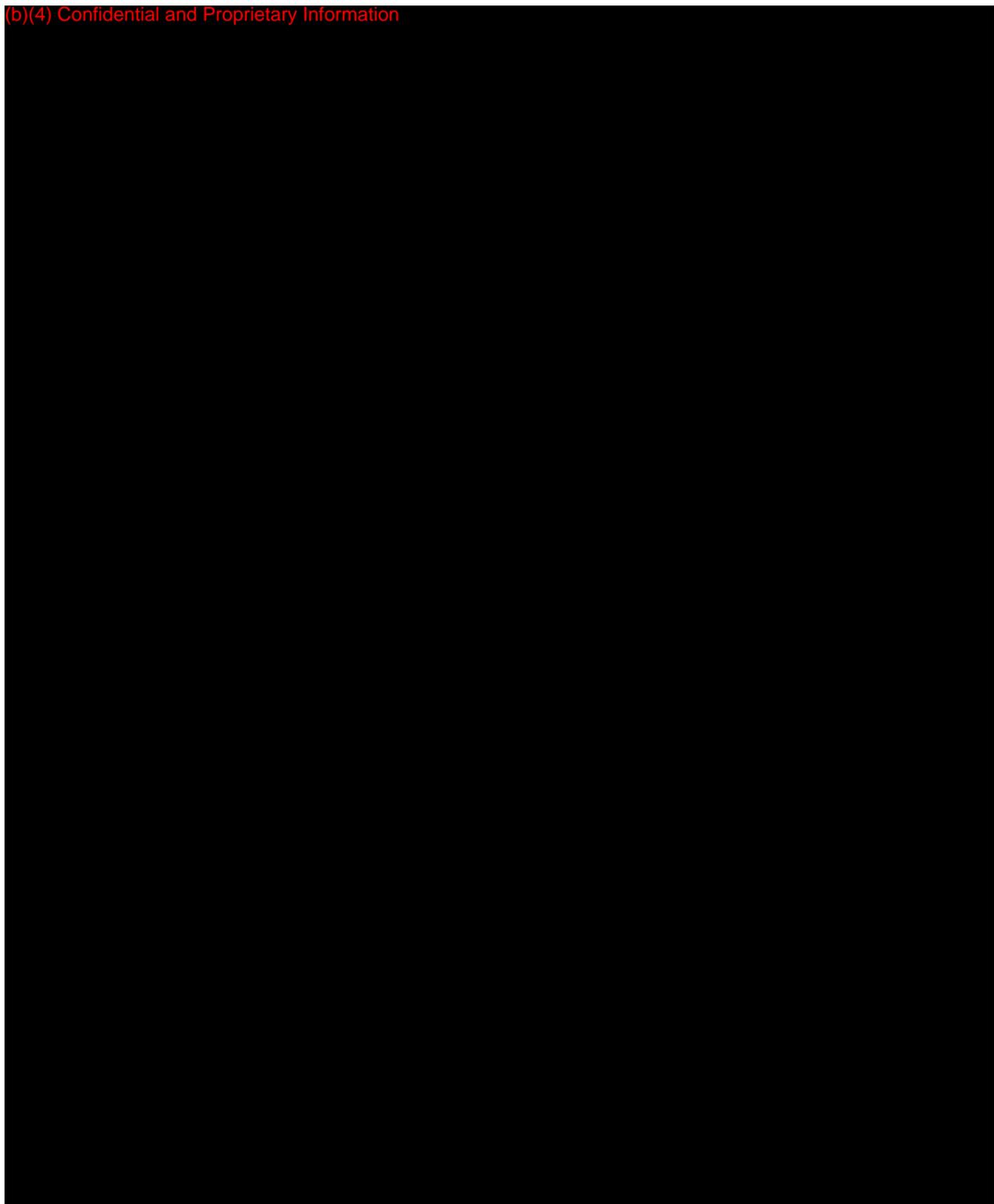
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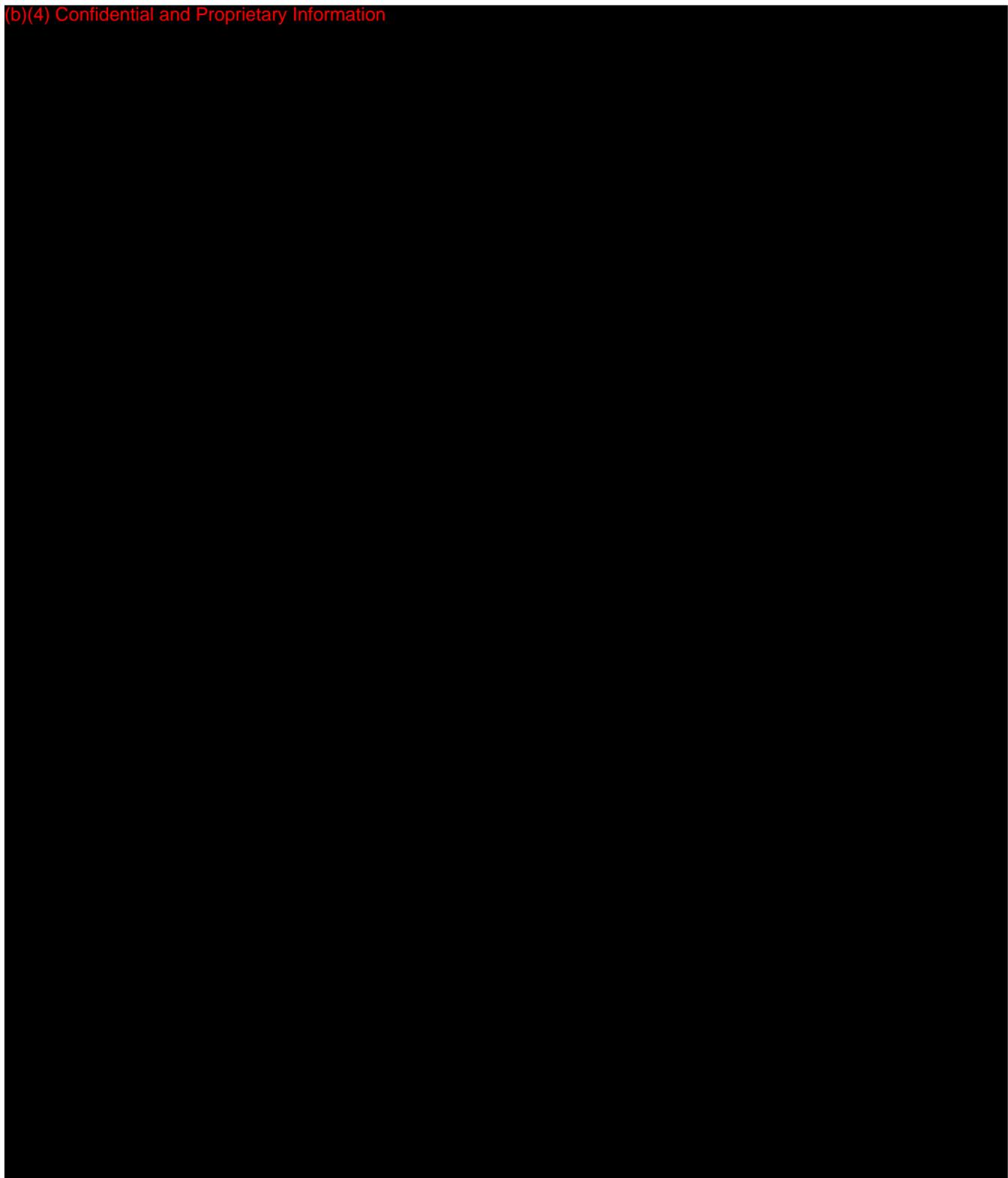
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(b)(4) Confidential and Proprietary Information



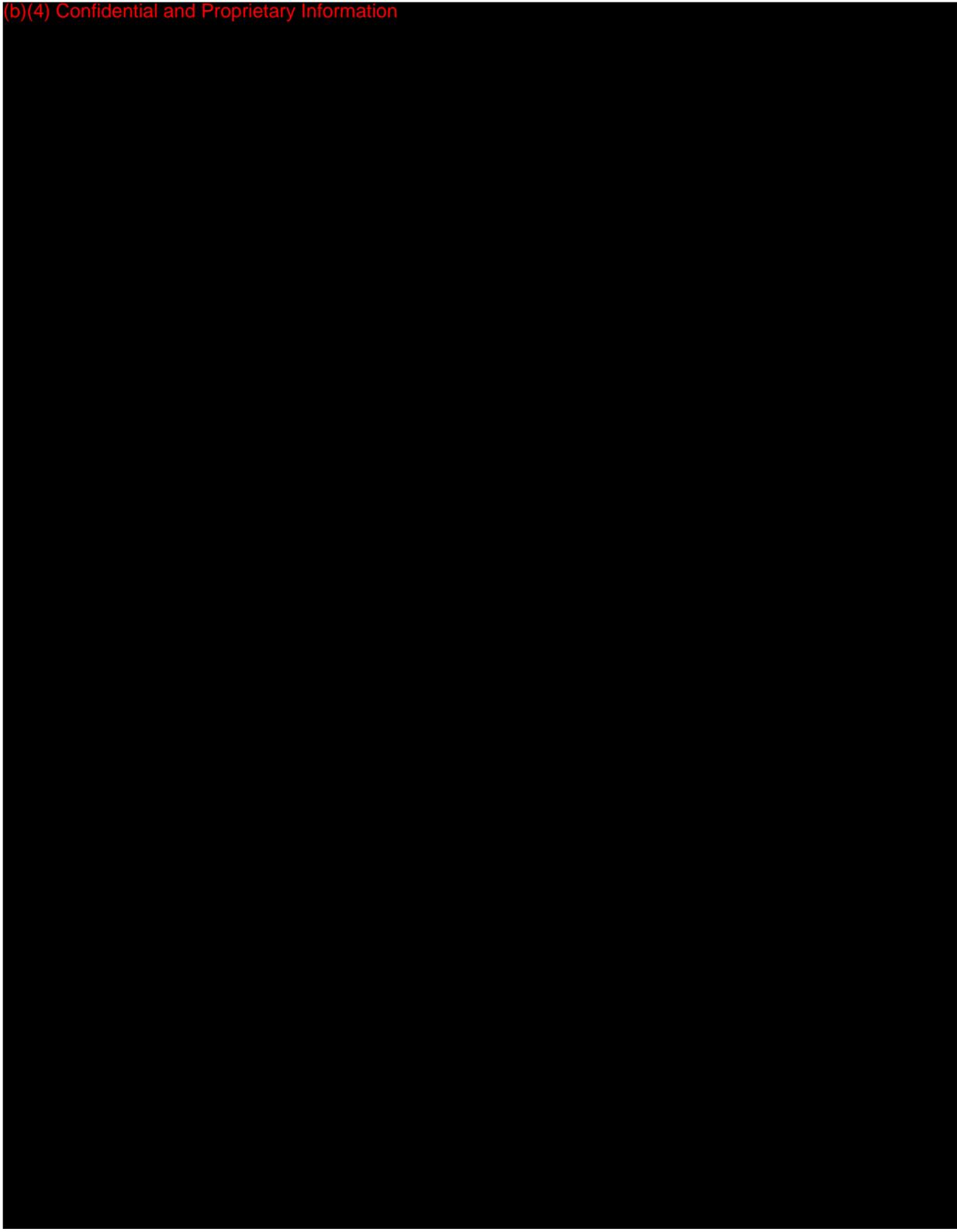
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(b)(4) Confidential and Proprietary Information



(b)(4) Confidential and Proprietary Information



Attachment 8.1 Stability report

Report no:

CMI-2010011B

Study Title:

Real time stability study

Test Article:

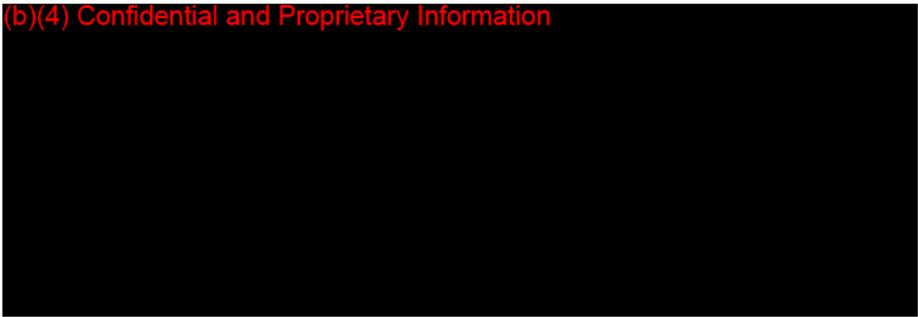
CollaDental Barrier

JAN, 2010

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1st Floor, No. 50-1, Keyen Road, Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

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Approved by

Date

Jasper Chou

2010. 1. 31

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INTRODUCTION

CollaDental Barrier is a barrier membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. This collagen-based device provides a biodegradable scaffold conducive for wound healing. The dressing is packaged in a blister pouch sealed with lidding material to maintain its quality. The proposed shelf life is two months.

MATERIALS AND METHODS

Test article: CollaDental Barrier. See Table 1 for product information.

Table 1 Information on CollaDental Barrier

Dimension	15mm x 20mm
Feature	Membrane
Sterility	Gamma ray irradiation
Color	White to off white
Component(s)	Porcine collagen
Packaging	Device houses in a PET blister, sealed with lidding material
Storage condition	23°C ± 2°C, 60% Relative humidity
Storage duration	3 months
Sampling plan	Day 0, 7 days, 14 days, 1 month and 2 months
Continued sampling plan	3 months, 6 months, 12 months, 24 months and 36 months

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(b)(4) Confidential and Proprietary Information

ACCEPTANCE CRITERIA

Table 2 Stability evaluation tests and the acceptance criteria

Tests	Acceptance criteria
(b)(4) Confidential and Proprietary Information	

RESULTS

CollaDental Barrier (b)(4) Confidential and Proprietary Information

was retrieved according to pre-determined sampling plan stated in Table 1. Samples were being evaluated for its hydroxyproline content, bioburden and packaging integrity. Results summarized in Table 3 demonstrated that the sterile CollaDental Barrier remained stable throughout the study and the outcome of each test conformed to respective acceptance criterion listed in Table 2. No deviation was found during the entire course of study.

Table 3 Summary of real time stability of CollaDental Barrier

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DISCUSSION

CollaDental Barrier is a sterile, single use device intended for use in dental surgery procedures as a resorbable material for placement in the area of dental implants, bone defects or ridge reconstruction to aid in wound healing post dental surgery.

CollaDental Barrier is a gamma-sterilized, single use device individually housed in a PET blister pouch, sealed with porous lidding material. Since collagen is inherently unstable, it is therefore important to ensure the device remains stable when stored according to the recommended conditions.

CollaDental Barrier has been stored at recommended storage conditions concurrently for over three months and samples are retrieved at pre-specified time points to monitor its stability. Continued sampling plan for stability study is listed in Table 1.

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(b)(4) Confidential and is summarized in Table 3. No deviation from product specification has been found during the entire storage period. In summary, the proposed 2 month shelf life of CollaDental Barrier is justified.

Attachment 9.1 Cytotoxicity test

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Report no:

CMI-2009111B

Study Title:

ISO MEM Elution Cytotoxicity Test

Test Article:

CollaDental Barrier

November, 2009

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Page no. 02/11

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information

Sponsor:

Collamatrix Inc.

1st Floor, No. 50-1, Keyen Road, Jhunan Township,
Miaoli County, 350, Taiwan

Study announcement:

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(b)(4) Confidential and Proprietary Information and Collamatrix Inc.

Approved by

Date

Jasper Chou

2009. 11. 30

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The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

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SUMMARY

An *in vitro* biocompatibility study was conducted on the test article, CollaDental Barrier, to test the cytotoxic potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 5: Test for Cytotoxicity: *in vitro* methods guidelines. Duplicate extracts of the test articles were prepared using Minimum Essential Medium (MEM) supplemented with 5% of bovine serum and 2% antibiotics. The test extract was added onto three separate confluent monolayer cultures of L-929 mouse fibroblasts. Other separate monolayer cultures were fed with the medium control, negative control and positive controls. All monolayer cultures were incubated at 37°C in 5% (v/v) CO₂. After 48 hours, all monolayer cultures were examined microscopically to evaluate any change of cell morphology.

Under the test conditions described here, the MEM extract from CollaDental Barrier showed no evidence of cell lytic or toxic effect (grade 0). It met the requirement of the test since the grade was near a grade 0 (none cytotoxicity). The medium control, negative controls and positive control performed as expected.

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INTRODUCTION

The MEM elution method was used in this study. This test was designed to determine the cytotoxicity of extractable substances from the test article. An extract of the sample was added to cell monolayer and incubated for 2 days. The morphological features of L-929 cell monolayer were examined and scored based on the degree of cytopathy (see Table 1).

Table 1. Classification of cytopathic effects

Cell morphology	Reactivity	Grade
No cell lysis, intracytoplasmic granules (ICP)	None	0
No more than 20% cell rounding and lysis	Slight	1
No more than 50% cell rounding and lysis	Mild	2
No more than 70% cell rounding and lysis	Moderate	3
Near complete cell lysis	Severe	4

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

Control articles:

Negative control: plastic high-density polyethylene

Positive control: tin stabilized polyvinylchloride

Cell line: (b)(4) Confidential and Proprietary Information

Single strength Minimum Essential Medium supplemented with 5% bovine serum and 1% antibiotics (1X MEM).

Experimental designs

Extract Preparation

Extraction vehicle –

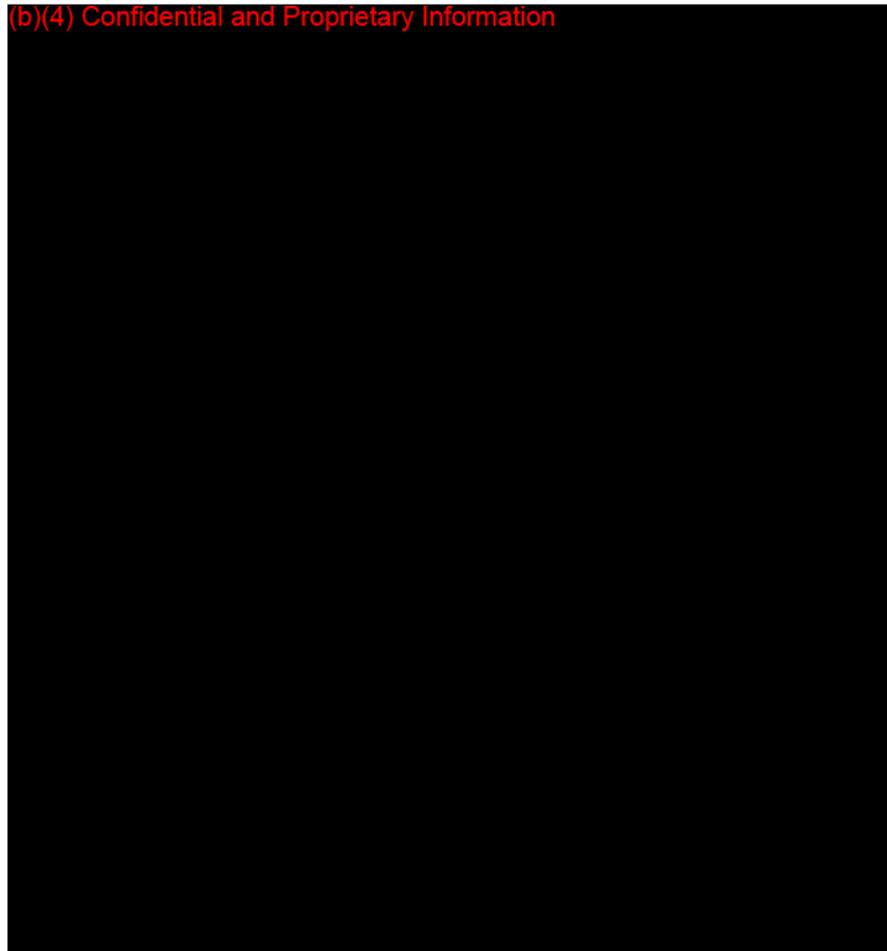
Test article –

Vehicle control –

Negative control –

Positive control –

(b)(4) Confidential and Proprietary Information



Cell Preparation

L-929 cells were propagated and maintained in 1X MEM at 37°C in 5% CO₂. For this study, six well cell culture plates were seeded and incubated until 80~90% confluence prior to test.

Treatment method

After confluent cell monolayer achieved, the culture medium was removed and replaced with 2ml of test or control extracts. Triplicate culture wells were applied for each extract. The cells were incubated at 37°C with 5% CO₂ for 48 hours.

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Evaluation criteria

At the end of this assay, the cell morphological features were examined microscopically. The degree of cytopathic effects was scored according to the USP based criteria shown at the Table 1.

For the validation of this test, the vehicle control and negative control must have had a reactivity of none (grade) and the positive control must have been a grade 3 or 4. The test article met the requirements of the test only when the cytotoxicity was less than or equal to grade 2 (mild).

The averaged results from three wells represented as the final cytotoxic score.

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RESULT

The test results were shown in Tables 2 and 3.

Under the experimental conditions of this study, the test extracts showed no signs of causing cell lysis or round-off (none).

The medium control (none), negative control (none) and positive control (severe) performed as expected.

CONCLUSION:

The 1X MEM extract from CollaDental Barrier showed no signs of cytotoxicity and met the requirements of the test (the grade 0).

CollaDental Barrier does not cause cytotoxic effect in the test conditions of an ISO MEM elution method.

REFERENCES:

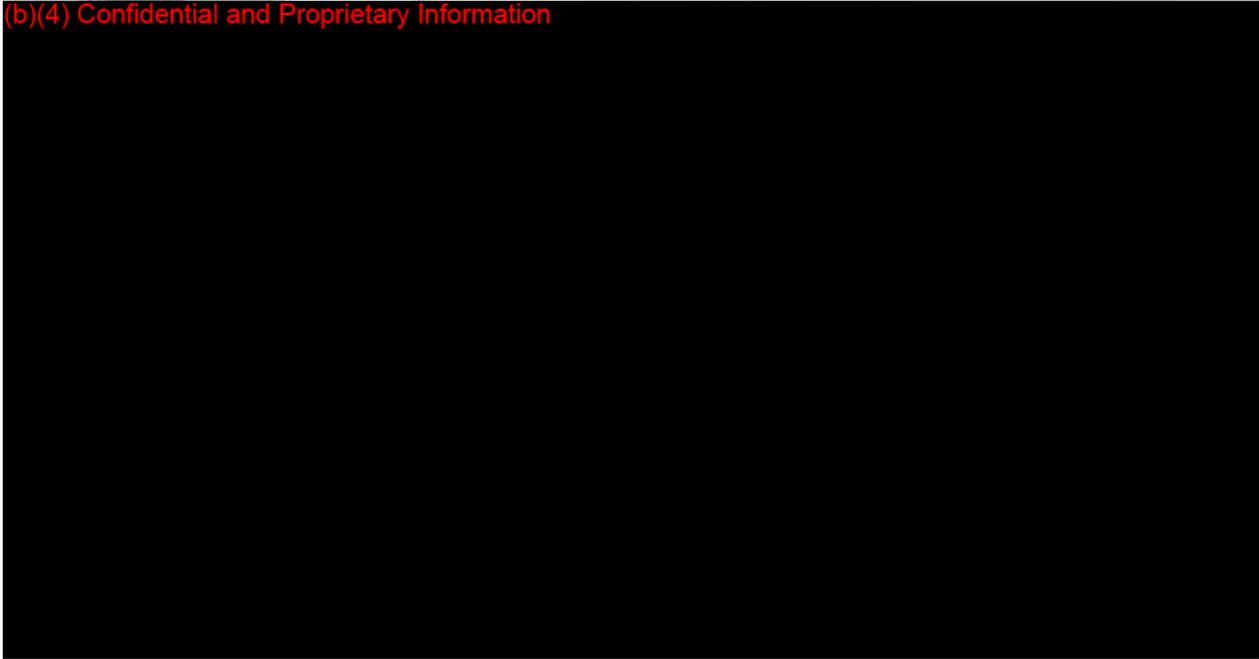
The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 5: Test for Cytotoxicity: *in vitro* method.

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

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Table 2. Grade of cytotoxic effect

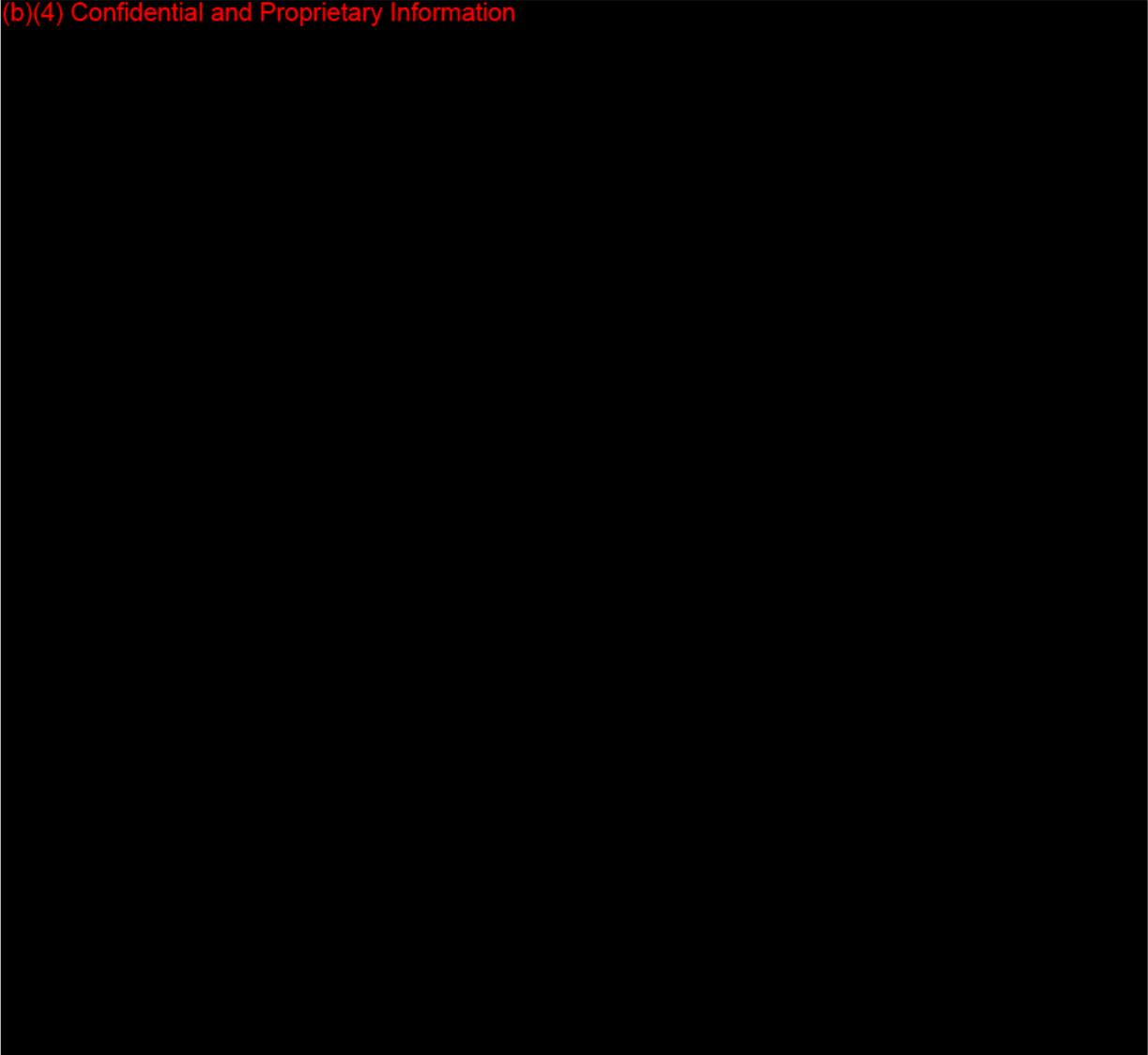
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Table 3. Cytopathic effect observations

(b)(4) Confidential and Proprietary Information



COLLAMATRIX INC

Sterilization Validation Report Of Gamma Radiation Using ISO 11137:2006

COLLAMATRIX INC

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1.0 Abstract

This study was performed to establish a radiation dose and to validate the effectiveness of gamma irradiation for the sterilization of CollaDental Barrier. This study was based on practices recommended by the International Organization for Standardization, Sterilization of Health Care Products –Radiation Sterilization (ISO 11137-2006). A Sample Item Proportion (SIP) of one was utilized for testing. (b)(4) Confidential and Proprietary Information

was selected based upon the overall adjusted bioburden, (b)(4) Confidential and Proprietary, from testing of three separate manufacturing lots, lot numbers (b)(4) Confidential and Proprietary, respectively.

A total of (b)(4) Confidential and Proprietary randomly sampled from (b)(4) Confidential, exposed to the verification dose and the sterility of irradiated products were tested. The sterility test results of the (b)(4) Confidential and Proprietary were acceptable in accordance with ISO 11137-2:1995.

There was none positive culture out of the (b)(4) Confidential and Proprietary. These results met the acceptance criteria of no more than two non-sterile cultures per (b)(4) Confidential and Proprietary tested stated in Method 1 of ISO 11137:2006. This result indicates that under the conditions of the study, an exposure dose of (b)(4) Confidential has been determined as adequate for routine sterilization. This exposure dose provides a Sterility Assurance Level (SAL) of 10^{-6} (a probability of more than a single survivor for each one million product units exposed to the SAL dose).

Approved by: _____

COLLAMATRIX INC

Sterilization Validation Report of Gamma Radiation Using ISO 11137:2006	Date	20091215
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2.0 Objective

The objective of this study is to validate gamma radiation sterilization on the product, CollaDental Barrier, manufactured by COLLAMATRIX. The verified irradiation dose is then intended to be used to substantiate the sterilization dose for validation and routine control irradiation sterilization.

3.0 Introduction

This study was performed to establish a radiation dose and validate the effectiveness of gamma irradiation for the sterilization of CollaDental Barrier. This study was based on practices recommended by the ISO 11137-2006 Sterilization of Health Care Products – Radiation Sterilization. Pre-gamma irradiation bioburden levels were determined and used to select an appropriate verification dose for this product. Recommendations for a routine minimum sterilization were based upon evaluation of microbial survival following exposure of products to the verification dose. The recommended full process dose is designed to provide a Sterility Assurance Level (SAL) of 10^{-6} or no more than one non-sterile unit for each one million units sterilized at that dose level.

The bioburden test was performed to determine the number of viable microorganism present naturally on the product through microbiological analysis in accordance with the ANSI/AAMI/ISO 11737-1:1995 Sterilization of medical devices Microbiological methods Part 1: Estimation of the population of microorganisms on product. The verification dose can be calculated using the closest tabulated average bioburden that is greater than or equal to the calculated average bioburden for the entire product and reading the dose necessary to achieve the desired SAL.

COLLAMATRIX INC

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A total of (b)(4) Confidential from one production lot was selected and exposed to this irradiation dose and product's sterility was tested according to ANSI/AAMI/ISO 11737-2:1995 Sterilization of medical devices—Microbiological methods—Part 2: Tests of sterility performed in the validation of a sterilization process and USP-NF <71> sterility test.

4.0 Sample Information

Name of test item: CollaDental Barrier

Lots: (b)(4) Confidential and Proprietary Information

Total sample amount used in this study

(b)(4) Confidential samples from three lots, (b) from each lot, was used for bioburden enumeration

(b)(4) Confidential samples from one lot were used for sterility test

5.0 Procedures

5.1 Bioburden Enumeration test

Thirty non-sterile samples were randomly sampled from 3 lots of CollaDental Barrier, lot number (b)(4) Confidential and Proprietary Information respectively. The Sample Item Proportion (SIP)

used (b)(4) Confidential. Each sample lot was first extracted via (b)(4) Confidential and Proprietary Information in

(b)(4) Confidential and Proprietary Information

COLLAMATRIX INC

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Device was completely immersed in (b)(4) Confidential and Proprietary, vortex for (b)(4) Confid before the supernatant was collected and filtered through (b)(4) Confidential. Filter membrane was placed on either Tryptic Soy agar (TSA) plate or Potato Dextrose agar (PDA) plate. TSA plate was incubated at $35^{\circ}\text{C}\pm 2^{\circ}\text{C}$ for 24 hours while PDA plate was incubated at $23^{\circ}\text{C}\pm 2^{\circ}\text{C}$ for 72 hours. The results of pre-gamma irradiation bioburden were recorded (Attachment 1).

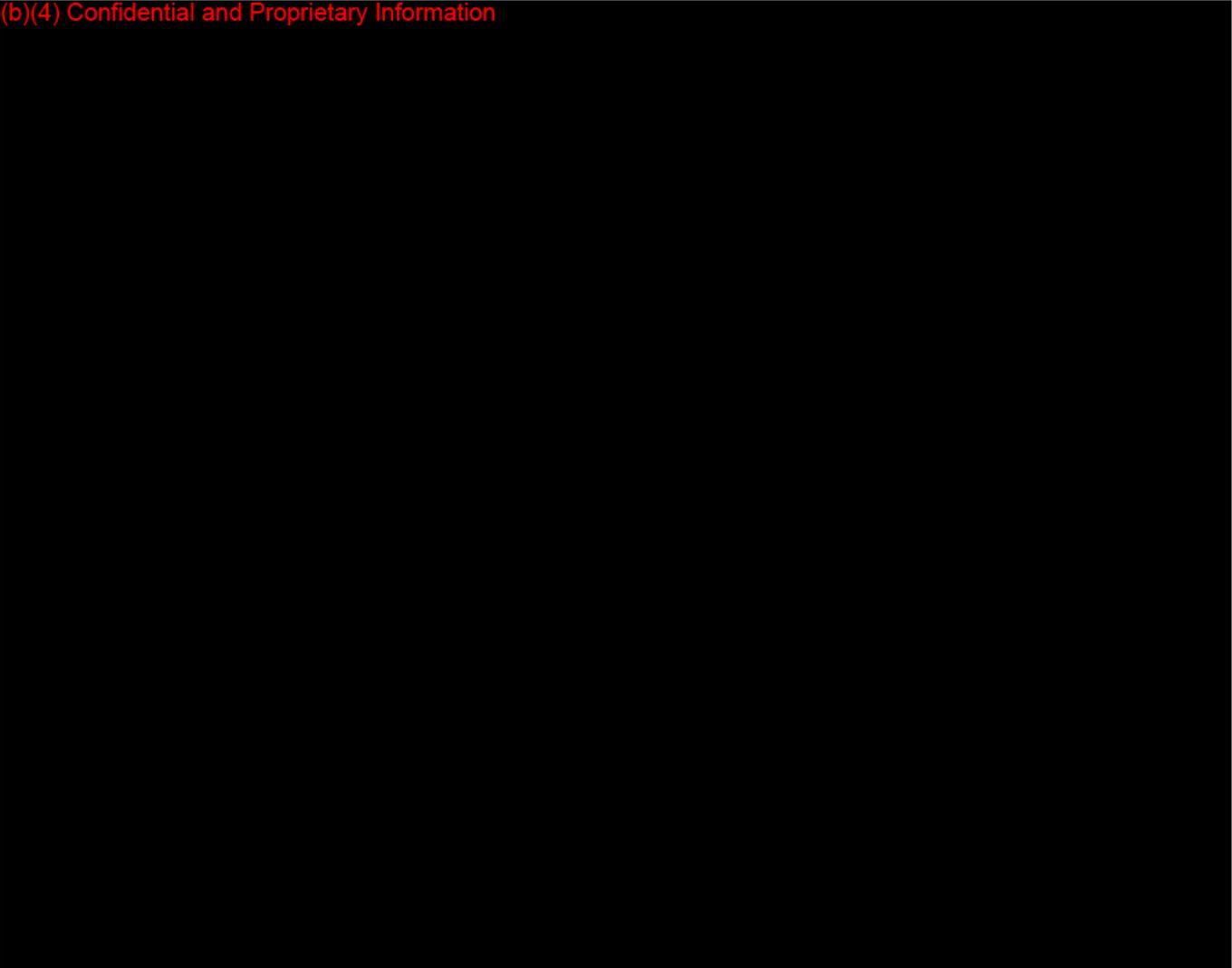
5.2 Dose setting method

The verification dose can be established using the “Table 6-Radiation dose (kGy) required to achieve a given SAL for an average (b)(4) Confidential and Proprietary having the standard distribution of resistances”, given in ISO 11137:2006 Part 2 - Establishing the sterilization dose shown below. The results were recorded in the Irradiated Dose Calculation form in Attachment 3. The maximum tolerance of deviation between the actual and calculated verification dose should be no more than 10% of the calculated dose as shown in Attachment 3.

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Sterilization Validation Report of Gamma Radiation Using ISO 11137:2006	Date	20091215
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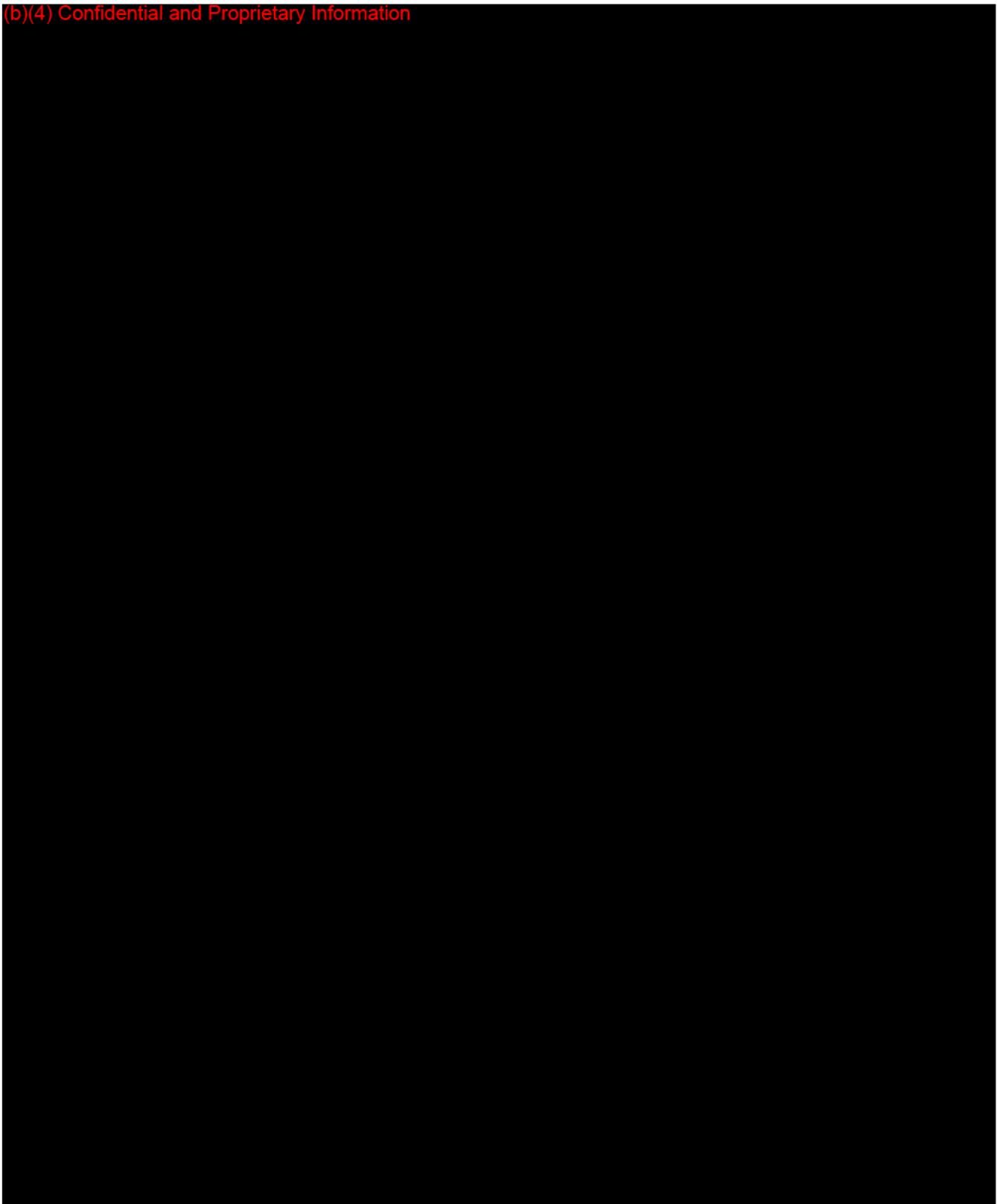
(b)(4) Confidential and Proprietary Information



COLLAMATRIX INC

Sterilization Validation Report of Gamma Radiation Using ISO 11137:2006	Date	20091215
	Page	6/11

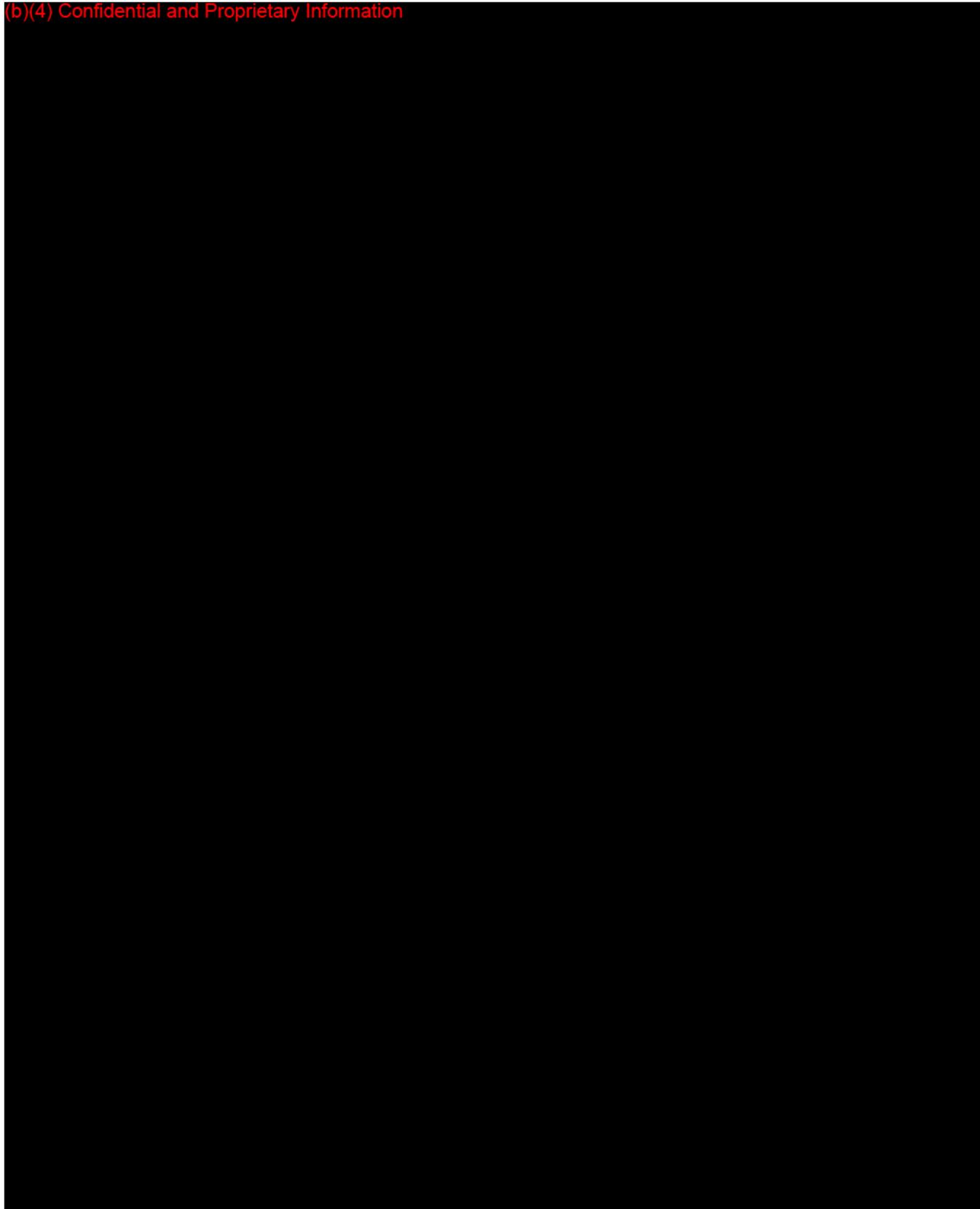
(b)(4) Confidential and Proprietary Information



COLLAMATRIX INC

Sterilization Validation Report of Gamma Radiation Using ISO 11137:2006	Date	20091215
	Page	7/11

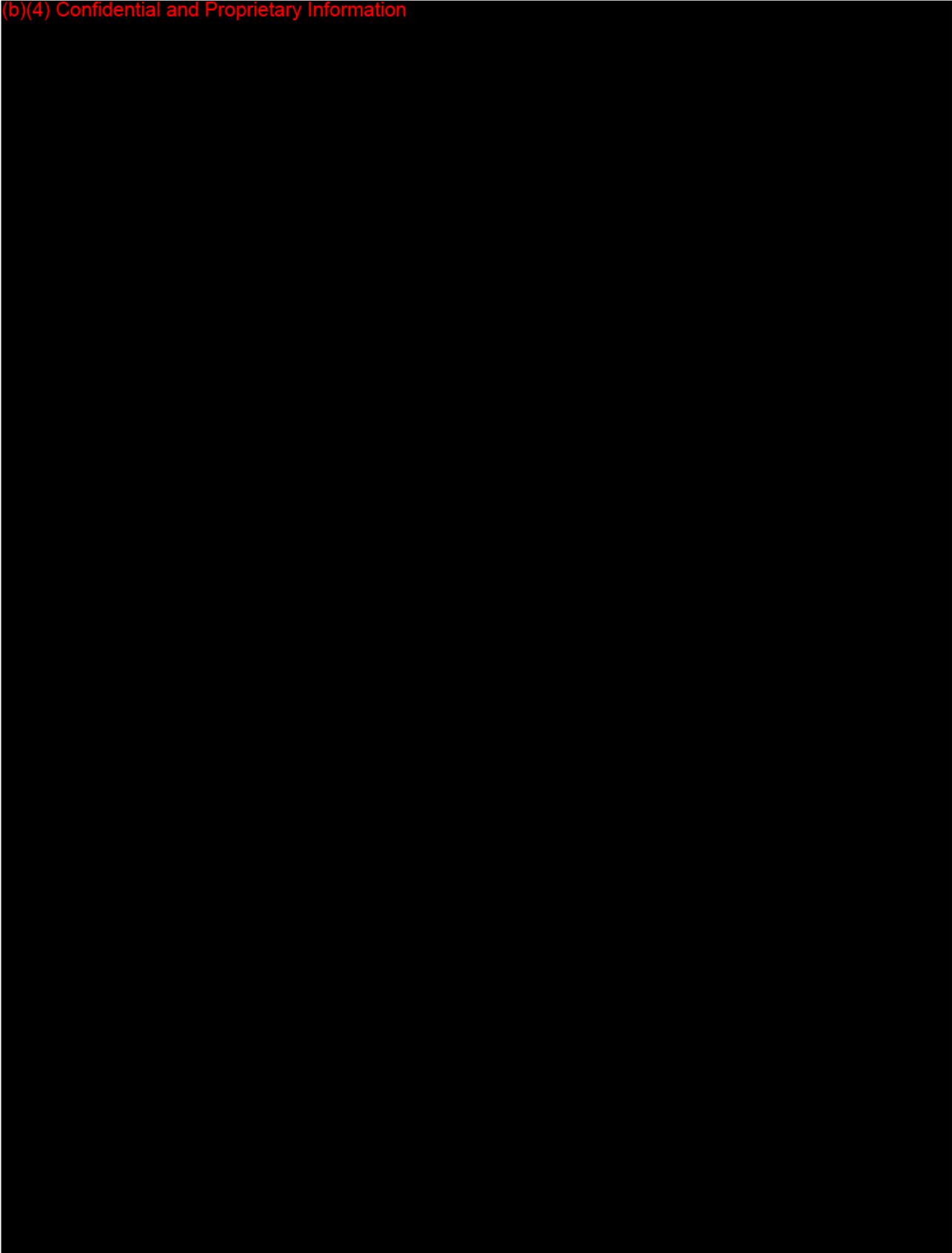
(b)(4) Confidential and Proprietary Information



COLLAMATRIX INC

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(b)(4) Confidential and Proprietary Information



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5.3 Sterility test

Sterility of (b)(4) irradiated CollaDental Barrier samples was conducted using a (b)(4) Confidential and Proprietary CollaDental Barrier sample was transferred directly to Thioglycollate broth and Tryptic Soy broth (TSB) culture media aseptically and then incubated for at 35°C ± 2°C (bacteria) and 23°C ± 2°C (yeast/mold) respectively for 14 consecutive days with constant monitoring to examine the gamma irradiation sterilization effect. Un-inoculated Thioglycollate culture media and TSB culture media were used as negative control. The culture media was being observed daily for the growth of microorganisms. The final result was record in Attachment 4.

6.0 Results

The bioburden result of thirty non-sterile samples is summarized as follows:

Description	Average bioburden
(b)(4) Confidential and Proprietary Information	

Based on the results of bioburden enumeration studies, the average bioburden was determined to be (b)(4) Confidential and Proprietary. Therefore the adjusted average bioburden value was (b)(4) Confidential and Proprietary (Attachment 1).

The adjusted average bioburden was applied in Table 6 of ISO 11137:2006. The verification dose of (b)(4) Confidential and Proprietary was then obtained for the products to be irradiated.

Products were irradiated at the verification dose of (b)(4) Confidential and Proprietary (Attachment 2 for the Certificate of Irradiation).

COLLAMATRIX INC

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It was the contract sterilization facility's responsibility to ensure that sufficient number of calibrated dosimeters was used to monitor three sterilization processes. The deviation between the actual irradiation dose and the calculated verification dose was checked to confirm that the deviation was within 10% of the acceptable range.

In the sterility test, none of the irradiated CollaDental Barrier was found to be positive on both Thioglycollate and Tryptic Soy broth (TSB) culture media after 14 days of incubation. (Attachment 4)

In the study of package integrity, package material subject to (b)(4) Confide irradiation was testing for its material intactness and sealing capability. Package was manually torn or completely immersed in water and incubated in a (b)(4) Confidential and Proprietary Information, package did not shown signs of damage or leakage after the tests.

7.0 Discussion

The verification dose of (b)(4) Confide was applied to 100 CollaDental Barrier samples to be irradiated at this dosage with 10% deviation. No positive result was found in the sterility tests indicating that the verification dose is valid.

COLLAMATRIX INC

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8.0 Conclusion

In conclusion, the sterilization validation of gamma irradiation for CollaDental Barrier was completed and met the requirements of ISO 11137:2006 based on the testing results of bioburden evaluation, dose setting, and sterility tests. The product, CollaDental Barrier is therefore valid for dosimetric release using (b)(4) Confidential sterilization dose.

A dose audit is necessary every three months to ensure that the sterilization dose remains valid.

9.0 References

1. ISO 11137:2006 Sterilization of Health Care Products – Radiation Sterilization
2. ANSI/AAMI/ISO 11737-1:1995 Sterilization of medical devices Microbiological methods Part 1: Estimation of the population of microorganisms on product.
3. USP-NF <71 > Sterility test
4. ANSI/AAMI/ISO 11737-1:1995 Sterilization of medical devices—Microbiological methods—Part 2: Tests of sterility performed in the validation of a sterilization process.

膠原科技股份有限公司

COLLAMATRIX TAIWAN LTD. *CollaDental Barrie*

Batch Record: Bioburden

Product: *pre-σ*

1. Lot number: (b)(4) Confidential and Proprietary Information

原料檢驗

巡迴檢驗

成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	李	Jasper
2. Direct plate out method	<input type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted <input type="checkbox"/> _____ dilution	李	Jasper
4. Perform filtration per SOP			
5. Perform direct plate out per SOP		李	Jasper
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE <input checked="" type="checkbox"/> TSA <input type="checkbox"/> PDA		
7. <input checked="" type="checkbox"/> Incubate at 35°C±2°C (16 hrs) for bacteria	<input type="checkbox"/> YM broth <input type="checkbox"/> Thioglycollate <input type="checkbox"/> Other: _____	李	Jasper
8. <input type="checkbox"/> Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input checked="" type="checkbox"/> 35°C±2°C <input type="checkbox"/> 23°C±3°C (RT)		
9. Check number of colony forming unit (CFU):	<input type="checkbox"/> Not detected <input checked="" type="checkbox"/> < 150 cfu <input type="checkbox"/> 150-250 cfu <input type="checkbox"/> TNTC	李	Jasper
10. Determine total viable count : CFU/mL CFU/g	_____ CFU/mL		
(b)(4) Confidential and Proprietary Information	(b)(4) Confidential and Proprietary Information	李	Jasper
11. Comments	(b)(4) Confidential and Proprietary Information		

Date: *2009.11.12*

Operator: *李俊男*

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Callawarmel Berries

Batch Record: Bioburden

Product: *pre-gummi*

1. Lot number:

(b)(4)
Confidential and
Proprietary
Information

原料檢驗

巡迴檢驗

成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	李	Jasper
2. Direct plate out method	<input type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted	李	Jasper
	<input type="checkbox"/> _____ dilution		
4. Perform filtration per SOP	OK	李	Jasper
5. Perform direct plate out per SOP			
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE <input type="checkbox"/> TSA <input checked="" type="checkbox"/> PDA <input type="checkbox"/> YM broth <input type="checkbox"/> Thioglycollate <input type="checkbox"/> Other: _____ <input type="checkbox"/> 35°C±2°C <input checked="" type="checkbox"/> 23°C±3°C (RT)	李	Jasper
7. [] Incubate at 35°C±2°C (16 hrs) for bacteria			
8. [✓] Incubate at 23°C±3°C (72 hrs) for yeast/mold			
<i>yeast</i>			
9. Check number of colony forming unit (CFU):	<input type="checkbox"/> Not detected <input checked="" type="checkbox"/> < 150 cfu <input type="checkbox"/> 150-250 cfu <input type="checkbox"/> TNTC	李	Jasper
10. Determine total viable count : CFU/mL CFU/g	_____ CFU/mL	李	Jasper
(b)(4) Confidential and Proprietary Information	(b)(4) Confidential and Proprietary Information		
11. Comments		李	Jasper
(b)(4) Confidential and Proprietary Information	(b)(4) Confidential and Proprietary Information		

Date: *2009.11.12*

Operator: *李俊男*



CHINA BIOTECH CORPORATION

誠信正直 · 顧客感動 · 社會公道

TEL: 886-4-23597515 FAX: 886-4-23597080

台中市工業區33路10號

10, 33rd Road, Taichung Industrial Park,

Taichung, Taiwan R.O.C 407

DATE : 2009/12/31

照射證明書 CERTIFICATE OF IRRADIATION

行政院原能會核准設立照射廠執照証號 IRRADIATION PLANT NO : 物字第 1100223 號

客戶名稱 CUSTOMER NAME : 膠原科技(股)公司

照射日期 IRRADIATION RUN DATE : 2009/11/20

照射批號 IRRADIATION RUN NUMBER : (b)(4) Confidential and Proprietary

客戶產品已照射 MATERIALS PROCESSED :

盒數	內容 DESCRIPTION	客戶產品批號 LOT NO
(b)(4) Confide	CollaDental Barrier	(b)(4) Confidential and Proprietary

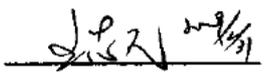
總數 TOTAL (b)(4) Confide 盒數

中國生化科技股份有限公司證明上述產品經本公司劑量偵測系統判讀，吸收劑量如下：
China Biotech Corporation certifies that the material listed above (has described by its manufacturer) received the following doses within the precision limits of the dosimetry system employed

最低劑量 MINIMUM DOSAGE (b)(4) Confide kGy ; 最高劑量 MAXIMUM DOSAGE (b)(4) Confidential kGy

使用放射性同位素 ISOTOPE UTILIZED : 鈷 60 COBALT-60

客戶劑量要求 DOSE REQUIREMENT : 最低劑量MIN (b)(4) Confid kGy ; 最高劑量MAX (b)(4) Confidential and kGy

確認者: 
CERTIFIED BY 品保部主管
QUALITY ASSURANCE

Dose calculation

Test article: CollaDental Barrier

Bioburden enumeration results:

Lot number:

(b)(4) Confidential
and Proprietary
Information

Overall average bioburden: (b)(4) Confidential
and Proprietary

Adjusted overall average bioburden: (b)(4) Confidential
and Proprietary

The adjusted overall bioburden (b)(4) Confidential
and Proprietary would be used to choose
a verification dose. And according to ISO11137 (b)(4)
Confidential the verification
dose is (b)(4) Confidential
and Proprietary In accordance with ISO11137 (b)(4)
Confidential one
hundred pieces of product should be selected from a single production
and irradiated at (b)(4) Confidential
and Proprietary

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

CollaDental Barrie
port 8

Batch Record: Bioburden

Product:

1. Lot number: (b)(4) Confidential and Proprietary Information 原料檢驗 巡迴檢驗 成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	<i>Dei</i>	<i>Jasper</i>
2. Direct plate out method	<input type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted	<i>Dei</i>	<i>Jasper</i>
	<input type="checkbox"/> _____ dilution		
4. Perform filtration per SOP		<i>Dei</i>	<i>Jasper</i>
5. Perform direct plate out per SOP			
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE	<i>Dei</i>	<i>Jasper</i>
	<input checked="" type="checkbox"/> TSA		
	<input type="checkbox"/> PDA		
	<input type="checkbox"/> YM broth		
	<input checked="" type="checkbox"/> Thioglycollate		
	<input type="checkbox"/> Other: _____		
7. <input checked="" type="checkbox"/> Incubate at 35°C±2°C (16 hrs) for bacteria	<input checked="" type="checkbox"/> 35°C±2°C		
8. <input type="checkbox"/> Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input type="checkbox"/> 23°C±3°C (RT)		
<i>Bacteria</i>			
9. Check number of colony forming unit (CFU):	<input checked="" type="checkbox"/> Not detected	<i>Dei</i>	<i>Jasper</i>
	<input type="checkbox"/> < 150 cfu		
	<input type="checkbox"/> 150-250 cfu		
	<input type="checkbox"/> TNTC		
10. Determine total viable count : CFU/mL CFU/g	_____ CFU/mL	<i>Dei</i>	<i>Jasper</i>
	<i>0</i> CFU/g		
11. Comments		<i>Dei</i>	<i>Jasper</i>
(b)(4) Confidential and Proprietary Information	(b)(4) Confidential and Proprietary Information		

Date: *2019.12.7*

Operator: *Dei Seah*

膠原科技股份有限公司 COLLAMATRIX TAIWAN LTD.

Batch Record: Bioburden

Product:

*CollaDental Dental
post 5*

1. Lot number:

(b)(4) Confidential and Proprietary Information

原料檢驗

巡迴檢驗

成品檢驗

Reagent and filtration	Results	Operator	Verifier
1. Filtration method	<input checked="" type="checkbox"/> Filtration	Dein	Jasper
2. Direct plate out method	<input type="checkbox"/> Plate out		
3. Dilution fold	<input checked="" type="checkbox"/> undiluted <input type="checkbox"/> _____ dilution	Dein	Jasper
4. Perform filtration per SOP		Dein	Jasper
5. Perform direct plate out per SOP			
6. Use mTGE or TSA for bacteria culture; PDA or YM broth for yeast/mold cultures	<input type="checkbox"/> mTGE <input type="checkbox"/> TSA	Dein	Jasper
7. [] Incubate at 35°C±2°C (16 hrs) for bacteria	<input checked="" type="checkbox"/> PDA		
8. [] Incubate at 23°C±3°C (72 hrs) for yeast/mold	<input type="checkbox"/> YM broth <input type="checkbox"/> Thioglycollate <input type="checkbox"/> Other: _____ <input type="checkbox"/> 35°C±2°C <input checked="" type="checkbox"/> 23°C±3°C (RT)		
9. Check number of colony forming unit (CFU):	<input checked="" type="checkbox"/> Not detected <input type="checkbox"/> < 150 cfu <input type="checkbox"/> 150-250 cfu <input type="checkbox"/> TNTC	Dein	Jasper
10. Determine total viable count : CFU/mL CFU/g	_____ CFU/mL <i>0</i> CFU/g	Dein	Jasper
11. Comments	(b)(4) Confidential and Proprietary Information	Dein	Jasper

Date: 2019.12.7

Operator: Dein Seah

Attachment 9.2 Irritation test

CMI-2009112B
Page no. 01/11

Report no:

CMI-2009112B

Study Title:

Skin Irritation Test

Test Article:

CollaDental Barrier

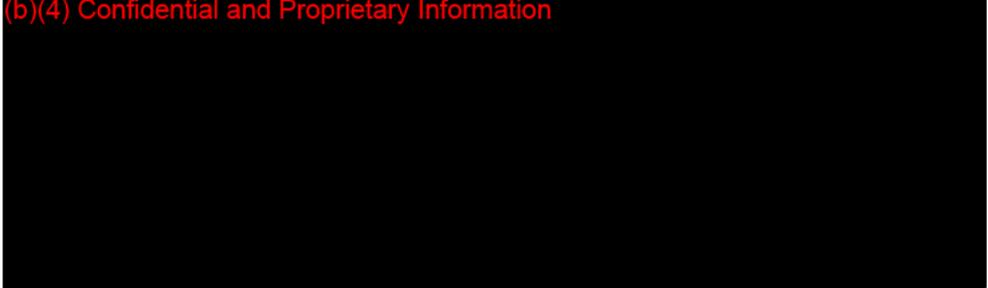
November, 2009

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Page no. 02/11

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

1. This report could not be reprinted or adapted without the permission from (b)(4) Confidential and Proprietary Information and Collamatrix Inc.
(b)(4) Confidential and Proprietary Information

Approved by

Date

Jasper Chou

2009.11.30

CMI-2009112B

Page no. 03/11

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

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CMI-2009112B

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SUMMARY

An ISO intracutaneous study was conducted on the test article, CollaDental Barrier, to test the skin-irritating potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Sensitization. Hydrophilic and hydrophobic extracts of the test articles were prepared using 0.9% sodium chloride and sesame oil. The test extracts were intracutaneously injected into the five separate sites on the right side of the back of each rabbit. The corresponding reagent controls were administered on the left side of the back of each rabbit. Two rabbits per extract were administered. The erythema and edema of injected sites were followed up at 24, 48, and 72 hours post-injection.

Under the test conditions described here, the extracts from CollaDental Barrier showed no evidence of skin-irritating effect. It met the requirement of the test since the Primary Irritation Indices of the test extracts were negligible. The negative controls performed as expected.

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INTRODUCTION

The Intracutaneous study was used in this study. This test was designed to determine whether extractable substances from the test article could cause skin irritation. A single dose of the test substance or control substances were injected intracutaneously into the back of rabbits. After administration, erythema and edema were examined at 24 hours, 48 hours and 72 hours.

MATERIALS AND METHODS

Materials

Test and control articles

Test article: CollaDental Barrier (15mm x 20mm)

Control articles: 0.9% sodium chloride and sesame oil

Test system

New Zealand White rabbit (*Oryctolagus cuniculus*), Male, Young adult

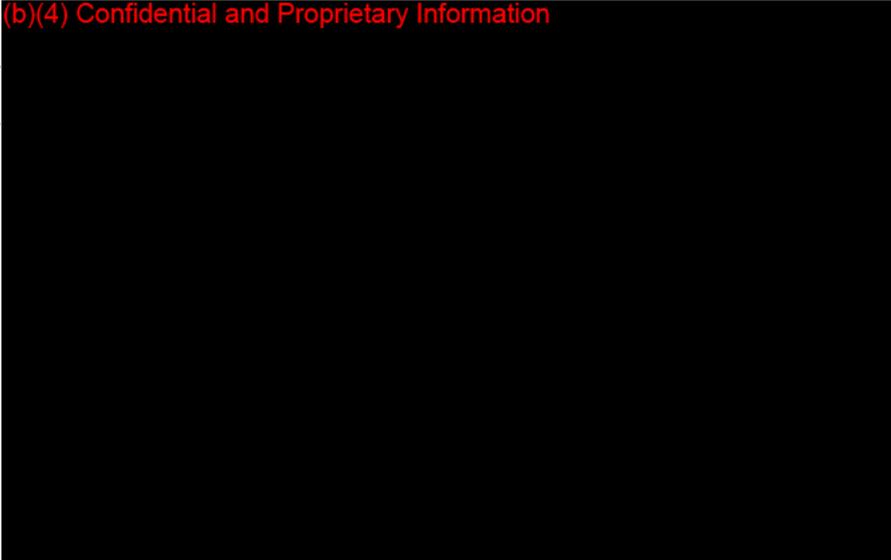
Experimental designs

Extract Preparation

Extraction vehicle —

Test article —

(b)(4) Confidential and Proprietary Information



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Vehicle control – (b)(4) Confidential and Proprietary Information

Two rabbits were prepared each pair of extracts and clipped free of fur from the back to yield a clear injection area. The clipped area was wiped with a 70% ethyl alcohol just before injection.

A single dose of 0.2ml of test extract was injected into five separate sites on the right side of the back of each rabbit. The vehicle control was injected into on the corresponding left side of the back.

The animals were examined for erythema and edema at 24 hours, 48 hours and 72 hours post-injection. Both reactions were scored according the Table 1.

Evaluation criteria

(b)(4) Confidential and Proprietary Information

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Table 1. Scoring Criteria for Irritation Reaction

Score	Erythema (ER)	Score	Edema (ED)
0	No erythema	0	No edema
1	Very slight erythema	1	Very slight edema
2	Well-defined erythema	2	Well-defined edema
3	Moderate erythema	3	Moderate edema (raised 1mm)
4	Severe erythema (beet redness) to eschar formation preventing grading of erythema	4	Severe edema (raised more than 1mm, and extending beyond exposure area)

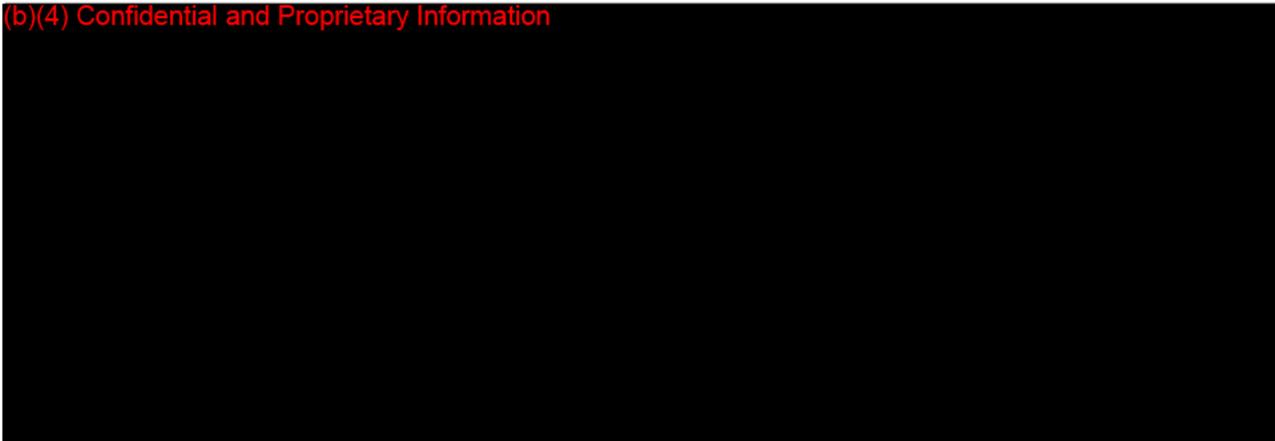
Table 2. Primary Irritation Index (PII)

PII value	Skin irritation effect
0 ~ 0.4	Negligible
0.5 ~ 1.9	Slight
2.0 ~ 4.9	Moderate
5.0 ~ 8.0	Severe

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RESULT

(b)(4) Confidential and Proprietary Information



CONCLUSION:

Under the test condition described above, CollaDental Barrier, does not be considered as a skin irritant.

REFERENCES:

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices — Part 10: Test for Irritation and Sensitization.

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

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Table 3. Primary Irritation Index (PII)

Extract	Animal	Score average		Primary irritation score	Total primary irritation score	Primary irritation index
		Test	Control			

(b)(4) Confidential and Proprietary Information



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Table 4. Individual scores

	Scoring time
Animal	(b)(4) Confidential and Proprietary Information
A	
B	
C	
D	

Attachment 9.3 Sensitization test

CMI-2009113B
Page no. 01/11

Report no:

CMI-2009113B

Study Title:

Skin Sensitization Test

Test Article:

CollaDental Barrier

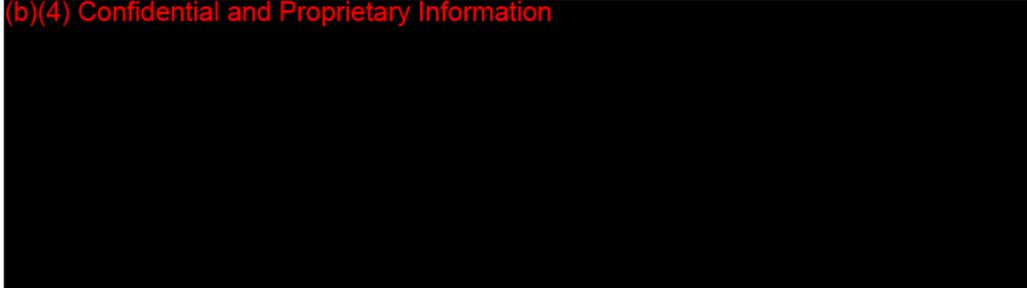
November, 2009

CMI-2009113B
Page no. 02/11

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Science Park
Miaoli County, 350, Taiwan

Study announcement:

1. This report could not be reprinted or adapted without the permission from (b)(4) Confidential and Proprietary Information and Collamatrix Inc.

Approved by

Date

Jasper Chou

2009.11.30

CMI-2009113B

Page no. 03/11

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

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SUMMARY

A skin biocompatibility study was conducted on the test article, CollaDental Barrier, to test the skin-sensitizing potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Sensitization. Hydrophilic and hydrophobic extracts of the test articles were prepared using 0.9% sodium chloride and DMSO. The 25 μ l extract from the test article was topical applied on the dorsum of the each ear for three days. The corresponding reagent controls were administrated similarly. Five mice were applied for each extract.

Under the test conditions described here, the extracts from CollaDental Barrier showed no evidence of skin-sensitizing activity. It met the requirement of the test since the Stimulation Index was less than 3.0. The negative and positive controls performed as expected.

INTRODUCTION

The murine local lymph node assay (LLNA) was used in this study. This test was designed to determine whether extractable substances from the test article could cause a proliferative increase of lymphocytes within the lymph nodes draining the ears. The increased proliferation of lymphocytes in lymph nodes adjacent to the administered site is an indication of skin sensitization.

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

Control articles:

Positive controls: Formaldehyde 10% (w/v) (for positive control of water-soluble substance)

2,4-dinitrochlorobenzene (DNCB) 0.25% (w/v) (for positive control of oil-soluble substance)

Extraction solvents: 0.9% sodium chloride and dimethylsulfoxide (DMSO)

Test system

Mouse (*Mus musculus*), Female, CBA/J strain, 8~10 weeks of age

Experimental designs

Extract Preparation

Extraction vehicle —

Test article —

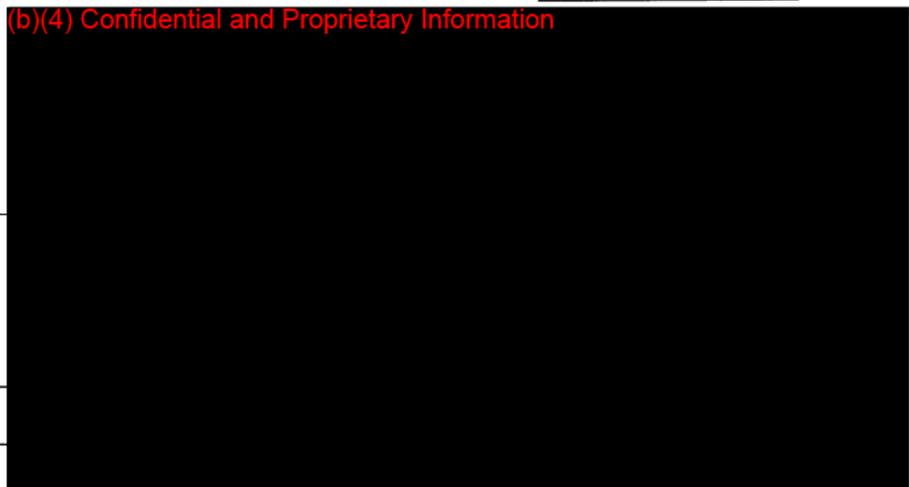
(b)(4) Confidential and Proprietary Information



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(b)(4) Confidential and Proprietary Information



Vehicle control

Positive control

Positive control

Treatment method

Five mice per extract were weighed and received 25 μ l of appropriate extract on the dorsum of each ear for 3 days.

After three-time dosing, the animals were observed for adverse reactions daily.

At the end of this study (day 6), the animals were weighed and injected intravenously with 250 μ l of normal saline containing 20 μ Ci of tritiated methyl thymidine. The animals were scarified 5 hours later and the lymph node draining the ear were collected and processed in normal saline and trichloroacetic acid. After an overnight precipitation at 5°C, the level radioactivity incorporated into cellular DNA was measured using a scintillation counter. The data were represented as disintegrations per minute (dpm).

Evaluation criteria

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Page no. 08/11

RESULT

(b)(4) Confidential and Proprietary Information



CONCLUSION:

Under the test condition described above, CollaDental Barrier could not be considered as a skin sensitizer.

REFERENCES:

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 10: Test for Irritation and Sensitization (ISO).

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

Table 1. Lymph node proliferation assay

	(b)(4) Confidential and Proprietary Information
SC negative control	
SC Test article extract	
Formaldehyde control	
DMSO negative control	
DMSO test article extract	
DNCB control	

NA: not applicable.

*: $p < 0.05$ (Statistically significant) as compared to the negative control.

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Table 2. Body weight observations

		Saline	DMSO
Group	(b)(4) Confidential and Proprietary Information		
Negative control			
Positive control			
Test extract			

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Page no. 11/11

Table 3. Individual counting data

		Saline	DMSO
Group	(b)(4) Confidential and Proprietary Information		
Negative control			
Positive control			
Test extract			

Attachment 9.4 Systemic toxicity test

CMI-2009114B
Page no. 01/10

Report no:

CMI-2009114B

Study Title:

Systemic toxicity Test

Test Article:

CollaDental Barrier

November, 2009

CMI-2009114B
Page no. 02/10

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Science Park
Miaoli County, 350, Taiwan

Study announcement:

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Approved by

Date

Jasper Chou

2009. 11. 30

CMI-2009114B
Page no. 03/10

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-2009114B
Page no. 04/10

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Page no. 05/10

SUMMARY

An systemic toxicity study was conducted on the test article, CollaDental Barrier, to test the potential of systemic toxic reactions in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 11: Tests for Systemic Toxicity. Hydrophilic and hydrophobic extracts of the test articles were prepared using 0.9% sodium chloride and sesame oil. A single dose of test extract was intraperitoneally (IP) injected into each of five mice per extract. The vehicle controls were also administrated into five mice per vehicle via the IP route.

Under the test conditions described here, the extracts from CollaDental Barrier showed no evidence of systemic toxicity. It met the requirement of the test since the no mortality or evidence of systemic toxicity was found. The negative controls performed as expected.

CMI-2009114B
Page no. 06/10

INTRODUCTION

The USP and ISO systemic toxicity method was used in this study. This test was designed to determine the systemic toxicity of extractable substances from the test article. A single dose of extract of the sample was injected into five mice and followed up for 3 days. The signs of systemic toxicity, such as death or decreased body weight, were examined.

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

Extraction solvents: 0.9% sodium chloride and sesame oil

Test system

Mouse (*Mus musculus*), Male, C57BL/6 strain, 4 weeks of age

Experimental designs

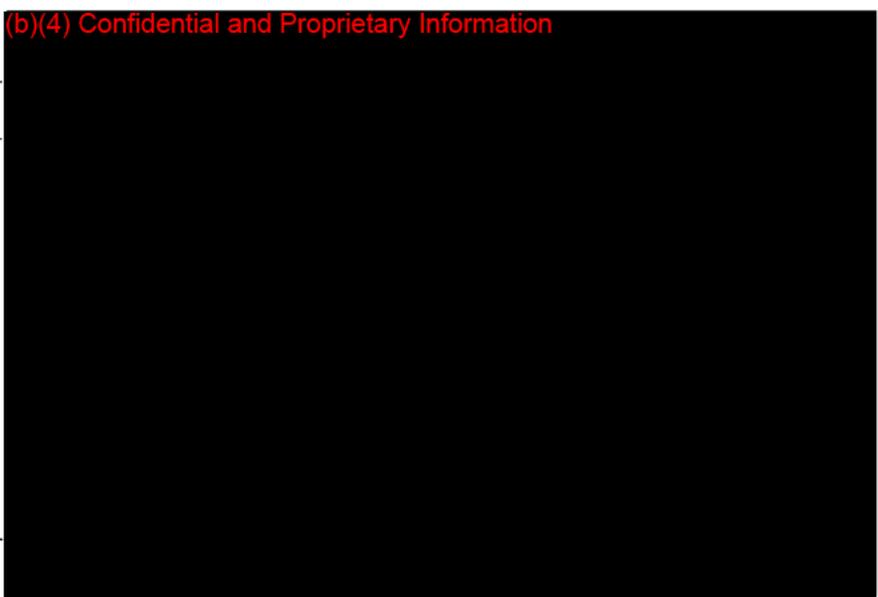
Extract Preparation

Extraction vehicle –

Test article –

Vehicle control –

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(b)(4) Confidential and Proprietary Information



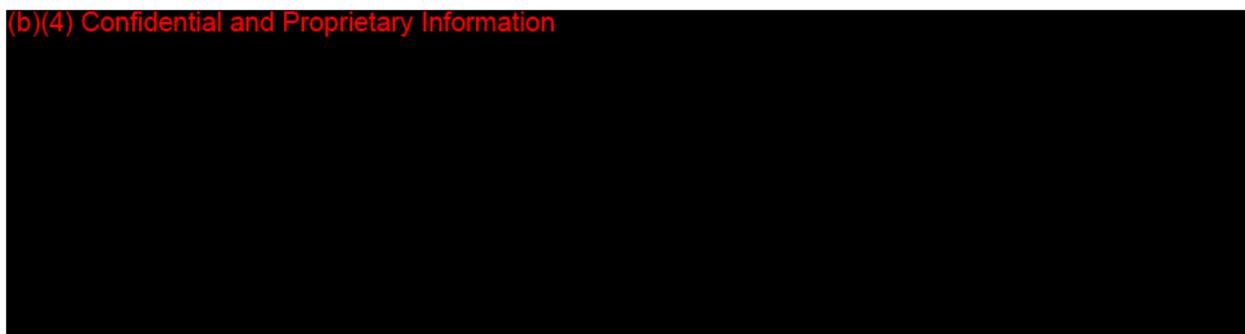
Treatment method

Five mice per extract were weighed and injected with the test extract at a dose of 50ml/kg. Another five mice were injected with the corresponding vehicle control. All extract and control were administered by the intraperitoneal (IP) route. The animals were kept at their cages.

After dosing, the animals were observed for adverse reactions immediately and at 4 hours, 24 hours, 48 hours, and 72 hours. At the end of this assay, all animals were weighed.

Evaluation criteria

(b)(4) Confidential and Proprietary Information

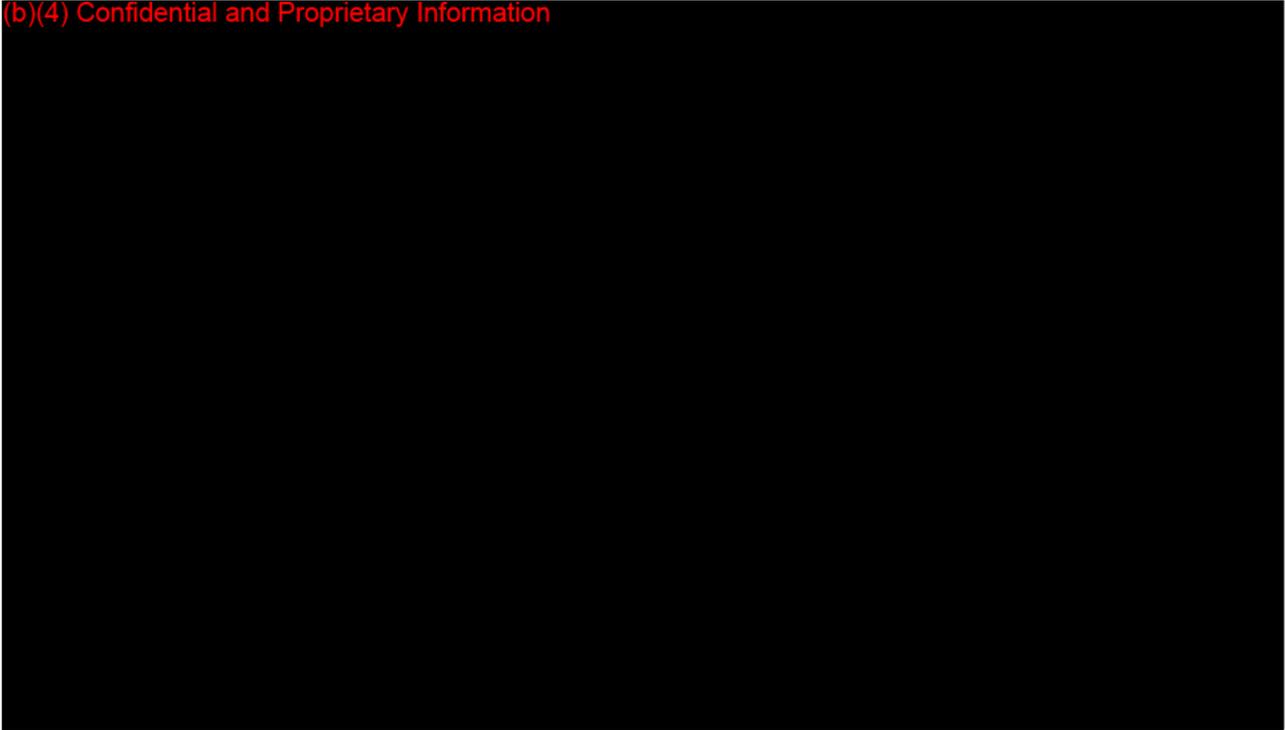


CMI-2009114B

Page no. 08/10

RESULTS

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CONCLUSION:

Under the test condition described above, CollaDental Barrier did not cause systemic toxic effect and could not be considered as an acutely toxic substance.

REFERENCES:

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 11: Tests for Systemic Toxicity (ISO).

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

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Page no. 09/10

Table 1. Body weight and mortality observations

	Test extract	Vehicle control
Extract vehicle, route, dose	(b)(4) Confidential and Proprietary Information	
0.9% NaCl, IP, 50ml/kg		
Sesame oil, IP, 50ml/kg		

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Page no. 10/10

Table 2. Clinical observations

	Test extract	Vehicle control
Immediate	(b)(4) Confidential and Proprietary Information	
4 hours		
24 hours		
48 hours		
72 hours		

Note: AN: appeared normal; U: Ungroomed.

Attachment 9.5 Ames test

CMI-2009115B
Page no. 01/12

Report no:

CMI-2009115B

Study Title:

***Salmonella typhimurium* reverse mutation (Ames)
test**

Test Article:

CollaDental Barrier

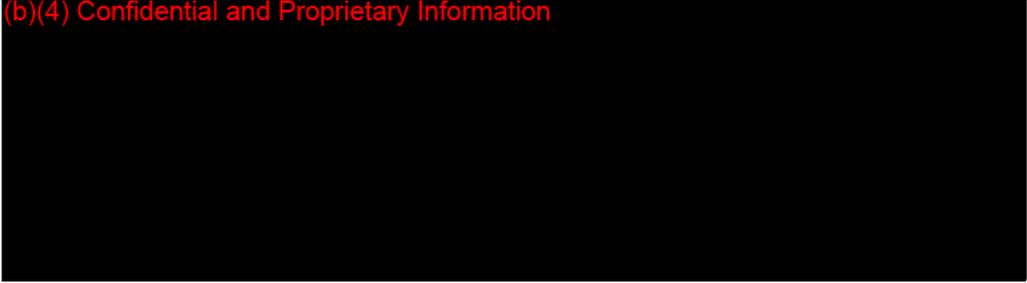
November, 2009

CMI-2009115B
Page no. 02/12

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



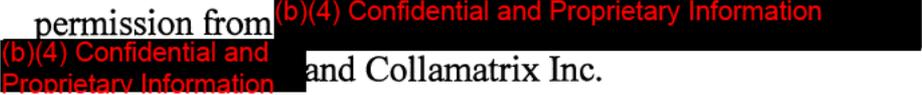
Sponsor:

Collamatrix Inc.

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Miaoli County, 350, Taiwan

Study announcement:

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Date

Jasper Chou

2009. 11. 30

CMI-2009115B
Page no. 03/12

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-2009115B
Page no. 04/12

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Page no. 05/12

SUMMARY

A mutagenic test was conducted on CollaDental Barrier to test its mutagenic potential in accordance with the International Organization for Standardization 10993: Biological Evaluation of Medical Devices – Part 3: Test for genotoxicity, carcinogenicity and reproductive toxicity.

Under the test conditions described here, CollaDental Barrier did not cause significant genetic alterations in the tester microorganism as compared with the negative controls. The positive controls performed as expected. These results suggested the CollaDental Barrier is non-mutagenic.

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Page no. 06/12

INTRODUCTION

The *Salmonella typhimurium* reverse mutation (Ames) test was used in this study. This is a bioassay addressing the genotoxic activity and is used to test for mutagenic activity of a substance. A substance is mutagenic if it causes a change in the genetic material of a living cell or organism. Several tester strains of *S. typhimurium* which require the amino acid histidine for growth were applied for this test (see Table 1).

Table 1 Characteristics of *S. typhimurium* tester strains

Parameter	<i>S. typhimurium</i> tester strains				
	97A	98	100	102	1535
<i>uvrB</i>	+	+	+	—	+
<i>R</i> -factor	+	+	+	+	—
<i>rfa</i>	+	+	+	+	+
Histidine requirement	+	+	+	+	+

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

Experimental designs

Positive controls:

Three positive controls were included in this test, including sodium azide, 4-nitro-0-phenylene-diamine (NPD), and 2-aminofluorene (2-AF). The expected of those controls were listed bellowed.

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Table 2. Expected result of positive controls used

Control item	Activation	Strains				
		97A	98	100	102	1535
Sodium azide	No	—	—	+	—	+
NPD	No	+	+	+	—	—
2AF	S-9	+	+	+	—	—

Tester stains culture and verification

The tester strains were cultured on minimal glucose agar plates fortified with biotin and histidine. Other characteristics were confirmed in Table 3. The culture plates were incubated at $37 \pm 2^\circ\text{C}$ for 48~72 hours. A single colony was used to inoculate nutrient broth. The broth cultures were allowed to grow at $37 \pm 2^\circ\text{C}$ for 10~14 hours on an orbital shaker at 100~120 rpm.

Table 3. Verification of tester strains

Parameter	Characteristics
<i>uvrB</i>	UV sensitive (lack nucleotide excision repair system)
<i>R-factor</i>	Ampicillin sensitivity (25 $\mu\text{g}/\text{ml}$)
<i>rfa</i>	Sensitivity of crystal violet (0.1%) in nutrient agar plate
<i>HIS-</i>	Survival in minimal glucose agar plates w/ or w/o biotin and histidine.

Metabolic activation of extracts from test or control articles

The treatment of S-9 activation system was used to identify for the presence of potential mutagens from the metabolic byproducts of the test article. Briefly, test substance and S9 preparation were incubated at 37°C for one hour, mixed with bacterial culture and soft

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agar, and added to minimal glucose agar plates.

Plate incorporation assay

Aliquots of top agar containing biotin and histidine were kept at $45 \pm 2^\circ\text{C}$. The top agar was plated on minimal glucose agar plates with or without 0.1ml of test substance (activated or not) and positive controls. Fourplicates per sample were performed. The culture plates were incubated at $37 \pm 2^\circ\text{C}$ for 48~72 hours.

Spot tests

Two ml aliquots of the top agar containing biotin and histidine and bacterial broth culture were mixed and poured on the minimal glucose agar plates. After hardening of the agar, 10 μl spot of test or positive substances were added on those plates. The culture plates were incubated at $37 \pm 2^\circ\text{C}$ for 48~72 hours.

Test criteria:

The criteria for acceptance of the Ames test and criteria for determination of a mutagen were listed below.

Test	Plate Incorporation test and Spot test are performed.
Tester stains	TA97A, TA98, TA100, TA102, and TA1535 are included.
Activation	In the presence and absence of liver microsomal enzymes (S-9)
Verification	All tester strains are verified and achieve the appropriate responses.
Positive controls	All positive controls included must give the appropriate responses.
Mutagen	A. A 2-fold increase over spontaneous reversion rat (>200%) B. A dose response curve when dilutions are tested
Non-mutagen	A. A less than 2-fold increase over spontaneous reversion rat (<200%) B. No dose response curve when dilutions are tested

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RESULTS

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CONCLUSION:

Under the experimental conditions of this study, the CollaDental Barrier is non-mutagenic.

REFERENCES:

Ames, B. N. and Maron D. M. 1983. Revised method for the *Salmonella* mutagenicity test. *Mutation Res.* 113:173-215.

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices – Part 3: Test for genotoxicity, carcinogenicity and reproductive toxicity.

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices – Part 12: Sample preparation and reference materials.

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Table 4. TA97A revertants record

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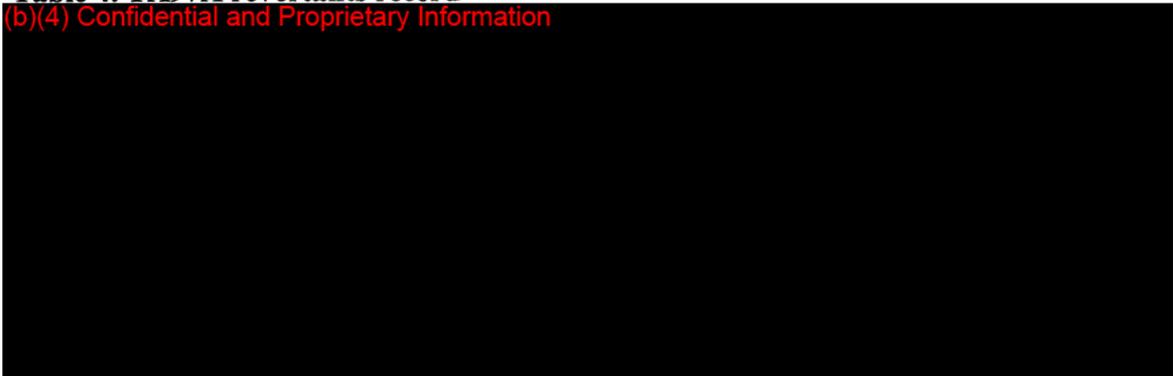


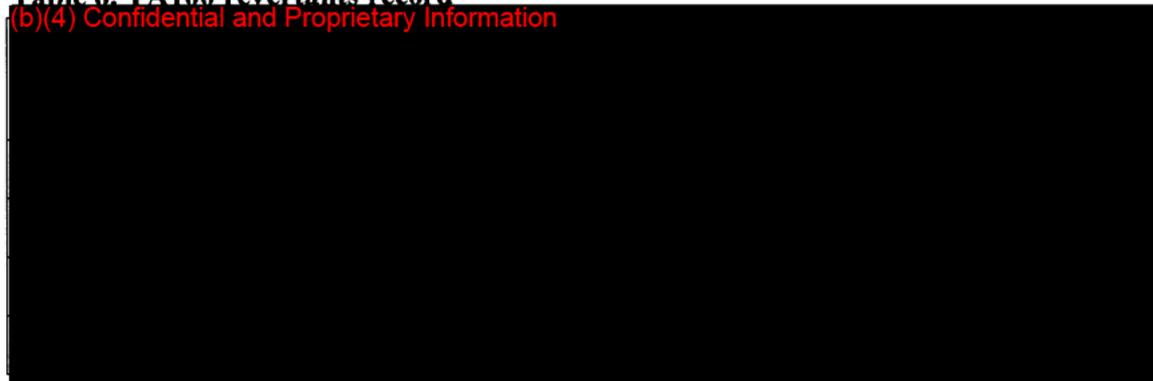
Table 5. TA98 revertants record

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Table 6. TA100 revertants record

(b)(4) Confidential and Proprietary Information



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Table 7. TA102 revertants record

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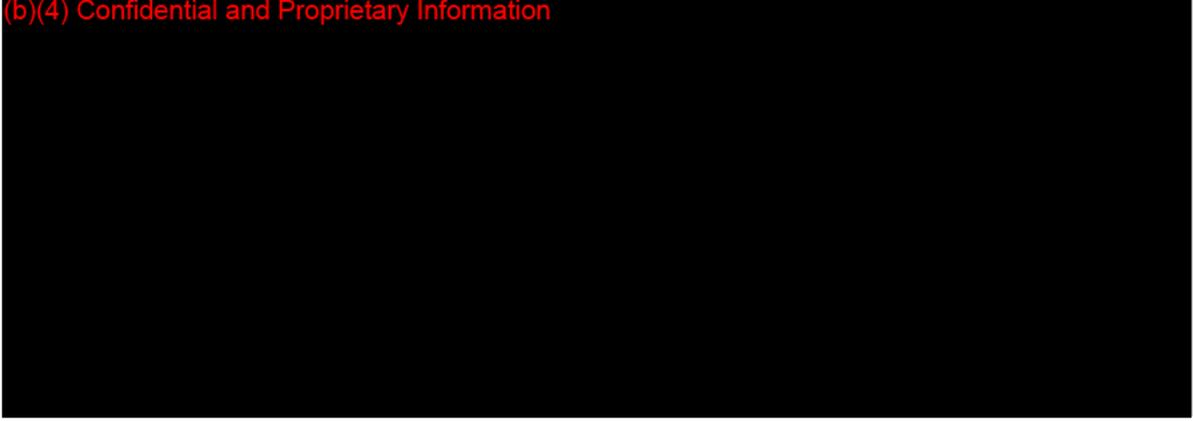


Table 8. TA1535 revertants record

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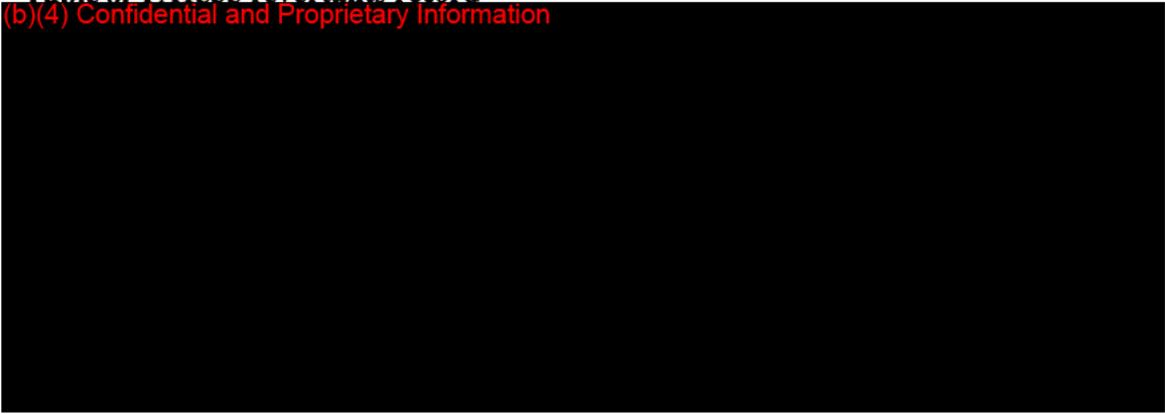


Table 9. Spot test record

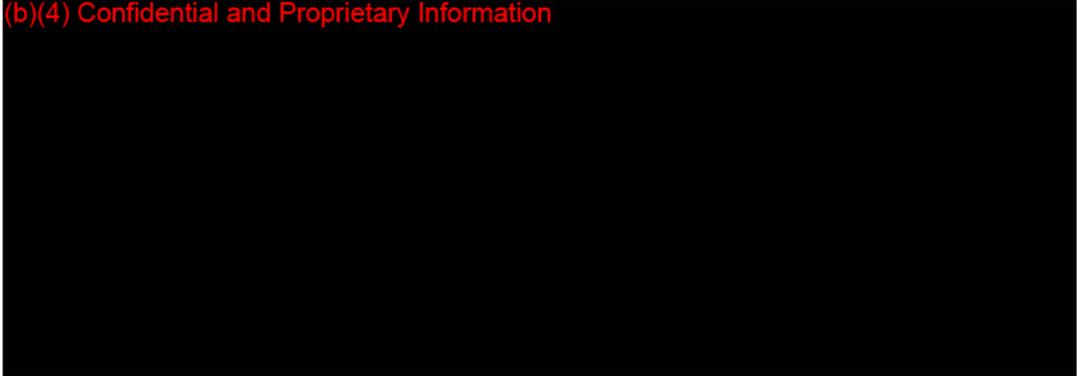
(b)(4) Confidential and Proprietary Information



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Table 10. Positive controls record

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Attachment 9.6 Micronucleus assay

CMI-2009119B
Page no. 1/9

Report no:

CMI-2009119B

Study Title:

Micronucleus assay

Test Article:

CollaDental Barrier

November, 2009

CMI-2009119B
Page no. 2/9

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information

Sponsor:

Collamatrix Inc.

1F, No. 50-1, Keyen Rd. Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

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Approved by

Date

Jasper Chou

2009. 11.30

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Page no. 3/9

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-2009119B
Page no. 4/9

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Page no. 5/9

SUMMARY

An ISO micronucleus assay was conducted on the test article, CollaDental Barrier, to detect the chromosomal damage potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 3: Tests for Genotoxicity, Carcinogenicity, and Reproductive Toxicity.

Under the test conditions described here, CollaDental Barrier did not cause significant micronucleus formation in the tester cell as compared with the negative controls. The positive controls performed as expected. These results suggested the CollaDental Barrier is non-genotoxic.

CMI-2009119B

Page no. 6/9

INTRODUCTION

The purpose of the in vitro micronucleus assay is to detect those agents which modify chromosome structure and segregation in such a way as to lead to induction of micronuclei in interphase cells. These micronuclei may originate from acentric fragments (chromosome fragments lacking a centromere) or whole chromosomes which are unable to migrate with the rest of the chromosomes during the anaphase of cell division.

MATERIALS AND METHODS

Test article

Test article: CollaDental Barrier (15mm x 20mm) was extracted with 0.9% sodium chloride solution and sesame oil.

Control

Concurrent negative (solvent or vehicle) and positive controls both with and without metabolic activation are included in each experiment.

Positive controls	without metabolic activation	with metabolic activation
Clastogen	Mitomycin C	Cyclophosphamide
Aneugen	Colchicine	-

Test system

V79 cell line was used in this test. Cells were propagated from stock cultures, seeded in culture medium at a density such that the cultures will not reach confluency before the time of harvest. Cell density was counted with a hemocytometer.

The treatment of S-9 activation system was used to identify for the presence of potential mutagens from the metabolic byproducts of the test article.

CMI-2009119B

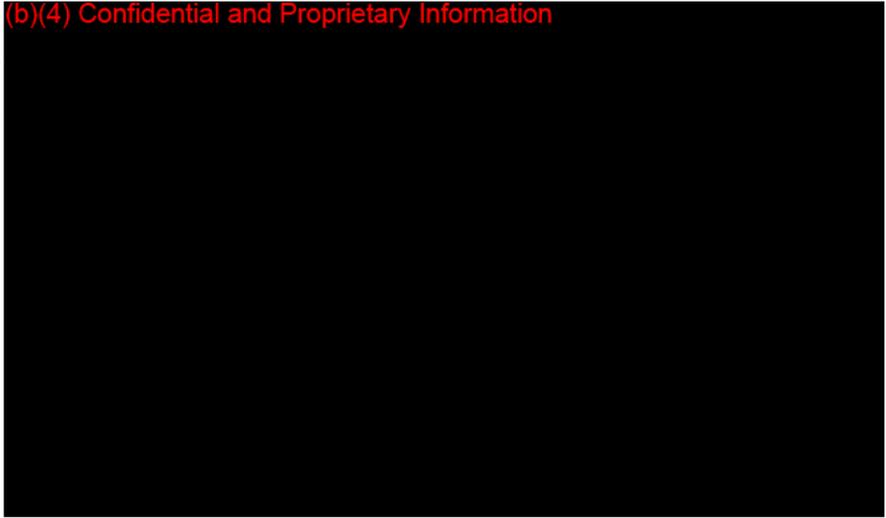
Page no. 7/9

Extract Preparation

Extraction vehicle –

Test article –

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Exposure concentration

In consideration of solubility and cytotoxicity the highest test item concentrations is 5µl /ml. At least three analysable concentrations are tested.

Incubation time

Cells are exposed continuously to test substances for 48 hours and then sampled.

Evaluation criteria

(b)(4) Confidential and Proprietary Information



CMI-2009119B

Page no. 8/9

RESULT

Table 1 Summary of mutagenicity assay, with S9

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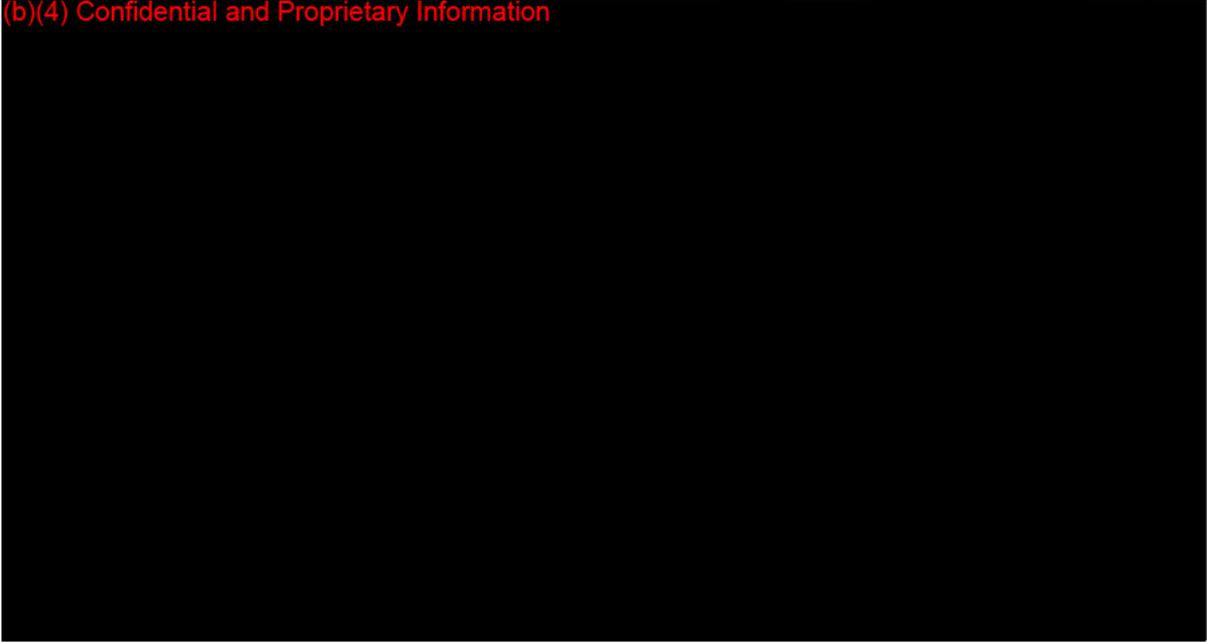
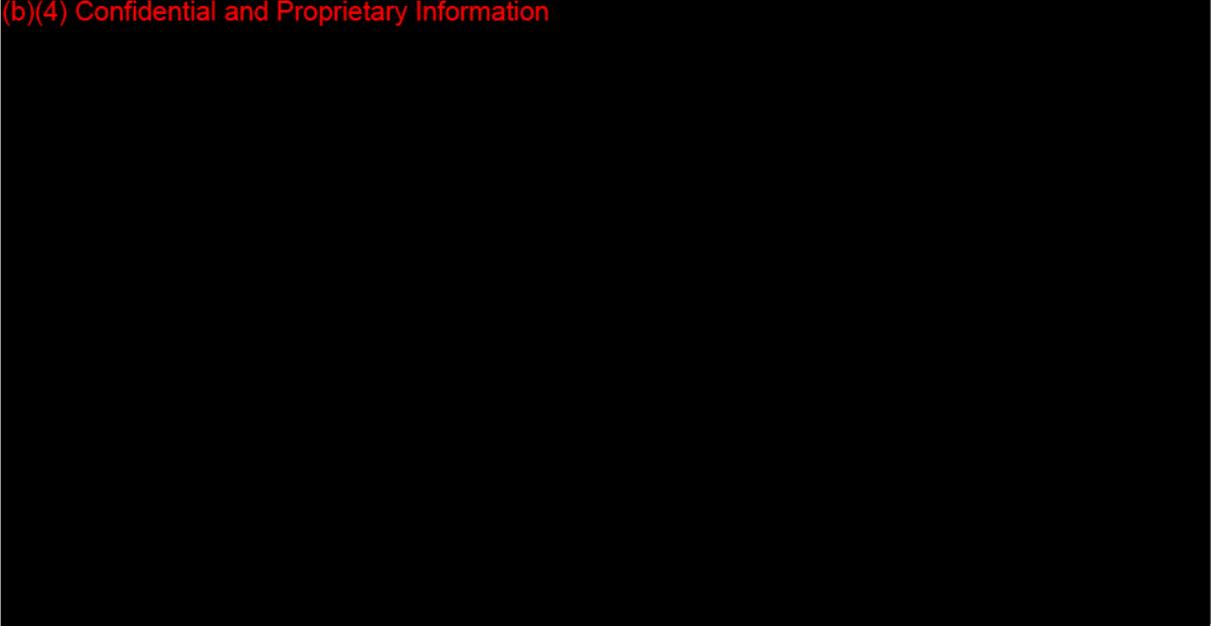


Table 2 Summary of mutagenicity assay, without S9

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Page no. 9/9

CONCLUSION:

Under the test condition described above and the result summaries shown in Table 1 and table 2, CollaDental Barrier could not be considered as a genotoxin.

REFERENCES:

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices —Part 3: Tests for Genotoxicity, Carcinogenicity, and Reproductive Toxicity.

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

Attachment 9.7 Mouse lymphoma assay

CMI-20091120B

Page no. 01/11

Report no:

CMI-20091120B

Study Title:

Mouse lymphoma assay

Test Article:

CollaDental Barrier

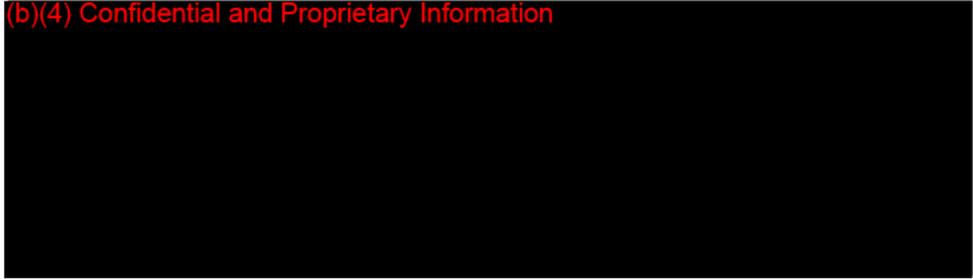
November, 2009

CMI-20091120B
Page no. 02/11

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

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Study announcement:

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Approved by

Date

Jasper Chou

2009. 11. 30

CMI-20091120B
Page no. 03/11

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-20091120B
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CMI-20091120B

Page no. 05/11

SUMMARY

An ISO mouse lymphoma assay was conducted on the test article, CollaDental Barrier, to detect the gene mutation potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 3: Tests for Genotoxicity, Carcinogenicity, and Reproductive Toxicity.

Under the test conditions described here, CollaDental Barrier did not cause significant gene mutation in L5178Y mouse lymphoma cells as compared with the negative controls. The positive controls performed as expected. These results suggested the CollaDental Barrier is non-genotoxic.

CMI-20091120B
Page no. 06/11

INTRODUCTION

The purpose of this study is to evaluate the mutagenic potential of the test article based on quantization of mutations caused by base pair changes, frameshift and small deletions at the thymidine kinase locus of L5178Y mouse lymphoma cells. Mutant cells, deficient in TK due to the forward mutation in the TK locus (from TK⁺ to TK⁻), are resistant to the cytotoxic effect of trifluorothymidine (TFT). The mutagenicity of the test agents is indicated by the increase in the number of mutants after treatment.

MATERIALS AND METHODS

Materials

Test and control article

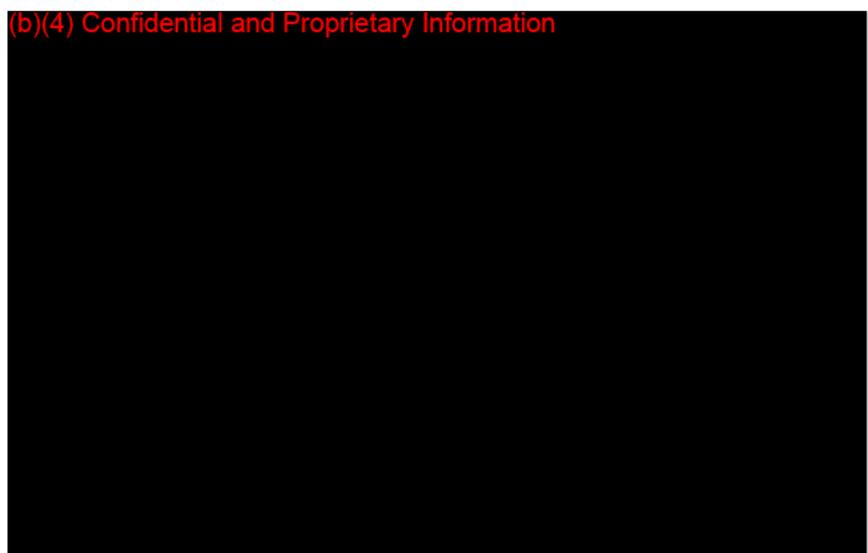
Test article: CollaDental Barrier (15mm x 20mm)

Extract Preparation

Extraction vehicle –

Test article –

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CMI-20091120B

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Dose selection

A preliminary range finding experiment will be conducted using 9 doses of test article extract, the highest concentration being the lowest insoluble dose in treatment medium range with 5000µg/mL as the top concentration. The procedures for range finding are identical to that used for mutagenesis except that the cultures are terminated after 24-48 hours without further cloning. The toxicity is indicated by the decrease of cell number in the suspension culture compared with that in untreated control. Four to five concentrations will be selected based on the result and used in the mutagenesis assay. The highest dose should produce a low level of survival (approximately 10-15%), and the survival in the lowest dose should be the same as the negative control.

Controls

0.9% sodium chloride and DMSO will be vehicle control. Methylmethanesulphonate (without S9 mixture) and Cyclophosphamide (with S9 mixture) will be used as the positive controls. Both mutagens are dissolved in DMSO. Both positive controls exhibited more than 2-fold increases in L5178T TK or TFT resistant colonies as compared to the vehicle control

Test system

L5178Y/TK^{+/-} mouse lymphoma cells are heterozygous at the normally diploid thymidine kinase (TK) locus. All treatment groups information are listed in Table 1.

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Page no. 08/11

Experimental designs

Metabolic activation of extracts from test or control articles

(b)(4) Confidential and Proprietary Information



Mutagenesis assay

a. Exposure

(b)(4) Confidential and Proprietary Information



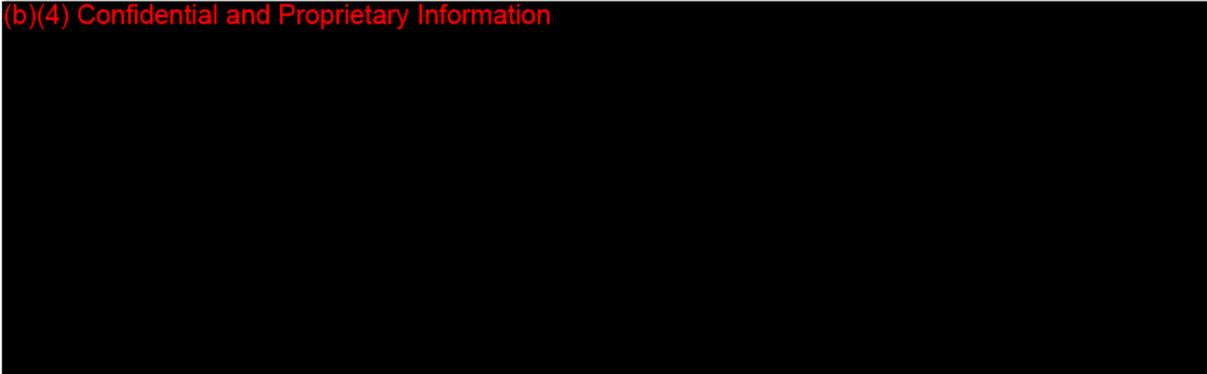
b. Expression:

(b)(4) Confidential and Proprietary Information



c. Cloning

(b)(4) Confidential and Proprietary Information



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Page no. 09/11

d. Colony counting and sizing:

Colonies are counted and sized 11-14 days after cloning using. The mutant frequency is calculated and adjusted based on the survival percentage.

Evaluation/Analysis

(b)(4) Confidential and Proprietary Information



Interpretation of results

A test agent will be considered to be positive in the mouse lymphoma cell mutagenesis assay if it induces a statistically significant dose-related increase in the mutant frequency, or generates a reproducible and statistically significant increase in the mutant frequency for at least one concentration.

Table 1 Treatment groups in the mutagenicity assay

Treatment groups	S9 activator
(b)(4) Confidential and Proprietary Information	

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Page no. 10/11

RESULTS

Evaluation of the potential mutagenic activity of CollaDental Barrier in the mouse lymphoma assay.

Table 2 Summary of mutagenicity assay, without S9

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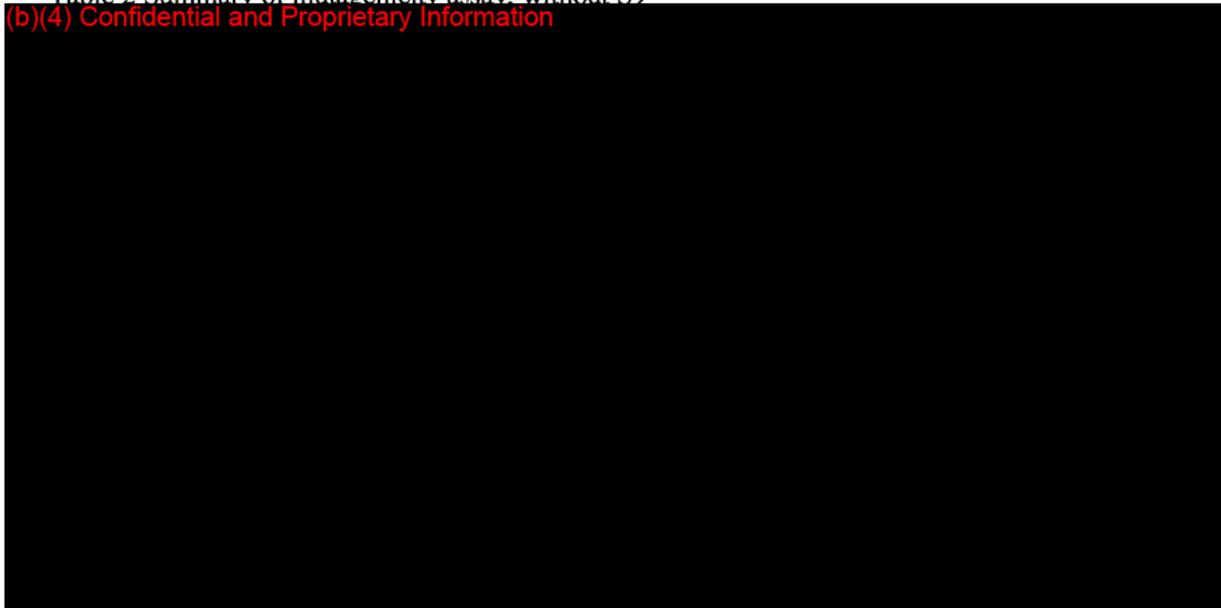


Table 3 Summary of mutagenicity assay, with S9

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Page no. 11/11

CONCLUSION:

Under the test condition described above and the result summaries shown in Table 2 and table 3, CollaDental Barrier could not be considered as a genotoxin.

REFERENCES:

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices —Part 3: Tests for Genotoxicity, Carcinogenicity, and Reproductive Toxicity.

The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

Attachment 9.8 Hemolysis test

CMI-2009116B
Page no. 01/10

Report no:

CMI-2009116B

Study Title:

Hemolysis Test

Test Article:

CollaDental Barrier

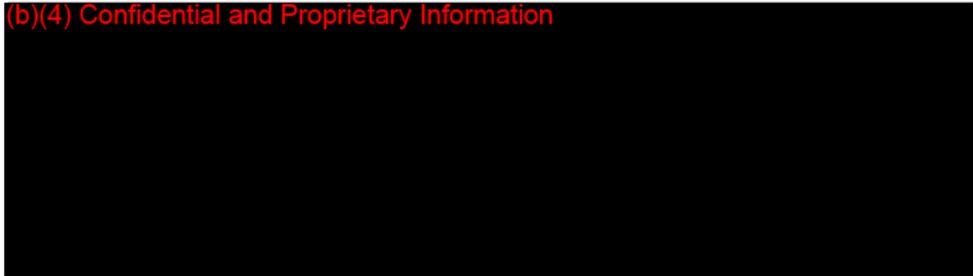
November, 2009

CMI-2009116B
Page no. 02/10

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1st Floor, No. 50-1, Keyen Road, Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

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Approved by

Date

Jasper Chou

2009. 11. 30

CMI-2009116B

Page no. 03/10

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-2009116B

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CMI-2009116B

Page no. 05/10

SUMMARY

An *in vitro* blood compatibility study was conducted on the test article, CollaDental Barrier, to test the hemolytic potential in accordance to the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 4: Selection of tests for interaction with blood. Duplicate extracts of the test articles were prepared using 0.9% sodium chloride. The test extract was incubated with rabbit blood. Both non-hemolytic and hemolytic controls were included. All extract-blood cultures were incubated at 37°C for 4h. After incubation, all samples were subjected to centrifugation and the supernatants were added to Drabkin's reagents. The absorption of samples at 540nm was detected spectrophotometrically.

Under the test conditions described here, the saline extract from CollaDental Barrier showed no evidence of hemolytic effect. It met the requirement of the test since the hemolytic index was very low and the hemolytic grade was near a nonhemolytic grade. The negative and positive controls performed as expected.

INTRODUCTION

The *in vitro* hemolysis method was used in this study. This test was designed to determine the blood biocompatibility of extractable substances from the test article. An extract of the sample was added to blood sample and incubated for 4 hours. After centrifugation, the absorbance (ABS) at a wavelength of 540nm of hemoglobin released was used to calculate the hemolytic grade (see Table 1).

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

Control articles:

Negative control: sterile USP negative control plastic high-density polyethylene

Positive control: sterile water

Extraction solvent: 0.9% sodium chloride

Test system

Clot-free blood samples for use in this test were collected from three male New Zealand White rabbits (*Oryctolagus cuniculus*) into EDTA vacuum tubes.

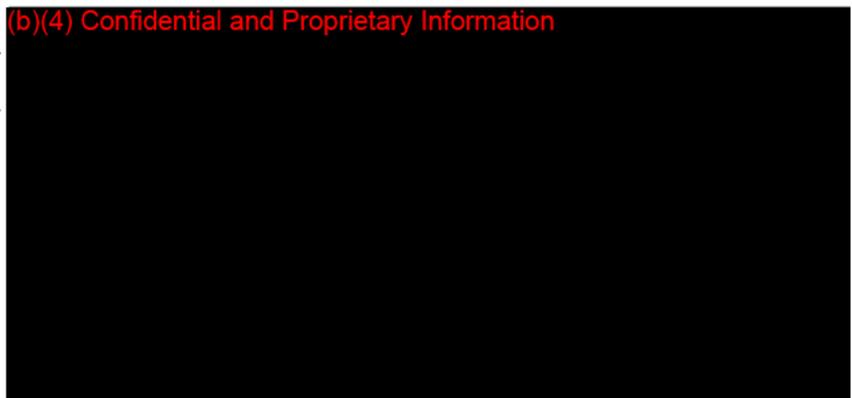
Experimental designs

Extract Preparation

Extraction vehicle –

Test article –

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CMI-2009116B

Page no. 07/10

Vehicle control

(b)(4) Confidential and Proprietary Information

Treatment method

The pooled rabbit blood was diluted with saline to a total hemoglobin concentration of 40 ± 5 mg/ml. A 1ml aliquot of diluted blood was added to four tubes containing 8ml of two test extracts (A and B), negative control extract, and positive control extract, respectively. The tubes were inverted gently to mix the contents and then kept stationary for 4h at $37 \pm 1^\circ\text{C}$.

At the end of this assay, the tubes were centrifuged at for 700-800 x g and the absorbance (ABS) of individual supernatants at 540nm wavelength was determined via a spectrophotometer. The degree of hemolytic effects was scored according to the table 1.

Table 1. Classification of hemolytic effects

Hemolytic Index	Hemolytic Grade
0 ~ 2 %	Nonhemolytic
3 ~ 10 %	Slightly Hemolytic
11 ~ 20 %	Moderately Hemolytic
21 ~ 40 %	Markedly Hemolytic
> 40 %	Severely Hemolytic

The hemolytic index was calculated as:

$$\frac{\text{ABS of test} - \text{ABS of negative control}}{\text{ABS of positive control} - \text{ABS of negative control}}$$

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Evaluation criteria

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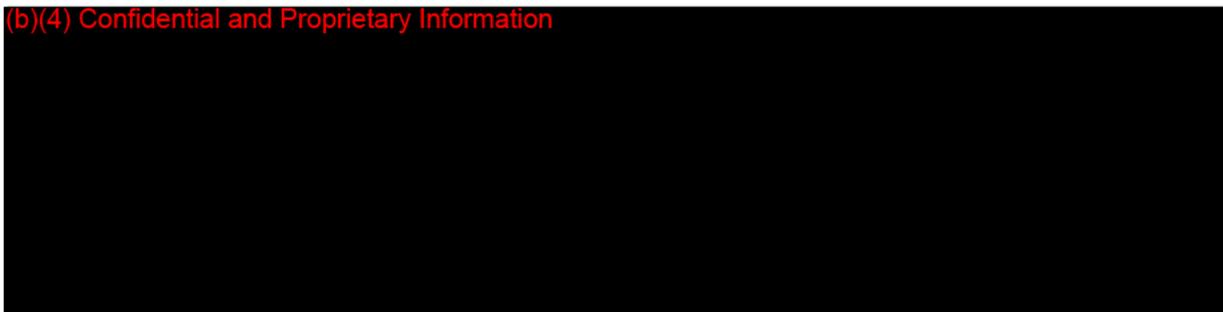


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RESULTS

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CONCLUSION:

The normal saline extract from CollaDental Barrier showed no signs of hemolytic effect and met the requirements of the test (nonhemolytic). CollaDental Barrier is a non-hemolytic device.

REFERENCES:

The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 4: Selection of tests for interaction with blood.

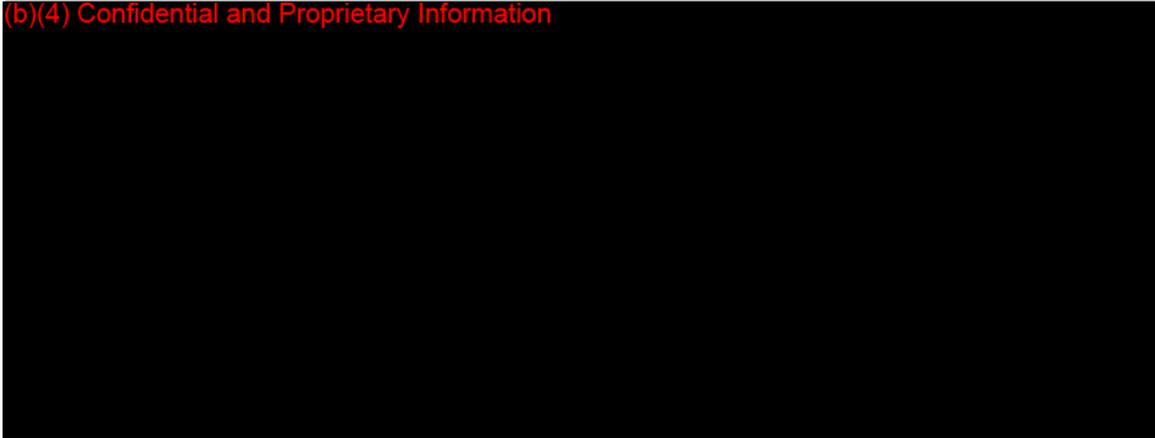
The International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

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Table I. Hemolytic activity observations

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Attachment 9.9 Endotoxin test

CMI-2009117B
Page no. 01/13

Report no:

CMI-2009117B

Study Title:

Limulus amoebocyte lysate (LAL) test

Test Article:

CollaDental Barrier

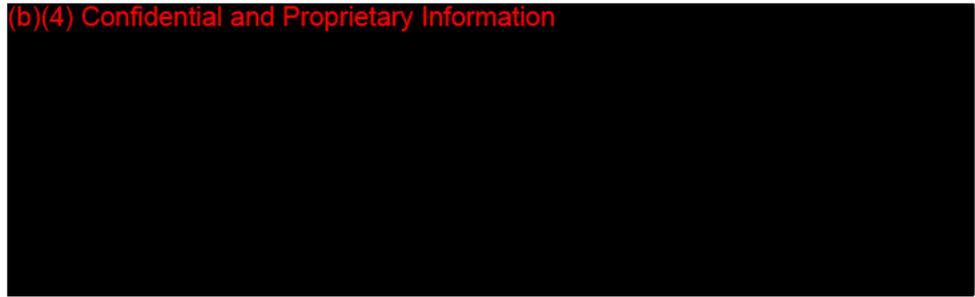
November, 2009

CMI-2009117B
Page no. 02/13

Study Report

Test Facility:

(b)(4) Confidential and Proprietary Information



Sponsor:

Collamatrix Inc.

1st Floor, No. 50-1, Keyen Road, Jhunan Township
Miaoli County, 350, Taiwan

Study announcement:

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Approved by

Date

Jasper Chou

2009. 11. 30

CMI-2009117B

Page no. 03/13

The sample provided by sponsor was identified as follow

Name	CollaDental Barrier
Packaging	Blister pouch
External feature	Membrane
Color	White to off white
Component(s)	Porcine collagen
Storage condition	Room temperature, Dry
Expiration date	Stable for duration intended testing
Sample disposition	Any remaining sample will be discarded

CMI-2009117B

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CMI-2009117B

Page no. 05/13

SUMMARY

An *in vitro* biocompatibility study was conducted on the test article, CollaDental Barrier, to test the pyrogenic potential in accordance to the United States Pharmacopeia (USP) Method 85 – Bacterial endotoxin testing: the *Limulus* Amebocyte Lysate (LAL) Gel Clot method. The amoebaocyte lysate from Horseshoe crab (*Limulus polyphemus*) was applied to detect bacterial endotoxin contamination in the test article.

The validation of LAL assay included sensitivity confirmation and inhibition/enhancement tests. Under the test conditions described here, the extract from CollaDental Barrier showed no evidence of detectable pyrogenic activity. It met the requirement of the test since the endotoxin of CollaDental Barrier was less than 10 Endotoxin Unit (EU) per device. All negative and positive controls performed as expected.

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Page no. 06/13

INTRODUCTION

The *Limulus* amoebocyte lysate (LAL) test, when used according to US FDA guidelines, may be substituted for the USP Pyrogen Test (Rabbit fever test) for the final product testing of “human injectable drugs (including biological products), animal injectable drugs and medical devices. The LAL test is recommended for the quantization of endotoxin in raw material used in production, including water, and for in-process monitoring of endotoxins level. Several techniques can be performed for the LAL test, including gel-clot or photometric techniques.

Here, the gel-clot techniques were used to detect or quantify endotoxins based on clotting of the LAL Reagent in the presence of endotoxin. The amoebaocyte lysate from Horseshoe crab contained a protein that interacts with the endotoxin and coagulates it. The concentration of endotoxin required to cause the lysate to clot under standard conditions is the labeled sensitivity of the LAL Reagent (0.25 EU/mL here). In general, the endotoxin limit for medical devices is 20 EU/ per device.

MATERIALS AND METHODS

Materials

Test article: CollaDental Barrier (15mm x 20mm)

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Endotoxin standard: *Escherichia coli* strain 113:H10 (2000 EU/ml).

Test system

Pyrotell LAL reagent (Associates of Cape Cod, Inc.)

It contains an aqueous extract of amoebocytes of *L. polyphemus*, 1.5% v/v of 25% human serum albumin (stabilizer), 3% NaCl, and other appropriate ions.

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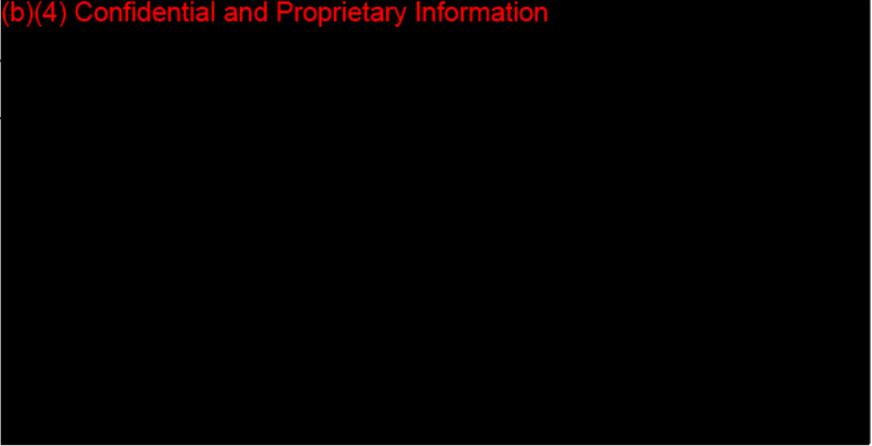
Experimental designs

Extract Preparation

Extraction vehicle

Sample solution

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Treatment method

The LAL assay was performed in duplicate using Pyrotell LAL reagent. The assay was performed in pyrogen-free test tubes to which 0.1ml of extract obtained from CollaDental Barrier and 0.1ml of LAL reagent were added. Following 60 minutes of undisturbed incubation at 37°C non-circulated water or dry bath, the test tubes were examined by 180° inversion for the presence of a stable solid clot. A clotted incubation mixture was considered to be a positive result. Endotoxin standard and pyrogen-free LAL reagent water, both provided by the manufacturer, were used as a control.

Confirmation of Labeled Endotoxin Sensitivity

To confirm the sensitivity of Pyrotell and quality of the technician by doing the LAL test on a series of twofold diluted endotoxins as shown in Table 1. The labeled sensitivity of the LAL Reagent (λ) or also known as the endpoint of the assay is the minimum concentration of reference standard endotoxin that causes gel-clot formation under standard conditions.

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Interfering factor test for the gel-clot technique

Prepare solutions a, b, c, and d as shown in Table 2, and perform the inhibition/enhancement test on the sample solution. Solutions A, B, C, and D are the blank that is free of detectable endotoxin, test group for possible interference, control group for labeled LAL Reagent sensitivity (λ) and negative control of LAL Reagent Water, respectively.

Titration analysis of endotoxin in test solution

Prepare solutions a, b, c, and d as shown in Table 3, and quantify the endotoxin levels in the sample solution by series of twofold dilutions. Solutions A included a series twofold diluted sample solution. Solutions B contain undiluted sample solution containing endotoxin standard. Solutions A included a series twofold diluted endotoxin solution. Solution D is the negative control of LAL Reagent Water.

Evaluation criteria

For medical devices, the endotoxin limit is not more than 20 Endotoxin Unit (EU) per device in accordance with the United States Pharmacopeia standard.

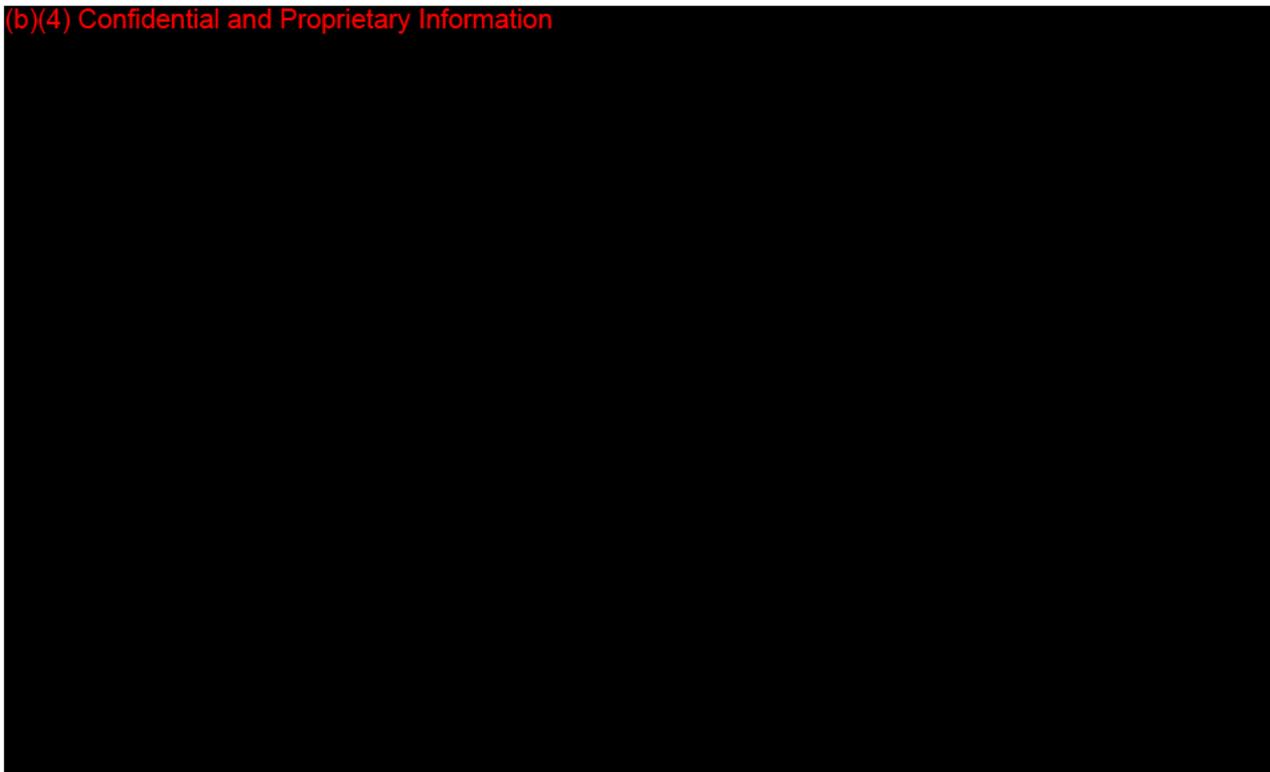
For validation of the test, the sample solution could not inhibit or enhance the LAL reaction and the sensitivity confirmation must be performed.

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RESULTS

(b)(4) Confidential and Proprietary Information



CONCLUSION:

The LAL test is valid because: (1) labeled endotoxin sensitivity was confirmed; (2) all negative control solutions failed to cause gel-clot; (3) all negative control solutions succeed to cause gel-clot; and (4) the sample solution did not inhibit or enhance the gel-clot reaction.

Under the study, no gel-clot formation was observed in sample solution (Table 3) indicated that the level of endotoxin presence in the sample solution is beyond the detection limit (0.25 EU/ml).

Therefore the result suggested endotoxin levels in CollaDental Barrier (1cm x 2cm) is <10 EU and met the endotoxin limit for medical device (<20 EU per device).

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REFERENCES:

The United States Pharmacopeia (USP) Chapter <85>: Bacterial endotoxin testing: the Limulus Amebocyte Lysate (LAL) Gel Clot method.

The US Food and Drug Administration's 1987 guidance document – Guideline on Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices

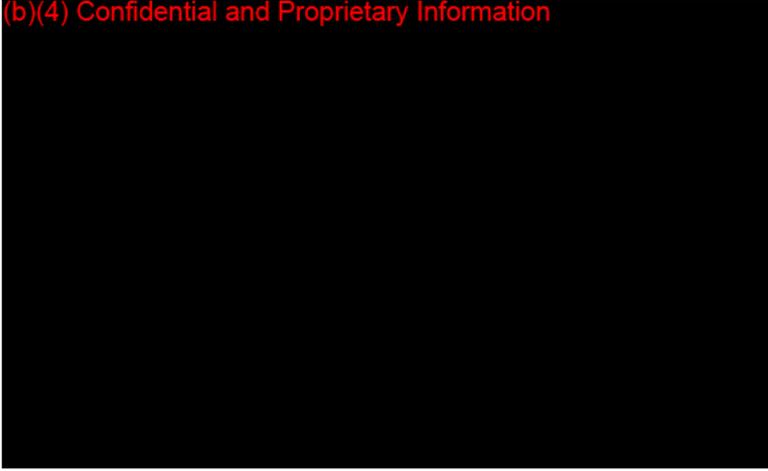
The international Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 12: Sample preparation and reference materials.

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Table 1. Sensitivity of standard endotoxin series

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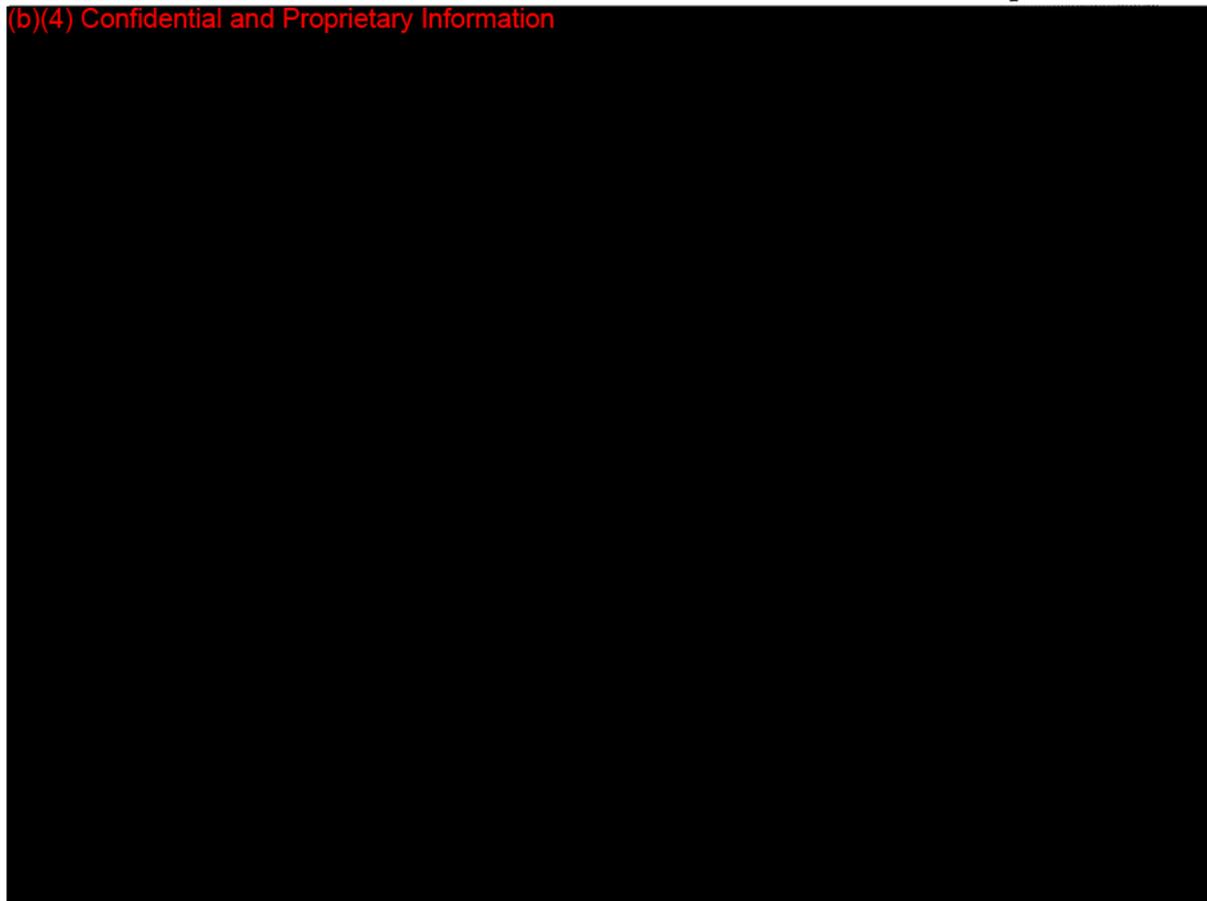


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Table 2. Results of the Inhibition/Enhancement Test for Gel-Clot Technique

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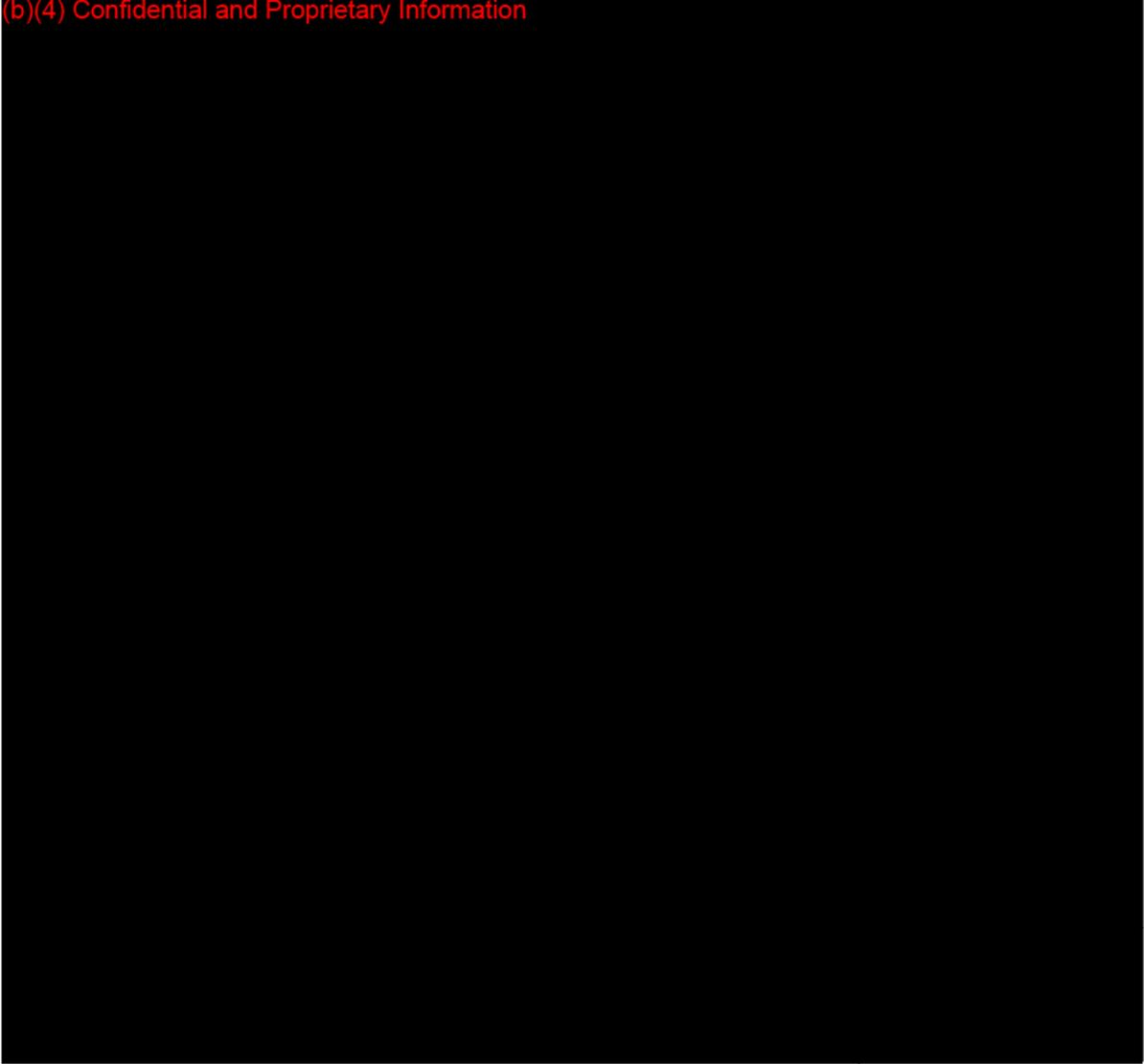


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Table 3. Results of Gel-Clot Technique

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Executive Summary

Device description

CollaDental Barrier is a membrane used in oral surgery and periodontal surgery to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. Such a method of preventing epithelial migration into a specific area is known as guided tissue regeneration (GTR). It comprises of odorless, hydrophilic (b)(4) Confidential and Proprietary Information porcine collagen membrane with a white appearance. It is water insoluble but lightly soluble in hot water and completely soluble in either acidic solution ($\text{pH} \leq 3$) or basic solution ($\text{pH} \geq 10$).

CollaDental Barrier is a white to off white, non-friable, conformable, resorbable, membrane consisting of purified type I collagen (purity>98%) derived from porcine dermis. CollaDental Barrier appears paper white in dry state. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the material is flexible and conforms to the contours of the defect site.

CollaDental Barrier is supplied sterile and for single use only. This device is available in three sizes 15mm x 20mm, 20mm x 30mm and 30mm x 40mm, respectively. CollaDental Barrier can be cut to any size or shape with scissors or scalpel in the wet and dry state, without tearing or fragmenting to meet the needs of the surgeon. CollaDental Barrier is individually housed in PET blister and sterilized by gamma irradiation.

Indication for use

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

Device comparison and performance results

The comparison of CollaDental Barrier to its predicate is tabulated as shown below. CollaDental Barrier has the same intended use as the predicates in dental surgery procedures. In the aspect of composition and technological characteristics, all devices are made of collagen and, in principle, are designed for providing a barrier to prevent epithelium from growing into an area in which another, more slowly-growing tissue type, such as bone, is desired. CollaDental Barrier is tested to be non-cytotoxic, non-irritant, non-sensitizer, non-toxic, non-genotoxic and non-hemolytic in accordance with ISO 10993 Biological evaluation of Medical devices Parts 4, 5, 10 and 11. The device is sterilized by gamma-irradiation according to ISO 11137 requirements and its sterility (SAL=10⁻⁶) is tested and established according to ISO 11137 sterility test. In summary, the claim of substantially equivalence of CollaDental Barrier to legally U.S. marketed predicate is substantiated by the intended use, technology characteristics, building material, biocompatibility and sterility requirements.

Device comparison table

Device name	CollaDental Barrier	BioMend Extend absorbable collagen membrane	BIO-GIDE®
Manufacturer	Collamatrix Inc.	Integra LifeSciences corp.	Ed. Geistlich Söhne AG für chemische Industrie.
510(k)	-	K992216	K042197
Product code	NPL	LYC	NPL
Intended use	augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided tissue regeneration procedures in periodontal defects.	Indicated for guided tissue regeneration procedures in periodontal defects to enhance regeneration of periodontal apparatus.	Simultaneous use of GBR-membrane and implants; augmentation around implants placed in immediate extraction sockets; augmentation around implants placed in delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects; guided tissue regeneration procedures in periodontal defects.

Contents	Collagen	Collagen	Collagen
Biocompatibility	Yes	Yes	Yes
Sterility	Yes	Yes	Yes
Compatible size	Yes	Yes	Yes

Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ASTM F2338 Standard Test Method for Nondestructive Detection of Leaks in Packages by Vacuum Decay Method

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d] www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include any adaptations used to adapt to the device under review (for example alternative test methods) choices made when options or a selection of methods are described deviations from the standard requirements not applicable to the device and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard The summary report includes information on all standards utilized during the development of the device

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE		
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JUSTIFICATION		
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TYPE OF DEVIATION OR OPTION SELECTED ♦		
DESCRIPTION		
JUSTIFICATION		
<p>* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of a deviation or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.</p> <p>♦ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.</p>		
Paperwork Reduction Act Statement		
<p>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:</p> <p style="text-align: center;">Center for Devices and Radiological Health 1350 Piccard Drive Rockville, MD 20850</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>		

Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 10993: Biological Evaluation of Medical Devices, Part 10: Test for irritation and sensitization

Please answer the following questions Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # G95-1

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
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Title of guidance: _____

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certification body involved in conformance assessment to this standard The summary report includes information on all standards utilized during the development of the device

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE		
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DESCRIPTION		
JUSTIFICATION		
<p>* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of a deviation or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.</p> <p>♦ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.</p>		
Paperwork Reduction Act Statement		
<p>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:</p> <p style="text-align: center;">Center for Devices and Radiological Health 1350 Piccard Drive Rockville, MD 20850</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>		

Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 10993: Biological Evaluation of Medical Devices, Part 3: Test for genotoxicity, carcinogenicity and reproductive toxicity

Please answer the following questions Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # G95-1

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d] www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include any adaptations used to adapt to the device under review (for example alternative test methods) choices made when options or a selection of methods are described deviations from the standard requirements not applicable to the device and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard The summary report includes information on all standards utilized during the development of the device

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DESCRIPTION		
JUSTIFICATION		
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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 10993: Biological Evaluation of Medical Devices, Part 4: Selection of tests for interaction with blood

Please answer the following questions Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # G95-1

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 10993: Biological Evaluation of Medical Devices, Part 5: Test for cytotoxicity: in vitro method

Please answer the following questions Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # G95-1

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

USP 71 sterility test

Please answer the following questions Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

USP chapter 85: Bacterial endotoxin testing: the Limulus Amebocyte Lysate (LAL) gel clot method

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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FOOD AND DRUG ADMINISTRATION

OMB No. 9010-0120
 Exp rat on Date: August 31, 2010.
 See OMB Statement on page 5.

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Date of Submission 03/06/2010	User Fee Payment ID Number (b) (4)	FDA Submission Document Number (if known)
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SECTION A TYPE OF SUBMISSION

PMA <input type="checkbox"/> Original Submission <input type="checkbox"/> Premarket Report <input type="checkbox"/> Modular Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment <input type="checkbox"/> Licensing Agreement	PMA & HDE Supplement <input type="checkbox"/> Regular (180 day) <input type="checkbox"/> Special <input type="checkbox"/> Panel Track (PMA Only) <input type="checkbox"/> 30 day Supplement <input type="checkbox"/> 30 day Notice <input type="checkbox"/> 135 day Supplement <input type="checkbox"/> Real time Review <input type="checkbox"/> Amendment to PMA & HDE Supplement <input type="checkbox"/> Other	PDP <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP	510(k) <input checked="" type="checkbox"/> Original Submission <input checked="" type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated (Complete section Page 5) <input type="checkbox"/> Additional information <input type="checkbox"/> Third Party	Meeting <input type="checkbox"/> Pre 510(K) Meeting <input type="checkbox"/> Pre DE Meeting <input type="checkbox"/> Pre PMA Meeting <input type="checkbox"/> Pre PDP Meeting <input type="checkbox"/> Day 100 Meeting <input type="checkbox"/> Agreement Meeting <input type="checkbox"/> Determination Meeting <input type="checkbox"/> Other (specify):
IDE <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	Humanitarian Device Exemption (HDE) <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	Class II Exemption Petition <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional information	Evaluation of Automatic Class III Designation (De Novo) <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional information	Other Submission <input type="checkbox"/> 513(g) <input type="checkbox"/> Other (describe submission):

Have you used or cited Standards in your submission? Yes No (If Yes, please complete Section I, Page 5)

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name Co amatr x nc	Establishment Registration Number (if known) 3005841971
Division Name (if applicable) Qua ty Assurance	Phone Number (including area code) (886) 2 7711 3299
Street Address 26F, No. 105, Section 2 Dunhua south road, Da-an d str ct	FAX Number (including area code) (886) 2 7711 3599
City Ta pe	State / Province Z P/Postal Code 106 Country Ta wan
Contact Name Denn s J. N. Seah	
Contact Title Manager	Contact E mail Address jnseah@co amatr x.com

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name	Phone Number (including area code) ()
Division Name (if applicable)	FAX Number (including area code) ()
Street Address	State / Province Z P/Postal Code Country
City	Contact Name
Contact Title	Contact E mail Address

SECTION D1

REASON FOR APPLICATION - PMA, FDP, OR HDE

<input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or Expanded indications <input type="checkbox"/> Request for Extension <input type="checkbox"/> Post approval Study Protocol <input type="checkbox"/> Request for Applicant Hold <input type="checkbox"/> Request for Removal of Applicant Hold <input type="checkbox"/> Request to Remove or Add Manufacturing Site	<input type="checkbox"/> Change in design component or specification <input type="checkbox"/> Software / Hardware <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Location change <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager
<input type="checkbox"/> Process change <input type="checkbox"/> Manufacturing <input type="checkbox"/> Sterilization <input type="checkbox"/> Packaging <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Labeling change <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Report Submission <input type="checkbox"/> Annual or Periodic <input type="checkbox"/> Post approval Study <input type="checkbox"/> Adverse Reaction <input type="checkbox"/> Device Defect <input type="checkbox"/> Amendment
<input type="checkbox"/> Response to FDA correspondence		<input type="checkbox"/> Change in Ownership <input type="checkbox"/> Change in Correspondent <input type="checkbox"/> Change of Applicant Address

Other Reason (*specify*):

SECTION D2

REASON FOR APPLICATION - IDE

<input type="checkbox"/> New Device <input type="checkbox"/> New indication <input type="checkbox"/> Addition of institution <input type="checkbox"/> Expansion / Extension of Study <input type="checkbox"/> RB Certification <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of Application <input type="checkbox"/> Unanticipated Adverse Effect <input type="checkbox"/> Notification of Emergency Use <input type="checkbox"/> Compassionate Use Request <input type="checkbox"/> Treatment DE <input type="checkbox"/> Continued Access	<input type="checkbox"/> Change in <input type="checkbox"/> Correspondent / Applicant <input type="checkbox"/> Design / Device <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing Process <input type="checkbox"/> Protocol Feasibility <input type="checkbox"/> Protocol Other <input type="checkbox"/> Sponsor	<input type="checkbox"/> Repose to FDA Letter Concerning <input type="checkbox"/> Conditional Approval <input type="checkbox"/> Deemed Approved <input type="checkbox"/> Deficient Final Report <input type="checkbox"/> Deficient Progress Report <input type="checkbox"/> Deficient investigator Report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request Extension of Time to Respond to FDA <input type="checkbox"/> Request Meeting <input type="checkbox"/> Request Hearing
<input type="checkbox"/> Report submission <input type="checkbox"/> Current investigator <input type="checkbox"/> Annual Progress Report <input type="checkbox"/> Site Waiver Report <input type="checkbox"/> Final		

Other Reason (*specify*):

SECTION D3

REASON FOR SUBMISSION - 510(k)

<input checked="" type="checkbox"/> New Device	<input type="checkbox"/> Additional or Expanded indications	<input type="checkbox"/> Change in Technology
--	---	---

Other Reason (*specify*):

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed				Summary of or statement concerning safety and effectiveness information	
1	NPL	2		3	
5		6		7	
				<input checked="" type="checkbox"/> 510 (k) summary attached <input type="checkbox"/> 510 (k) statement	

Information on devices to which substantial equivalence is claimed (if known)

	510(k) Number	Trade or Proprietary or Model Name	Manufacturer
1	K992216	BioMend Extend absorbable collagen	Integra Lifesciences Corp.
2	K042197	BioGide	Ed. Geistlich Sohne AG
3			
4			
5			
6			

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification

CollaDental Barrier

	Trade or Proprietary or Model Name for This Device	Model Number
1	CollaDental Barrier	
2		
3		
4		
5		

FDA document numbers of all prior related submissions (regardless of outcome)

1	2	3	4	5	6
7	8	9	10	11	12

Data included in Submission

- Laboratory Testing
 Animal Trials
 Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code NPL	C F R Section (if applicable) 872.3930	Device Class <input type="checkbox"/> Class <input checked="" type="checkbox"/> Class <input type="checkbox"/> Class <input type="checkbox"/> Unclassified
Classification Panel Dental		

Indications (from labeling)

CollaDental Barrier is intended for use in augmentation around implants placed in maxillary and mandibular extract sockets; augmentation around implants placed in delayed extract sockets; occlusal ridge augmentation for atrophic maxilla; a vertical ridge reconstruction for prosthetic treatment; filling of bone defects after root resection, cystectomy, removal of retained teeth; guided tissue regeneration procedures in periodontal defects.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FE) Number		<input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name Collamatrix Inc			Establishment Registration Number 3005841971		
Division Name (if applicable) Quality Assurance			Phone Number (including area code) (886) 2 7711 3299		
Street Address 1F, No. 50-1, Keyan Rd			FAX Number (including area code) (886) 2 7711 3599		
City Jhunan Township		State / Province Miaoli		Z P/Postal Code 350	Country Tawan
Contact Name Dennis J. N. Seah		Contact Title Manager		Contact E mail Address jnseah@collamatrix.com	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FE) Number		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name			Establishment Registration Number		
Division Name (if applicable)			Phone Number (including area code) ()		
Street Address			FAX Number (including area code) ()		
City		State / Province		Z P/Postal Code	Country
Contact Name		Contact Title		Contact E mail Address	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FE) Number		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name			Establishment Registration Number		
Division Name (if applicable)			Phone Number (including area code) ()		
Street Address			FAX Number (including area code) ()		
City		State / Province		Z P/Postal Code	Country
Contact Name		Contact Title		Contact E mail Address	

SECTION I

UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a *Declaration of Conformity to a Recognized Standard* statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	11137:2006	ISO	Sterilization of health care products - Radiation.	-	
2	ISO 10993	ISO	Biological evaluation of medical devices.		
3					
4					
5					
6					
7					

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
 CDRH (HFZ 342)
 9200 Corporate Blvd
 Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control

Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 10993: Biological Evaluation of Medical Devices, Part 11: Test for systemic toxicity

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # G95-1

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d] www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include any adaptations used to adapt to the device under review (for example alternative test methods) choices made when options or a selection of methods are described deviations from the standard requirements not applicable to the device and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard The summary report includes information on all standards utilized during the development of the device

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE		
STANDARD TITLE		
CONFORMANCE WITH STANDARD SECTIONS*		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
TYPE OF DEVIATION OR OPTION SELECTED ♦		
DESCRIPTION		
JUSTIFICATION		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
TYPE OF DEVIATION OR OPTION SELECTED ♦		
DESCRIPTION		
JUSTIFICATION		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
TYPE OF DEVIATION OR OPTION SELECTED ♦		
DESCRIPTION		
JUSTIFICATION		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
TYPE OF DEVIATION OR OPTION SELECTED ♦		
DESCRIPTION		
JUSTIFICATION		
<p>* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of a deviation or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.</p> <p>♦ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.</p>		
Paperwork Reduction Act Statement		
<p>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:</p> <p style="text-align: center;">Center for Devices and Radiological Health 1350 Piccard Drive Rockville, MD 20850</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>		

Statement of indications for use

510(K) Number (if known):

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; localized ridge augmentation for later implantation; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Screening Checklist for Traditional/Abbreviated Premarket Notification [510(k)] Submissions

based on
**Guidance for Industry and FDA Staff
 Format for Traditional and Abbreviated 510(k)s**
<http://www.fda.gov/cdrh/ode/guidance/1567.html>

Title	Related Information	Present	Inadequate	N/A
MDUFMA Cover Sheet	Medical Device User Fee Cover Sheet www.fda.gov/oc/mdufma/coversheet.html	✓		
CDRH Premarket Review Submission Cover Sheet	CDRH Premarket Review Submission Cover Sheet www.fda.gov/opacom/morechoices/fdaforms/FDA-3514.pdf	✓		
510(k) Cover Letter	Appendix A of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Indications for Use Statement	Device Advice "Content of a 510(k)" Section D www.fda.gov/cdrh/devadvice/314312.html#link_6	✓		
510(k) Summary or 510(k) Statement	Device Advice "Content of a 510(k)" Section E www.fda.gov/cdrh/devadvice/314312.html#link_7	✓		
Truthful and Accuracy Statement	Device Advice "Content of a 510(k)" Section G www.fda.gov/cdrh/devadvice/314312.html#link_9	✓		
Class III Summary and Certification	Class III Summary and Certification Form www.fda.gov/cdrh/manual/stmnciii.html			✓
Financial Certification or Disclosure Statement	FORM FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators www.fda.gov/opacom/morechoices/fdaforms/FDA-3454.pdf FORM FDA 3455, Disclosure: Financial Interests and Arrangements of Clinical Investigators www.fda.gov/opacom/morechoices/fdaforms/FDA-3455.pdf Financial Disclosure by Clinical Investigators www.fda.gov/oc/guidance/financialdis.html			✓
Declarations of Conformity and Summary Reports (Abbreviated 510(k)s)	Use of Standards in Substantial Equivalence Determinations www.fda.gov/cdrh/ode/guidance/1131.html . FDA Standards program www.fda.gov/cdrh/stdsprog.html . Declaration of conformity www.fda.gov/cdrh/devadvice/3145.html#link_9 Required Elements for Declaration of Conformity to Recognized Standard www.fda.gov/cdrh/ode/regrecstand.html			✓
Executive Summary	See section 10 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		

Rev. 5/30/07

Title	Related Information	Present	Inadequate	N/A
Device Description	See section 11 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Substantial Equivalence Discussion	Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3), www.fda.gov/cdrh/k863.html	✓		
Proposed Labeling	Device Advice "Content of a 510(k)" Section H www.fda.gov/cdrh/devadvice/314312.html#link_10	✓		
Sterilization/Shelf Life	Updated 510(k) Sterility Review Guidance (K90-1) www.fda.gov/cdrh/ode/guidance/361.html For reuse of single use devices, see Guidance for Industry and FDA Staff – Medical Device User Fee and Modernization Act of 2002 Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices www.fda.gov/cdrh/ode/guidance/1216.html	✓		
Biocompatibility	FDA Blue Book Memo, G95-1, Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" www.fda.gov/cdrh/g951.html	✓		
Software	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices www.fda.gov/cdrh/ode/software.html			✓
Electromagnetic Compatibility/Electrical Safety	CDRH Medical Device Electromagnetic Compatibility Program www.fda.gov/cdrh/emc See also IEC 60601-1-2 Medical Electrical Equipment -- Part 1: General Requirements for Safety; Electromagnetic Compatibility -- Requirements and Tests (Second Edition, 2001)			✓
Performance Testing – Bench	See section 18 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Performance Testing – Animal	See section 19 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005			✓
Performance Testing – Clinical	See section 20 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005 Certification/Disclosure Forms: Financial Interests and Arrangements of Clinical Investigators www.fda.gov/opacom/morechoices/fdaforms/FDA-3454.pdf www.fda.gov/opacom/morechoices/fdaforms/FDA-3455.pdf			✓
Kit Certification	Device Advice http://www.fda.gov/cdrh/devadvice/314c.html			✓

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION MEDICAL DEVICE USER FEE COVER SHEET	PAYMENT IDENTIFICATION NUMBER: (b)(4) Confidential and Proprietary Information Write the Payment Identification number on your check.
---	---

A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: <http://www.fda.gov/oc/mdufma/cover sheet.html>

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)

COLLAMATRIX INC
26F, NO. 105
Section 2
DunHua South Road
Daan District
Taipei
TW

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)

2. CONTACT NAME

Dennis Seah

2.1 E-MAIL ADDRESS

jnseah@collamatrix.com

2.2 TELEPHONE NUMBER (include Area code)

+886 2 7711 3299

2.3 FACSIMILE (FAX) NUMBER (Include Area code)

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: <http://www.fda.gov/oc/mdufma>)

Select an application type:

- Premarket notification(510(k)); except for third party
 513(g) Request for Information
 Biologics License Application (BLA)
 Premarket Approval Application (PMA)
 Modular PMA
 Product Development Protocol (PDP)
 Premarket Report (PMR)
 Annual Fee for Periodic Reporting (APR)
 30-Day Notice

3.1 Select a center

- CDRH
 CBER

3.2 Select one of the types below

Original Application

Supplement Types:

- Efficacy (BLA)
 Panel Track (PMA, PMR, PDP)
 Real-Time (PMA, PMR, PDP)
 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)

YES, I meet the small business criteria and have submitted the required qualifying documents to FDA NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number:

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?

- YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.)
 NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see <http://www.fda.gov/cdrh/mdufma> for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.

- This application is the first PMA submitted by a qualified small business, including any affiliates The sole purpose of the application is to support conditions of use for a pediatric population
 This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

7. IS THIS A SUPPLEMENT TO A PREVIOUS PMA APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA)).

YES

NO

8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

07-Mar-2010

(b)(4) Confidential and Proprietary

["Close Window"](#) [Print Cover sheet](#)



DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

**Premarket Notification [510(k)] Review
Traditional/Abbreviated**

K100695/S001 *A3*

Date: November 12, 2010
To: The Record
From: Robert S. Betz, D.D.S.

Office: ODE
Division: DAGID
Branch: DEDB

Device Name: CollaDental Barrier
510(k) Holder: Collamatrix, Inc.
Contact: Dennis J. N. Seah

Phone: 886-277-113299
Fax: 886-277-113599
E-mail: jnseah@collamatrix.com

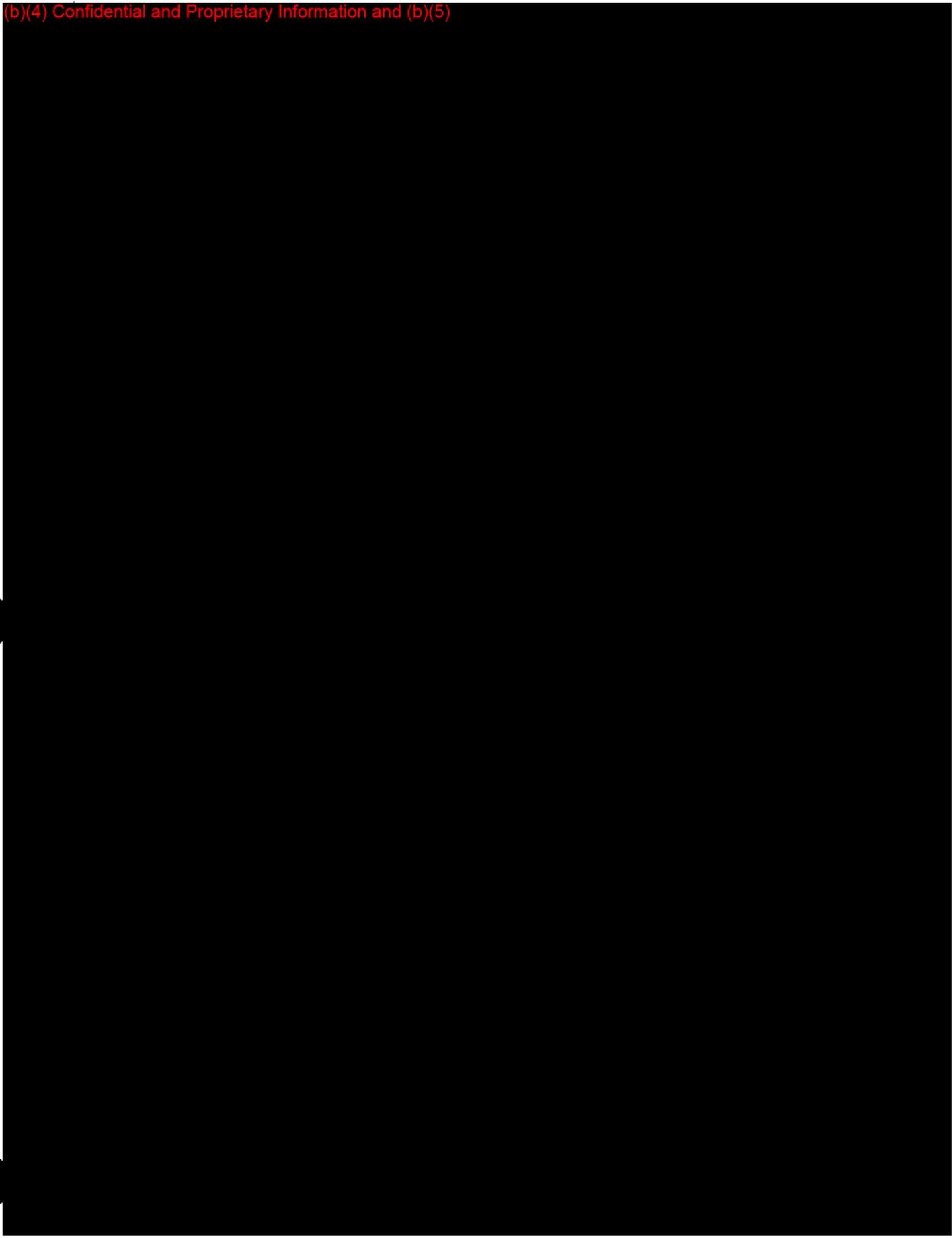
- I. **Purpose and Submission Summary** – This product is a collagen dental barrier material. Barrier membranes are Class II devices that have a Product Code of NPL. They are accessories to dental bone grafting materials which are described in 21 CFR 872.3930. Substantial equivalence is claimed to Integra Life Science's BioMend Extend (K992216), and BioGide (K042197). Conformance is claimed to:
1. ISO 11137 (Sterilization – Radiation),
 2. ISO 10993 (Biological Evaluation of Medical Devices) Part 3 – Genotoxicity, carcinogenicity and reproductive toxicity.
 3. ISO 10993 (Biological Evaluation of Medical Devices) Part 4 – Interaction with blood.
 4. ISO 10993 (Biological Evaluation of Medical Devices) Part 5 – Cytotoxicity.
 5. ISO 10993 (Biological Evaluation of Medical Devices) Part 10 – Irritation and sensitization.
 6. ISO 10993 (Biological Evaluation of Medical Devices) Part 11 – Systemic toxicity.
 7. ISO 2338 Package integrity using vacuum decay method.
 8. USP 71 – Sterility test
 9. USP 85 – Bacterial endotoxin testing

II. **Administrative Requirements**

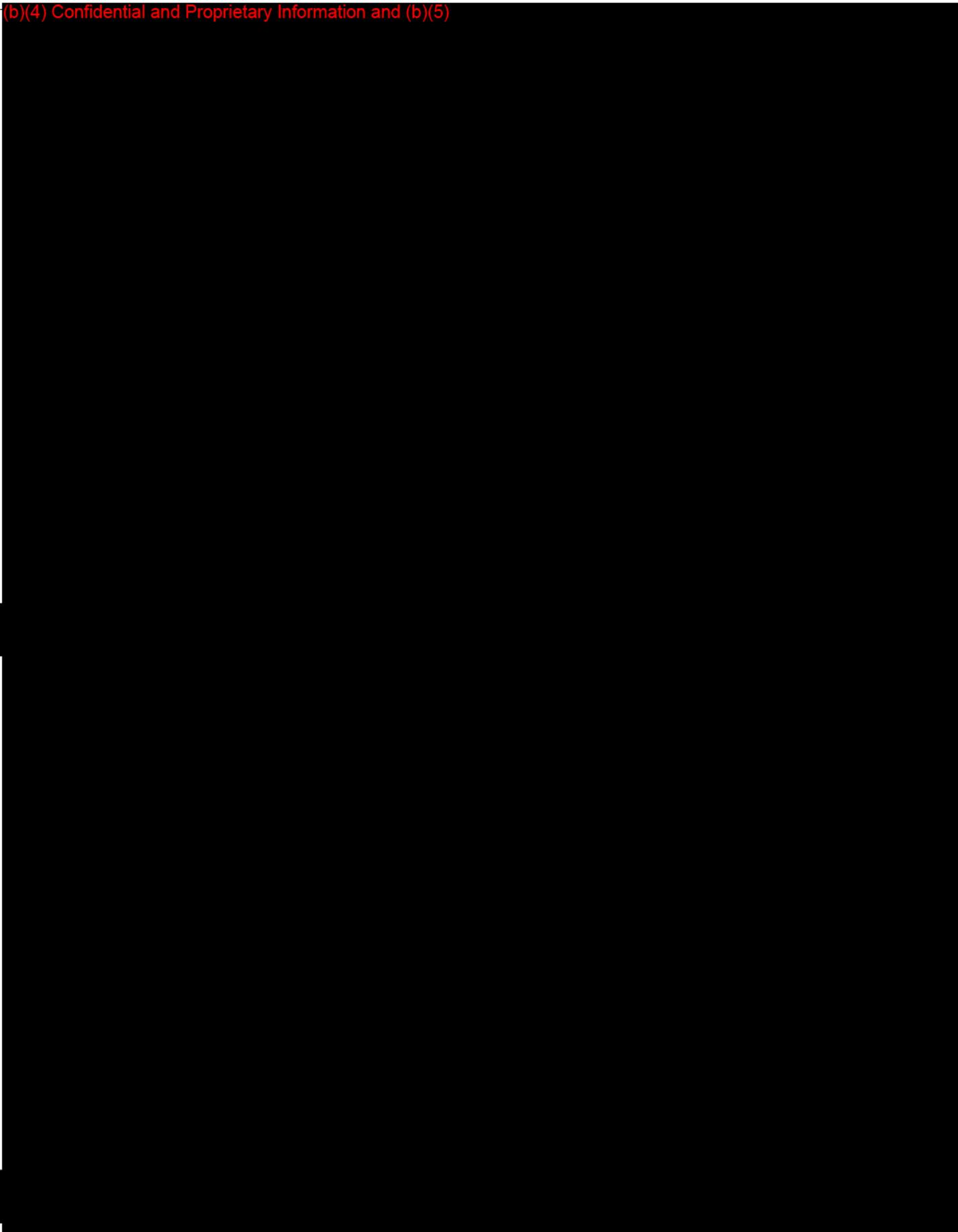
	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or OTC)	Rx		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	SUM		
Standards Forms	X		

(b)(4) Confidential and Proprietary Information and (b)(5)

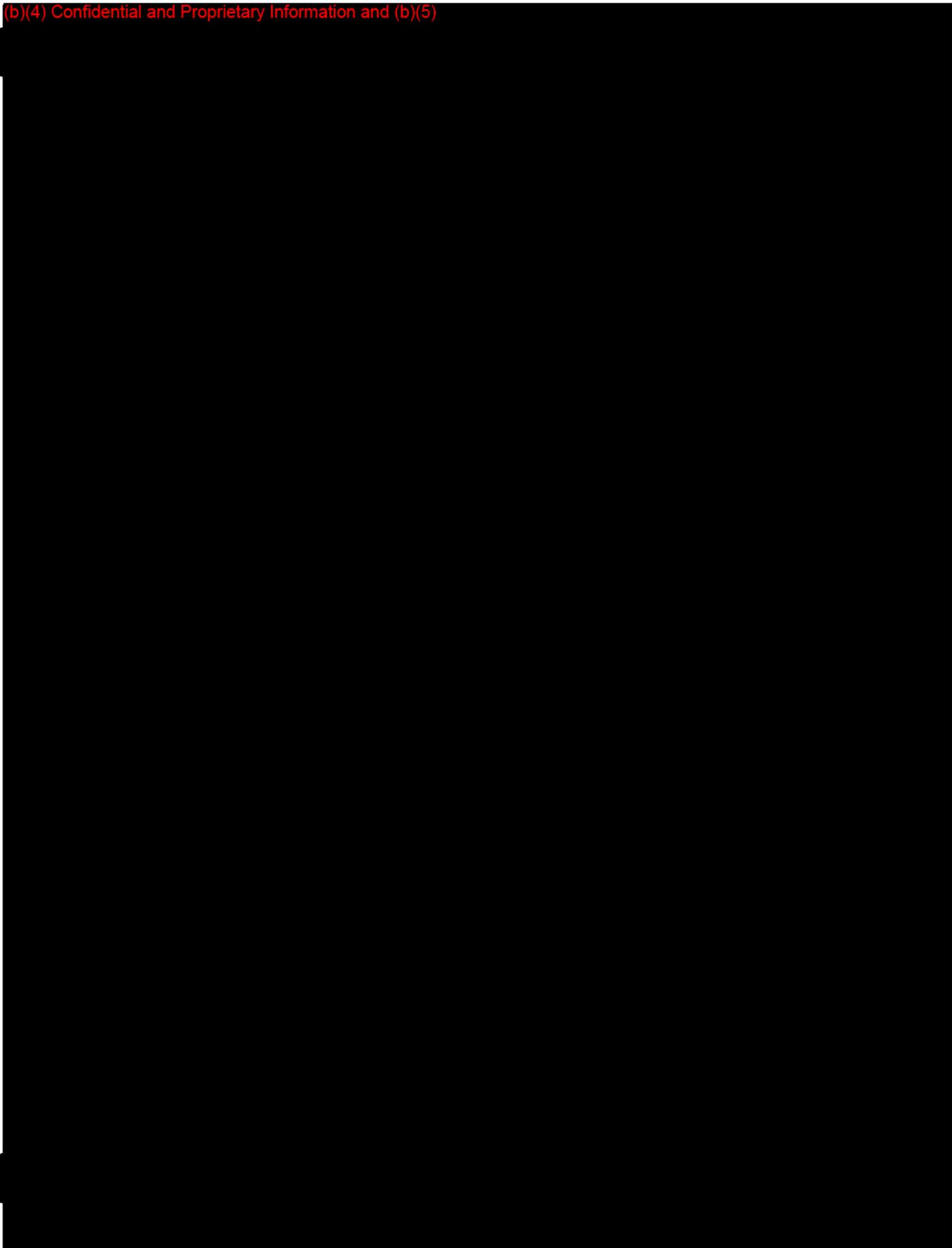
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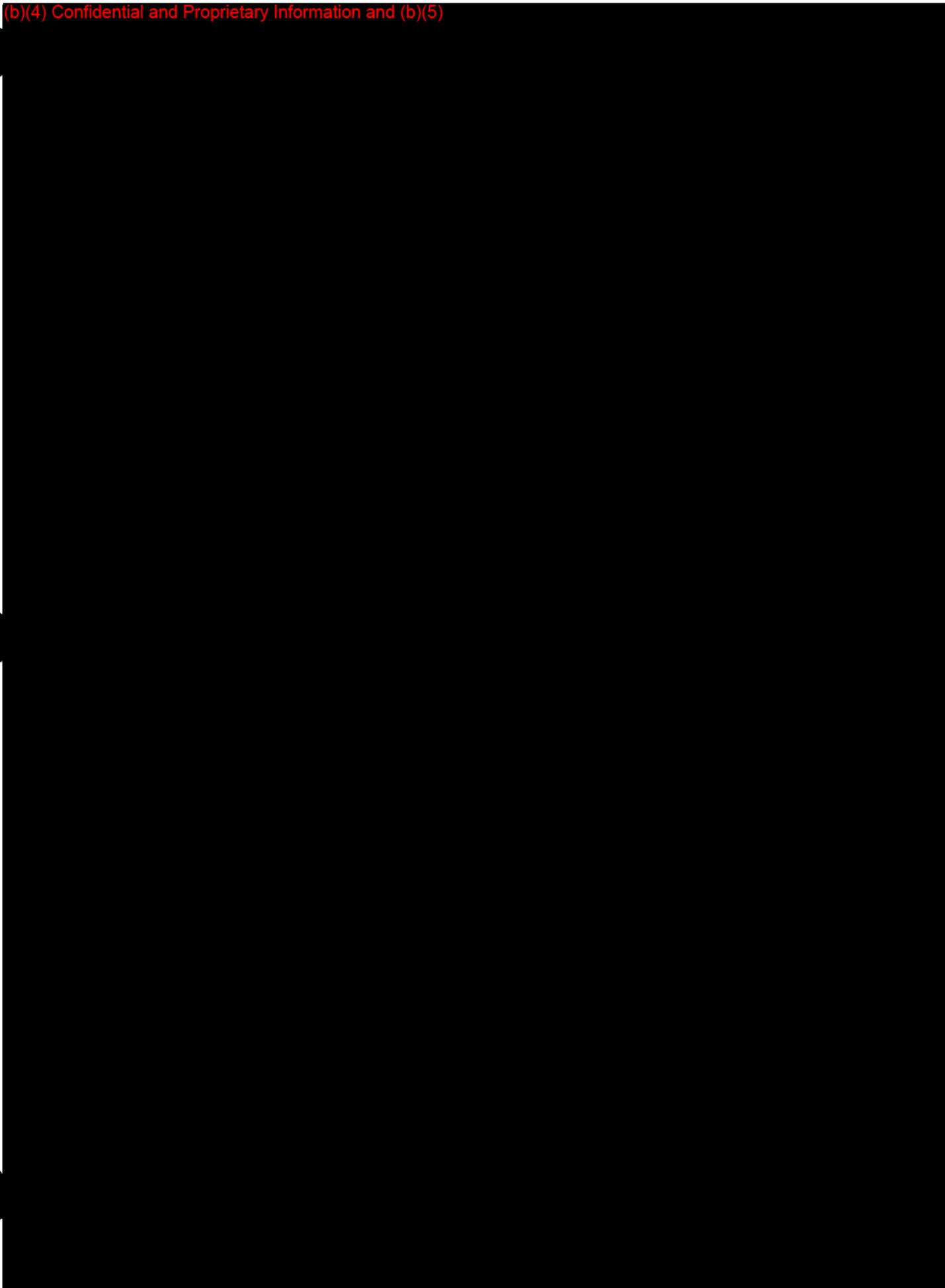
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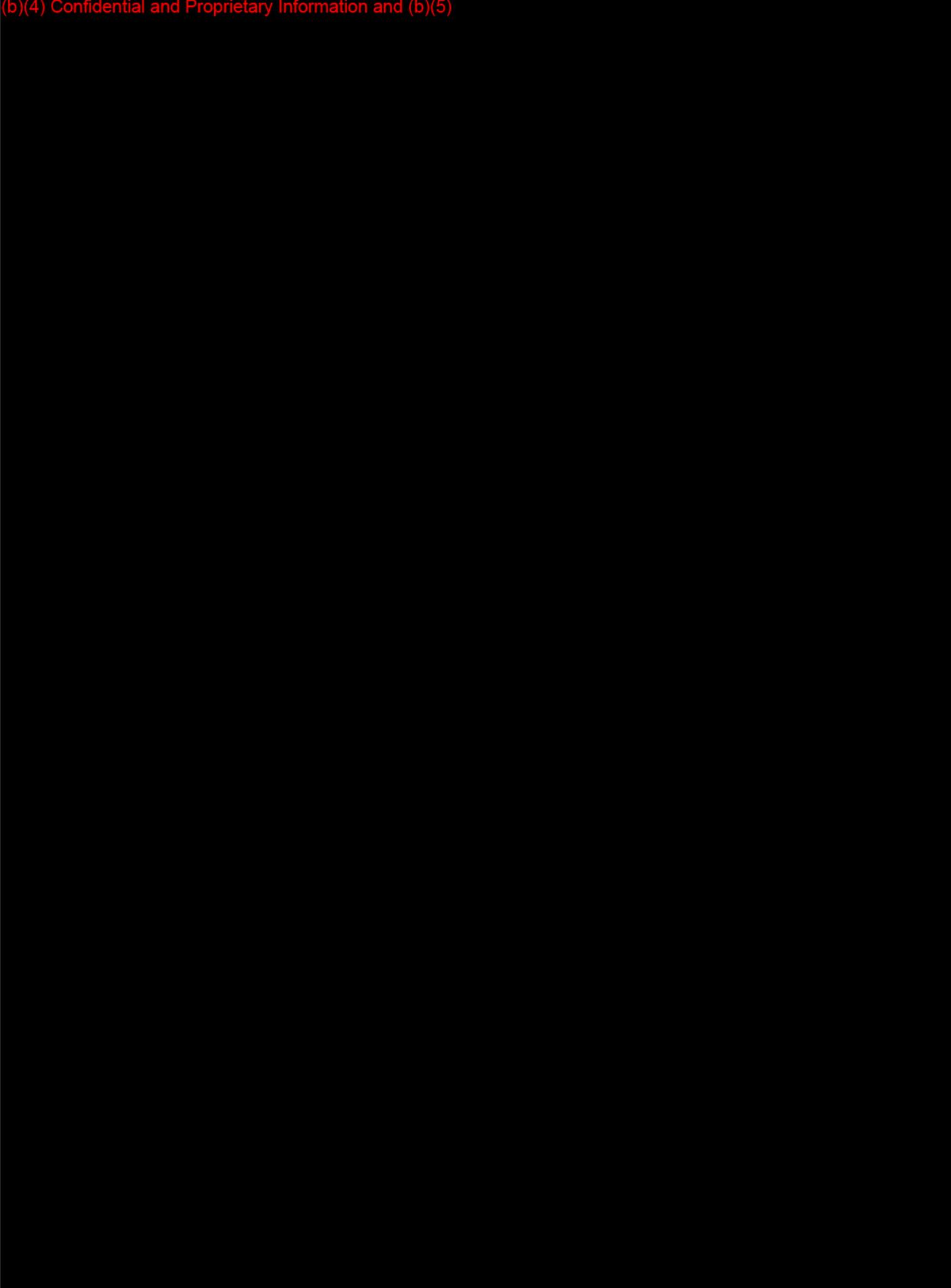
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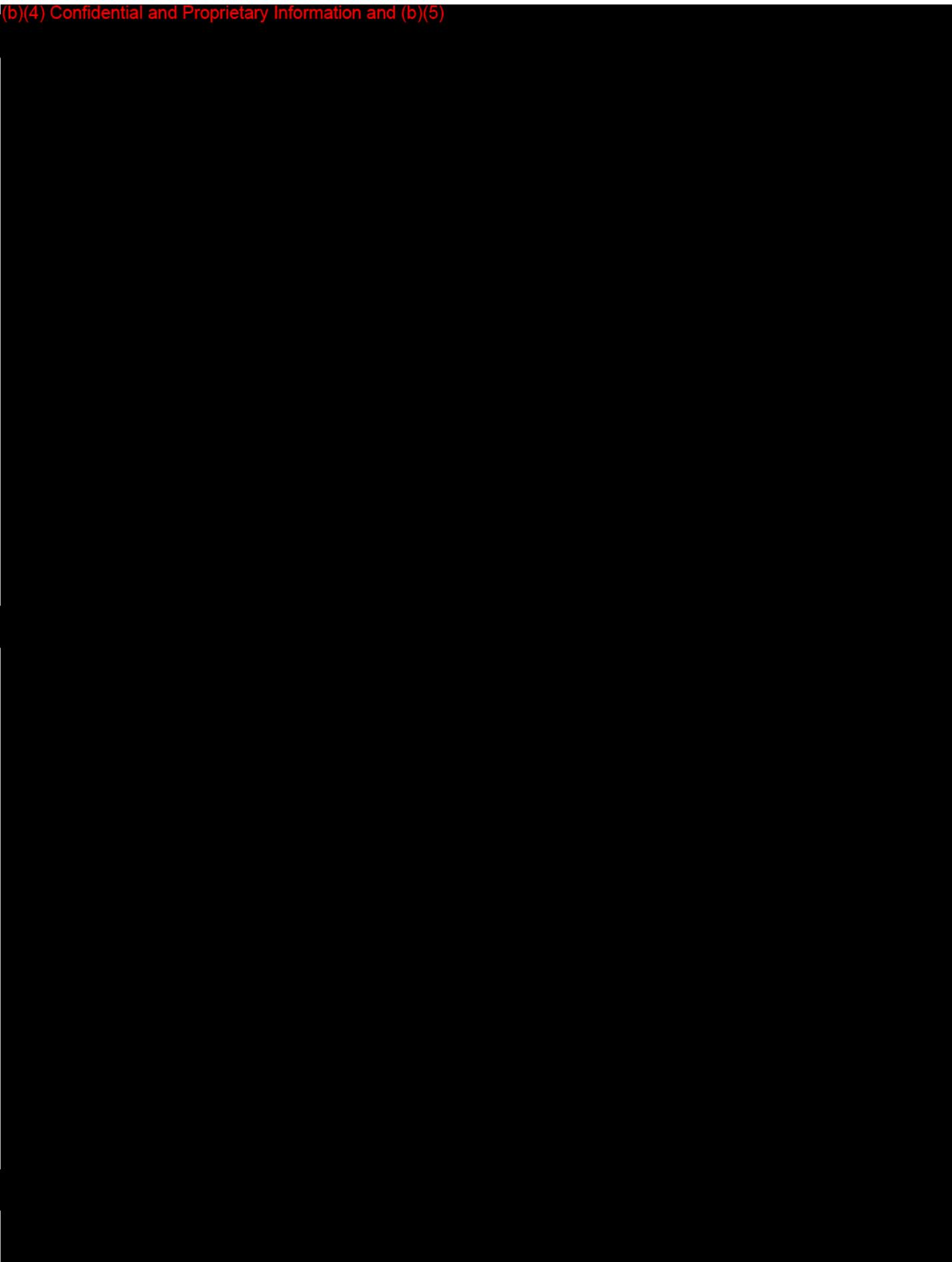
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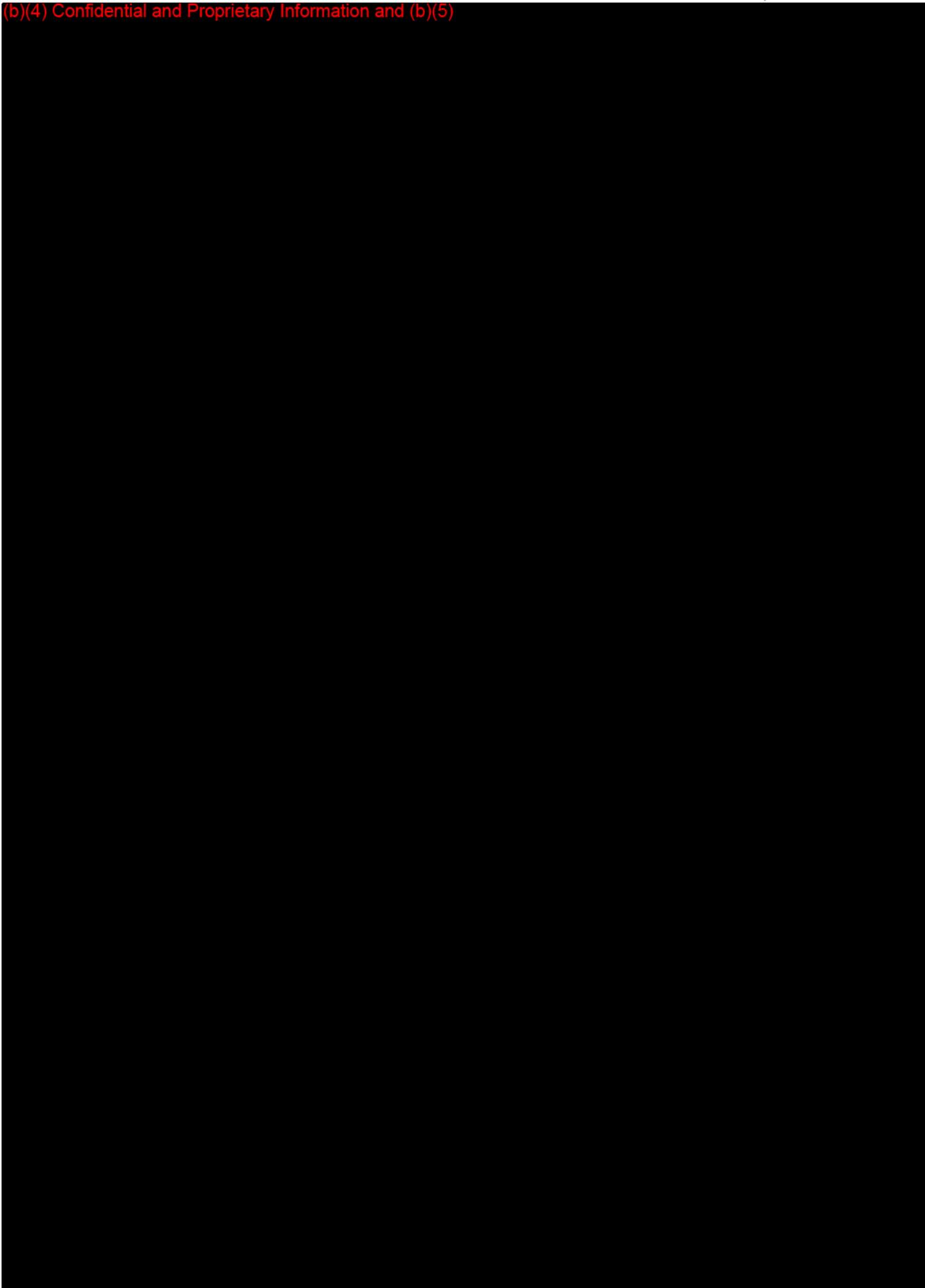
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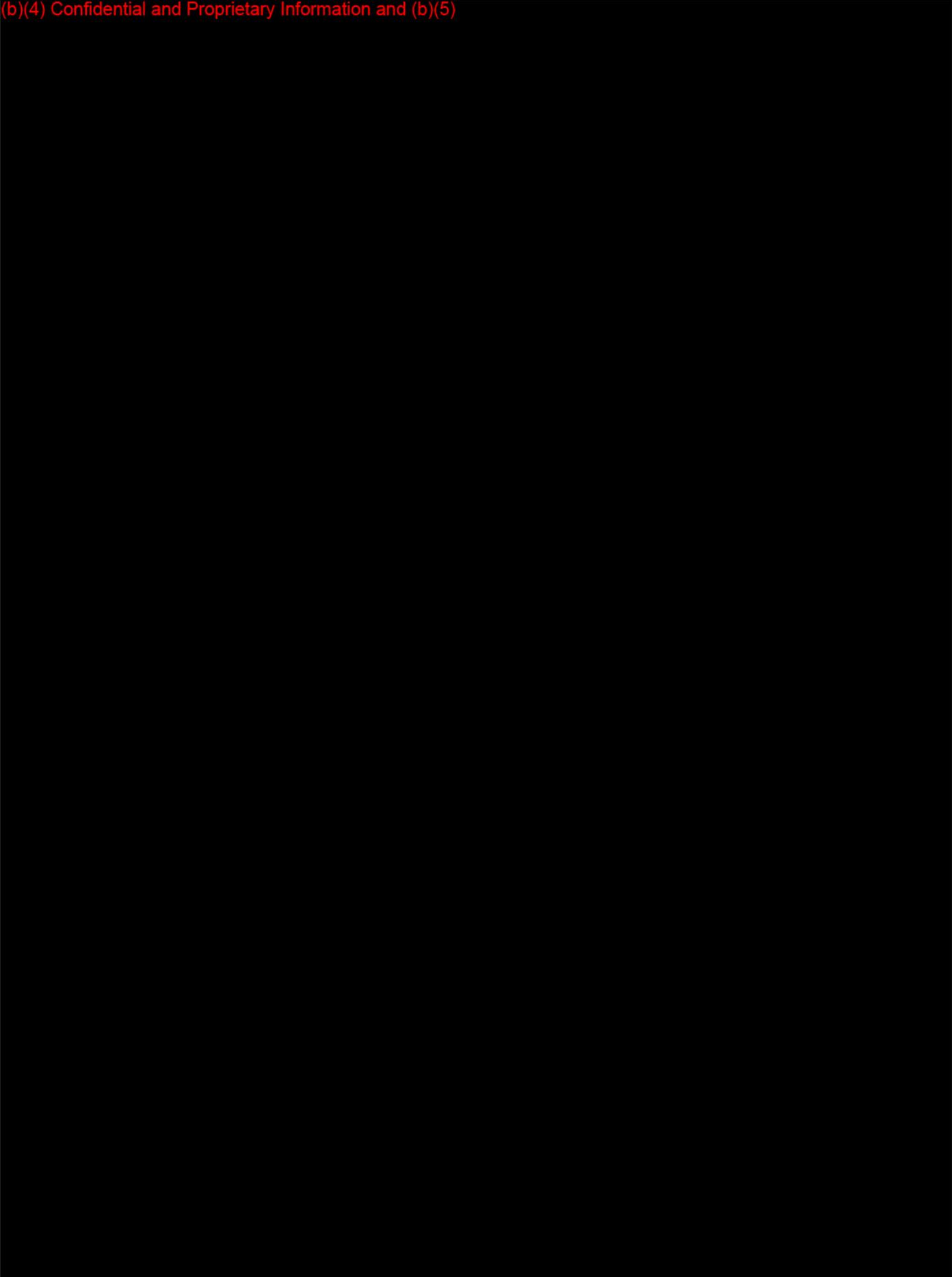
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(b)(4) Confidential and Proprietary Information and (b)(5)

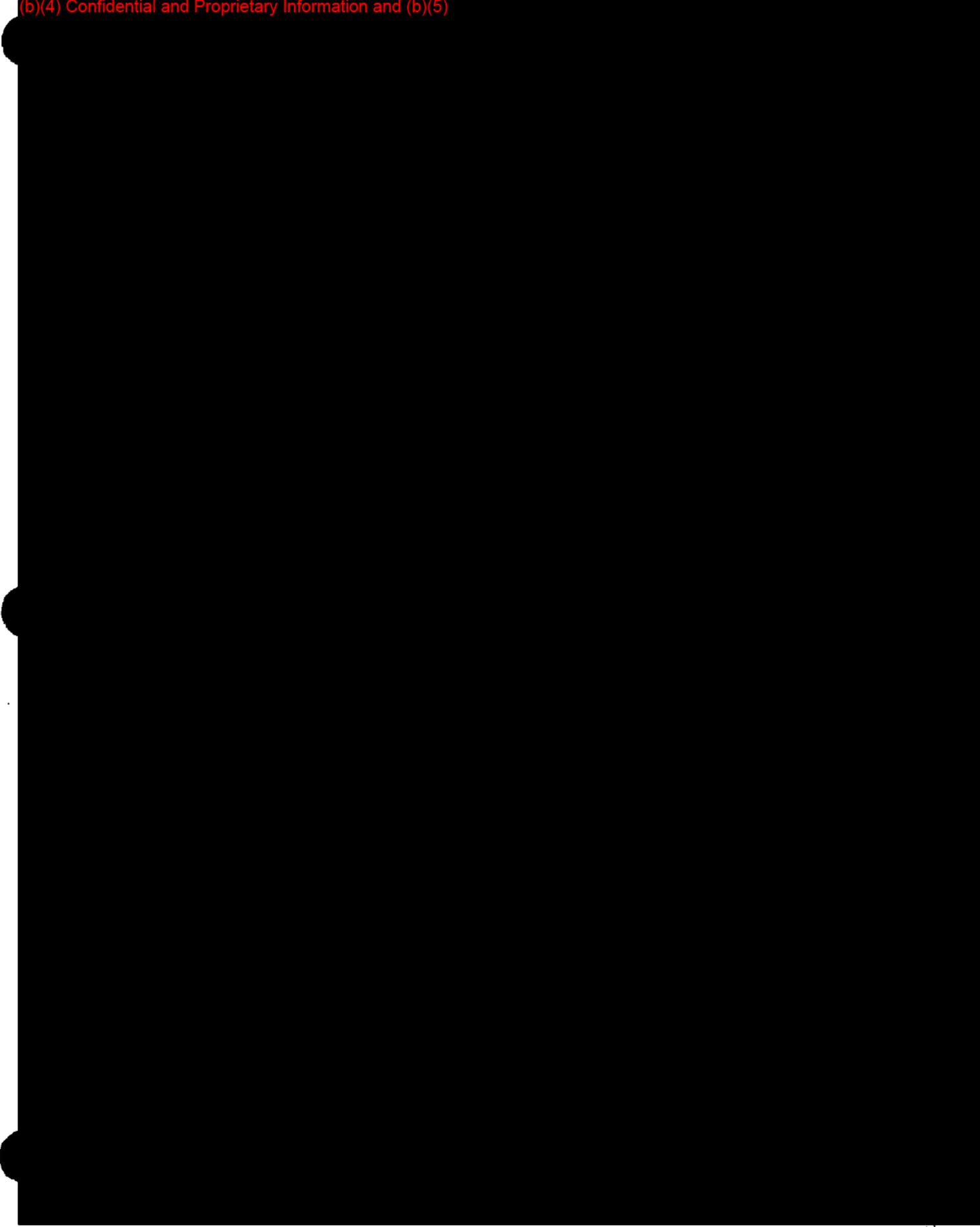


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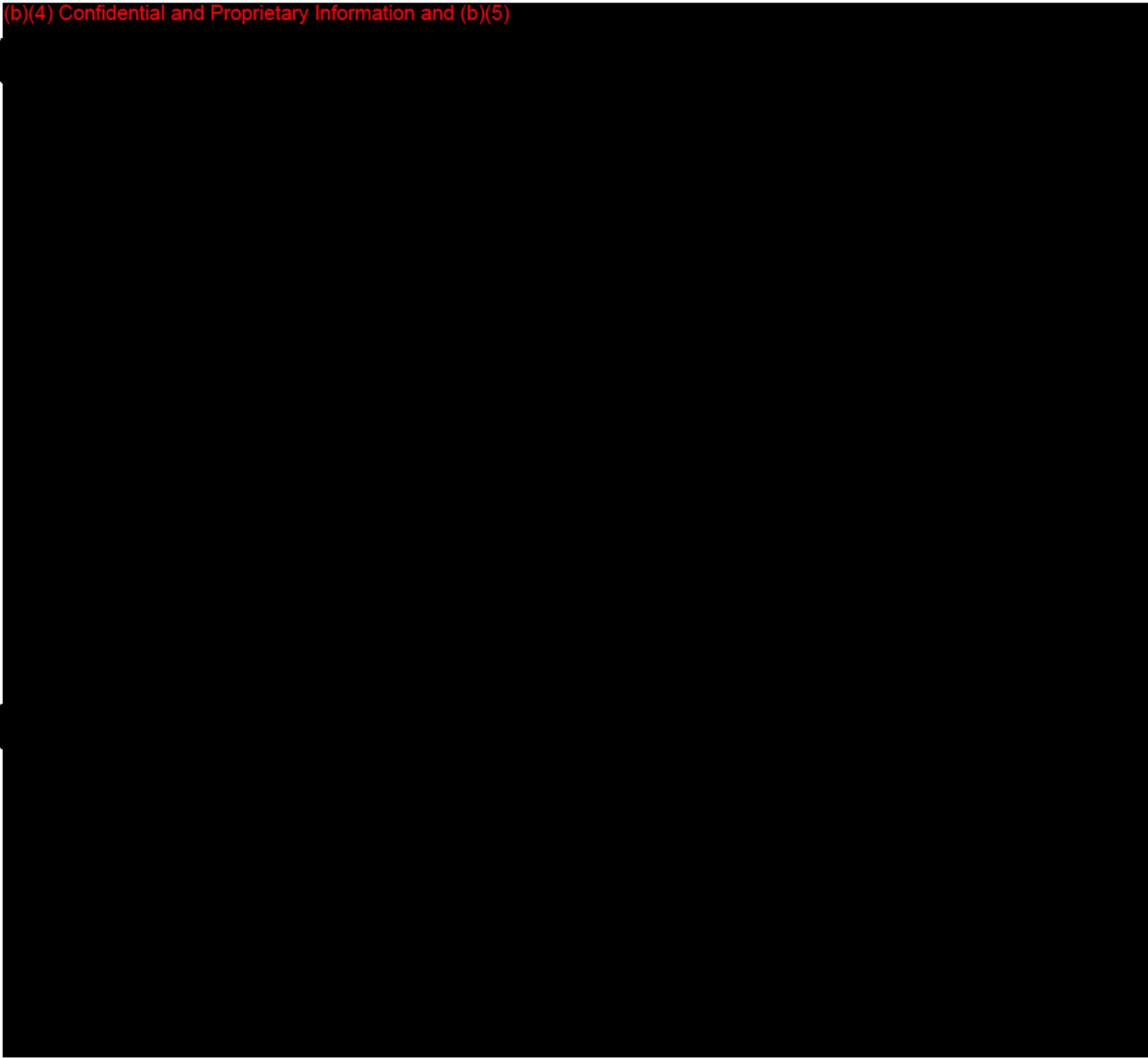


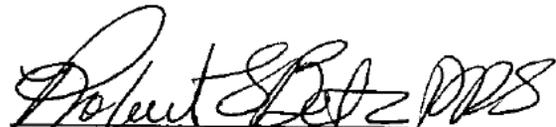
XV.

(b)(4) Confidential and Proprietary Information and (b)(5)



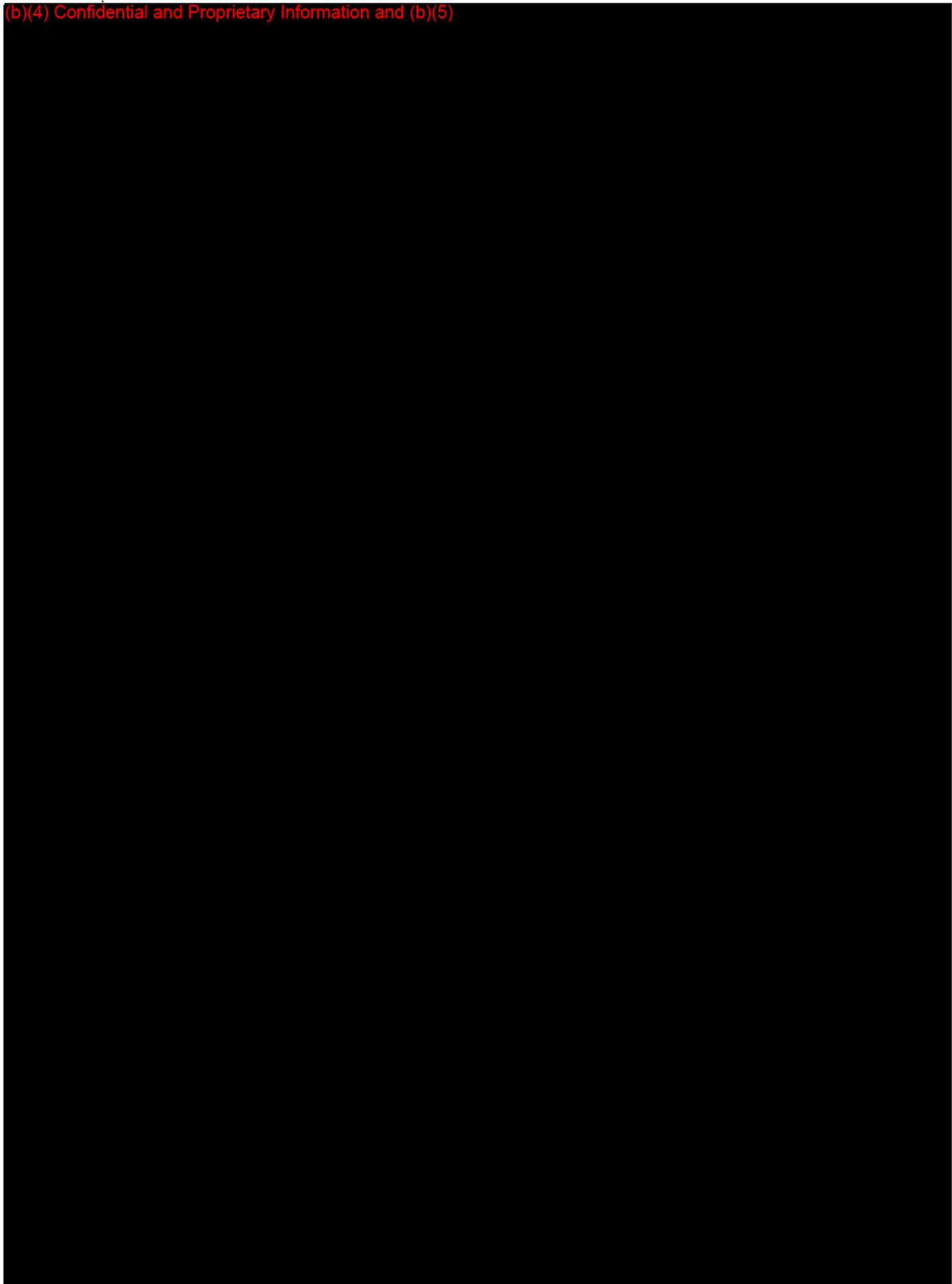
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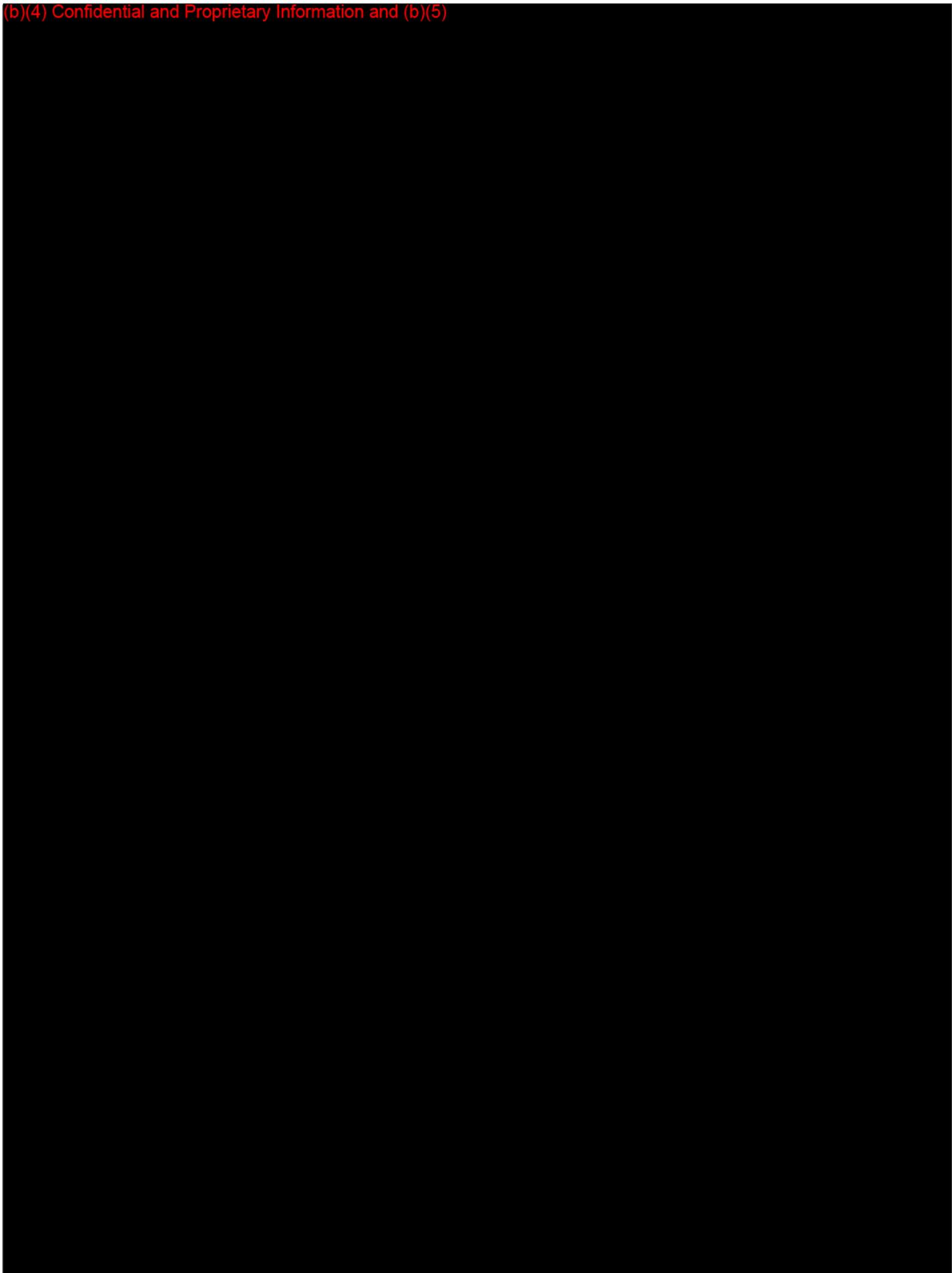

Robert S. Betz, DDS
DAGID/DEDB

December 1, 2010
Date

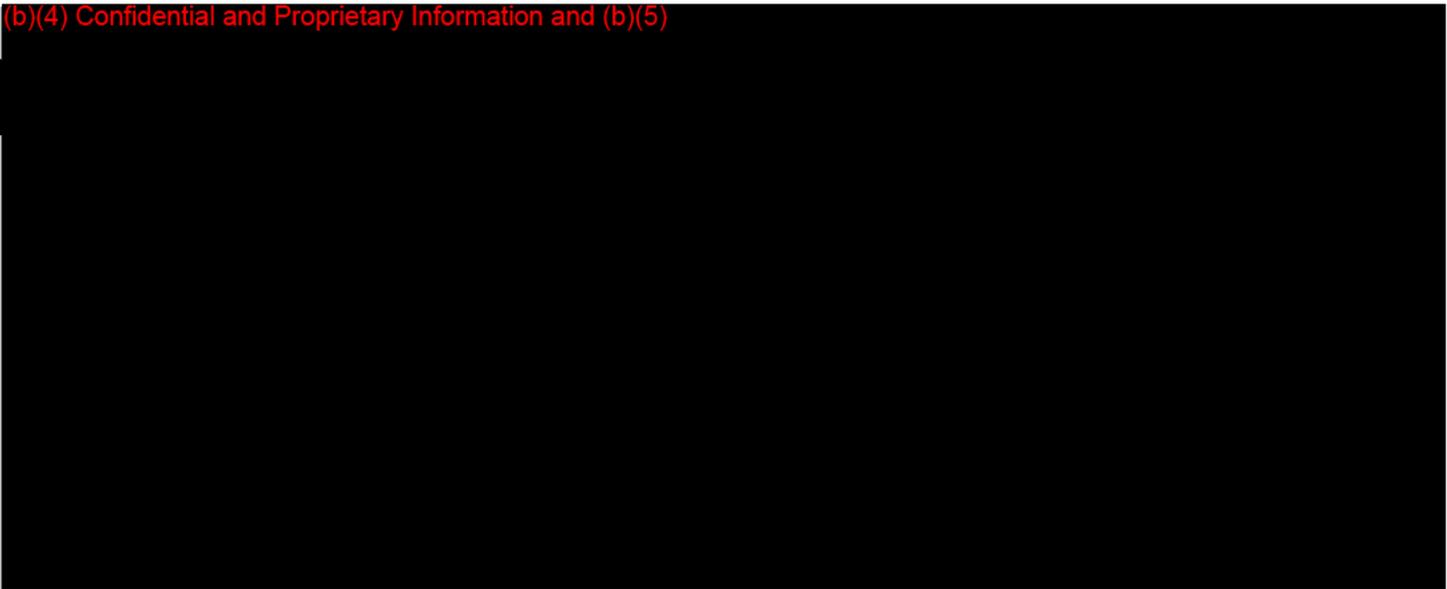
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(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

[Text of E-Mail Sent to Sponsor on November 12, 2010]

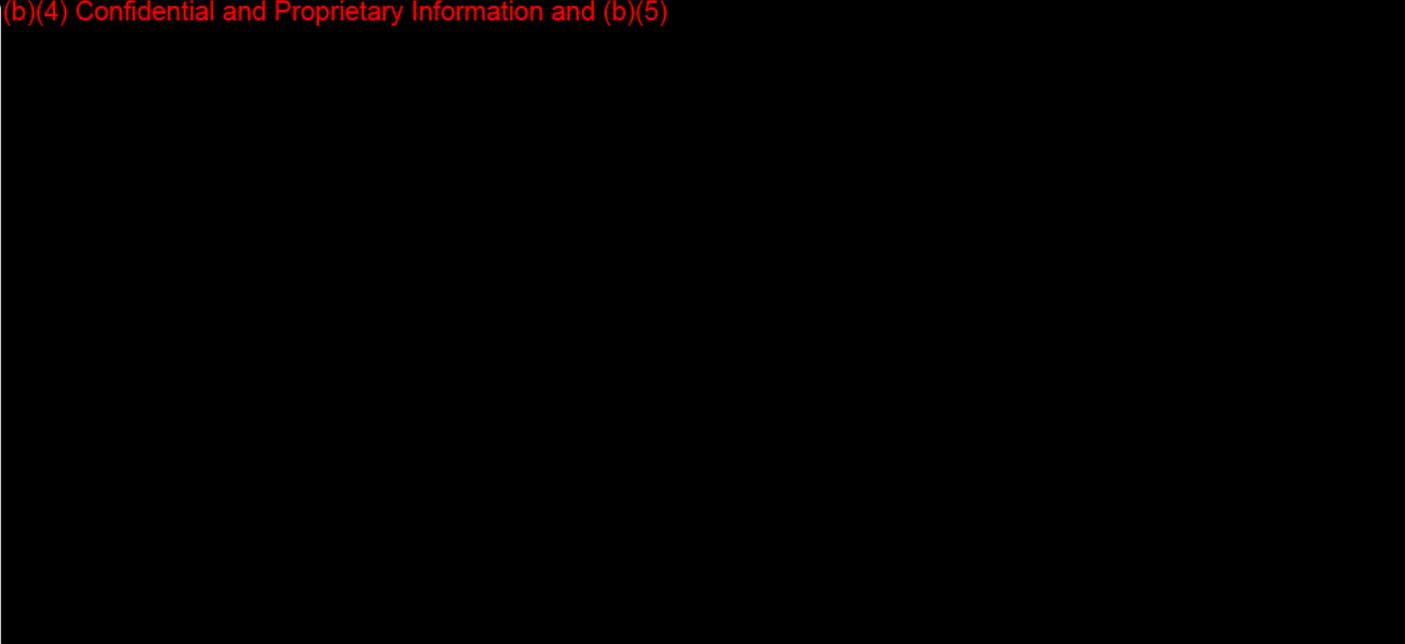
(b)(4) Confidential and Proprietary Information and (b)(5)



Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

[Text of E-mail Sent to Sponsor on December 1, 2010]

(b)(4) Confidential and Proprietary Information and (b)(5)



Thank you for your prompt response,

Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

Food and Drug Administration
Center for Devices and Radiological Health

Document Mail Center WO66-G609

10903 New Hampshire Avenue

Silver Spring, MD 20993-0002

November 23, 2010

Re: Information for CollaDental Barrier (K100695)

12-419

Dear Dr. Betz,

Please find enclosed revised Indications for use statement and revised 510k summary required for the application of CollaDental Barrier.

Thank you.

FDA CDRH DMC

NOV 29 2010

Received

Sincerely yours,



Dennis Seah

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. Date Prepared

March 3, 2010

2. Submitter name and address

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. Contact person

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. Device names

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. Device classification

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

6. Device description

CollaDental Barrier is a nonfriable, resorbable membrane made of purified type I collagen derived from pig skin using standardized controlled manufacturing process. The collagen is obtained from veterinary certified pigs and purified to avoid its antigenicity. The manufacturing process complies with the standards for virus inactivation. The CollaDental

COLLAMATRIX Co. Ltd.

Barrier has been tested for purity using standard purity testing procedures, sterilized by gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

CollaDental Barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

8. Statement of Substantial equivalence

CollaDental Barrier is a device similar to predicate devices that are previously approved by the agency. CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices, BioMend Extend absorbable collagen membrane (K992216) and BIO-GIDE® (K042197), each of which has been determined by FDA to be substantially equivalent to preamendment devices. CollaDental Barrier has the following similarities to the predicate devices in terms of indication for use, technological characteristics, material use and the process for sterilization. In summary, CollaDental Barrier is substantially equivalent to the predicate devices under the 510(k) regulations.

9. Biocompatibility

CollaDental Barrier has been demonstrated to be safe. To support the biocompatibility of this product, safety tests were conducted in accordance with ISO 10993 Part 1 Biological Evaluation of Medical Devices.

All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

COLLAMATRIX Co. Ltd.

10. Conclusion

CollaDental Barrier is essentially equivalent in indication for use, technological characteristics and material to the commercially available predicate device, and therefore meets the requirements as defined in 21 CFR § 807.

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; alveolar ridge reconstruction for prosthetic treatment; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dehiscence defects and guided tissue regeneration procedures in periodontal defects.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. Date Prepared

March 3, 2010

2. Submitter name and address

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. Contact person

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. Device names

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. Device classification

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

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COLLAMATRIX Co. Ltd.

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Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

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Prescription Use X
(Part 21 CFR 801 Subpart D)

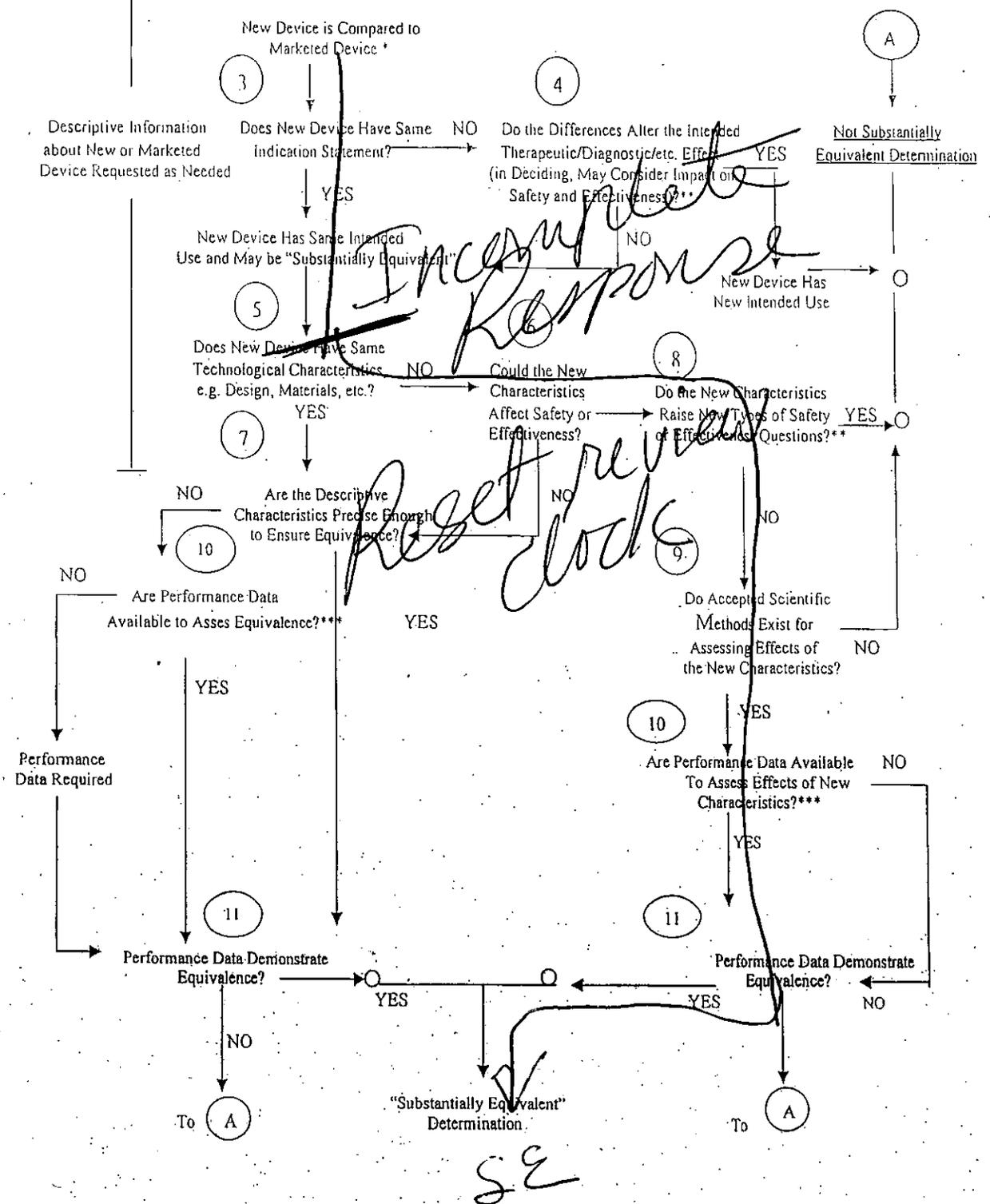
AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) "SUBSTANTIAL EQUIVALENCE"
DECISION-MAKING PROCESS



❖ 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 maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature. Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOIS STATUS@fda.hhs.gov or call 301-796-8118.



Do not remove this review

DEPARTMENT OF HEALTH AND HUMAN SERVICES

MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

**Premarket Notification [510(k)] Review
Traditional/Abbreviated**

K100695/S001

Date: November 12, 2010
To: The Record
From: Robert S. Betz, D.D.S.

Office: ODE
Division: DAGID
Branch: DEDB

Device Name: CollaDental Barrier
510(k) Holder: Collamatrix, Inc.
Contact: Dennis J. N. Seah

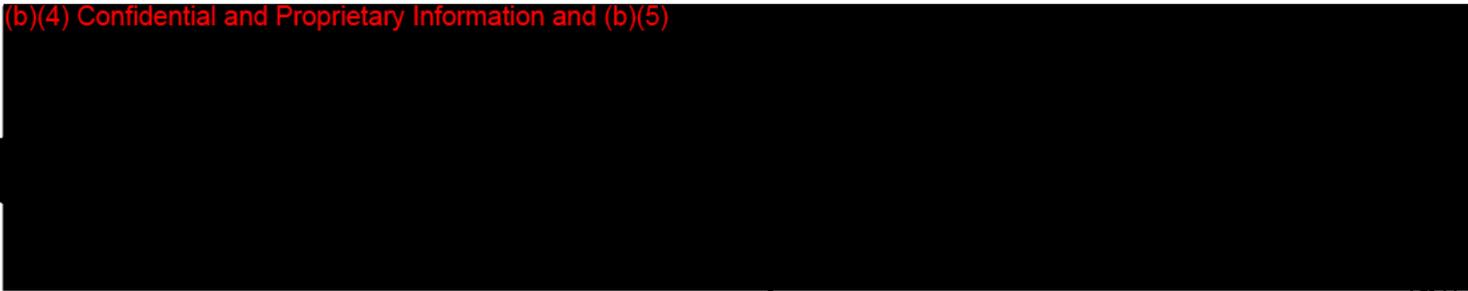
Phone: 886-277-113299
Fax: 886-277-113599
E-mail: jnseah@collamatrix.com

- I. **Purpose and Submission Summary** – This product is a collagen dental barrier material. Barrier membranes are Class II devices that have a Product Code of NPL. They are accessories to dental bone grafting materials which are described in 21 CFR 872.3930. Substantial equivalence is claimed to Integra Life Science's BioMend Extend (K992216), and BioGide (K042197). Conformance is claimed to:
1. ISO 11137 (Sterilization – Radiation),
 2. ISO 10993 (Biological Evaluation of Medical Devices) Part 3 – Genotoxicity, carcinogenicity and reproductive toxicity.
 3. ISO 10993 (Biological Evaluation of Medical Devices) Part 4 – Interaction with blood.
 4. ISO 10993 (Biological Evaluation of Medical Devices) Part 5 – Cytotoxicity.
 5. ISO 10993 (Biological Evaluation of Medical Devices) Part 10 – Irritation and sensitization.
 6. ISO 10993 (Biological Evaluation of Medical Devices) Part 11 – Systemic toxicity.
 7. ISO 2338 Package integrity using vacuum decay method.
 8. USP 71 – Sterility test
 9. USP 85 – Bacterial endotoxin testing

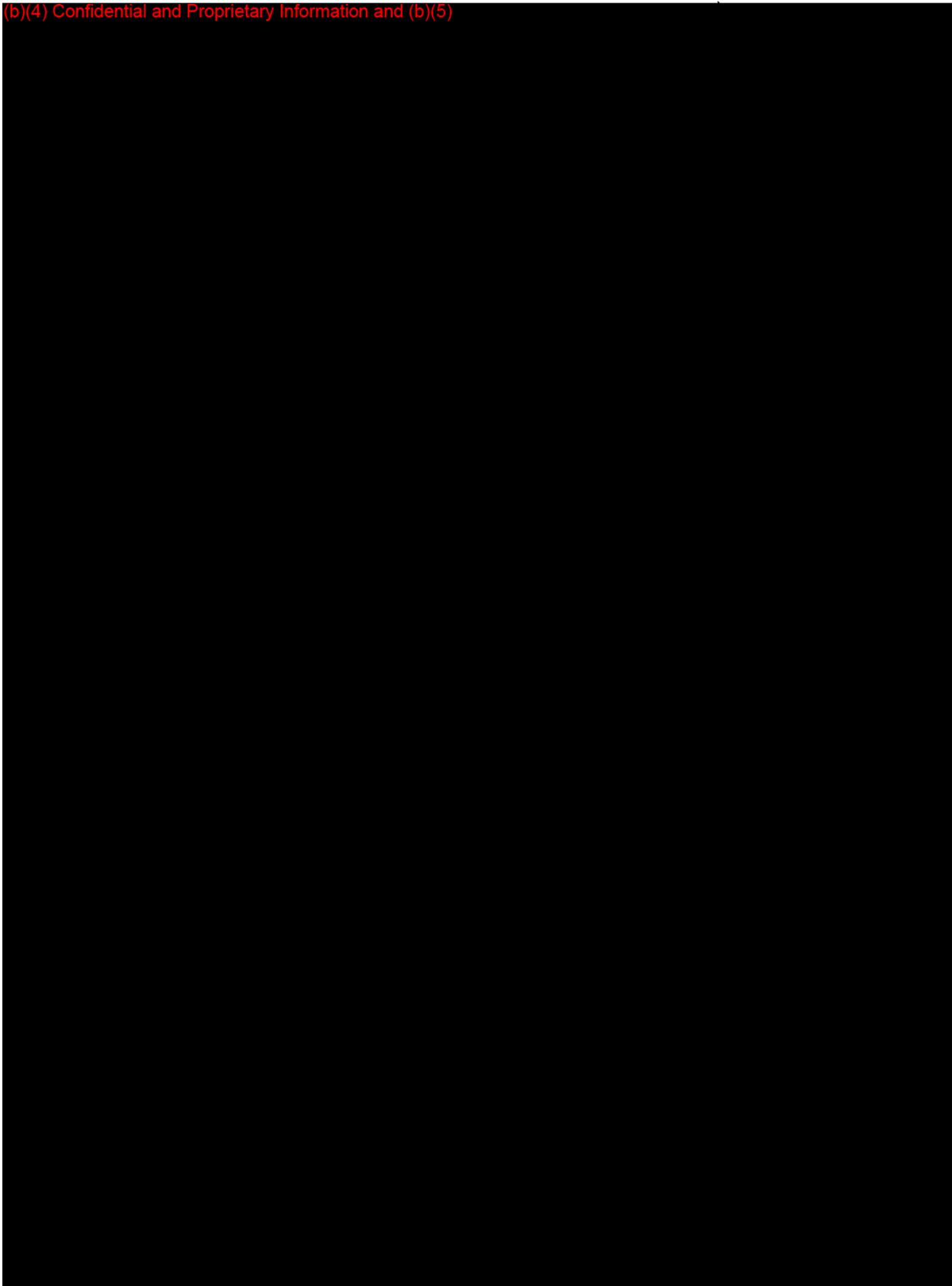
II. **Administrative Requirements**

	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or OTC)	Rx		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	SUM		
Standards Forms	X		

(b)(4) Confidential and Proprietary Information and (b)(5)



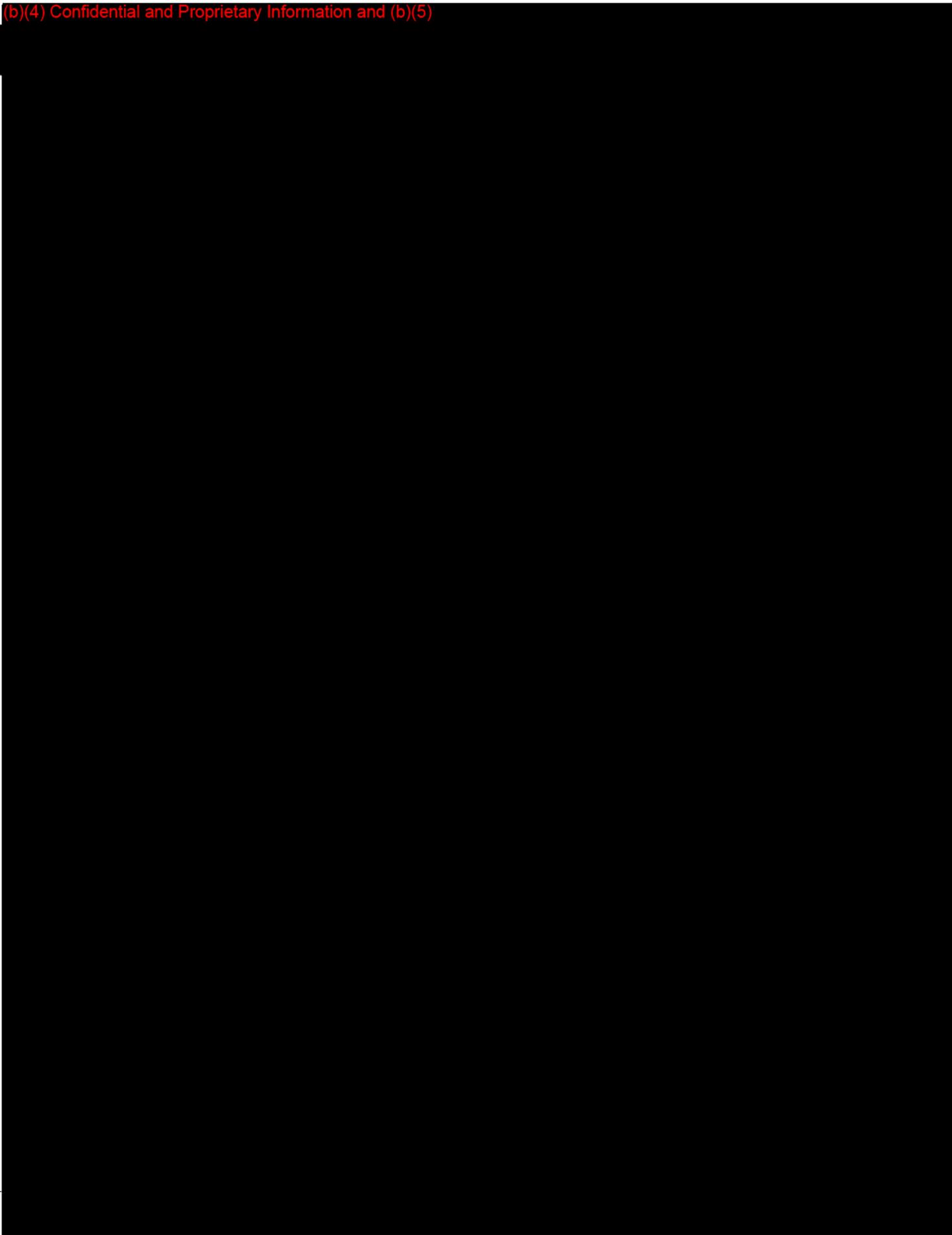
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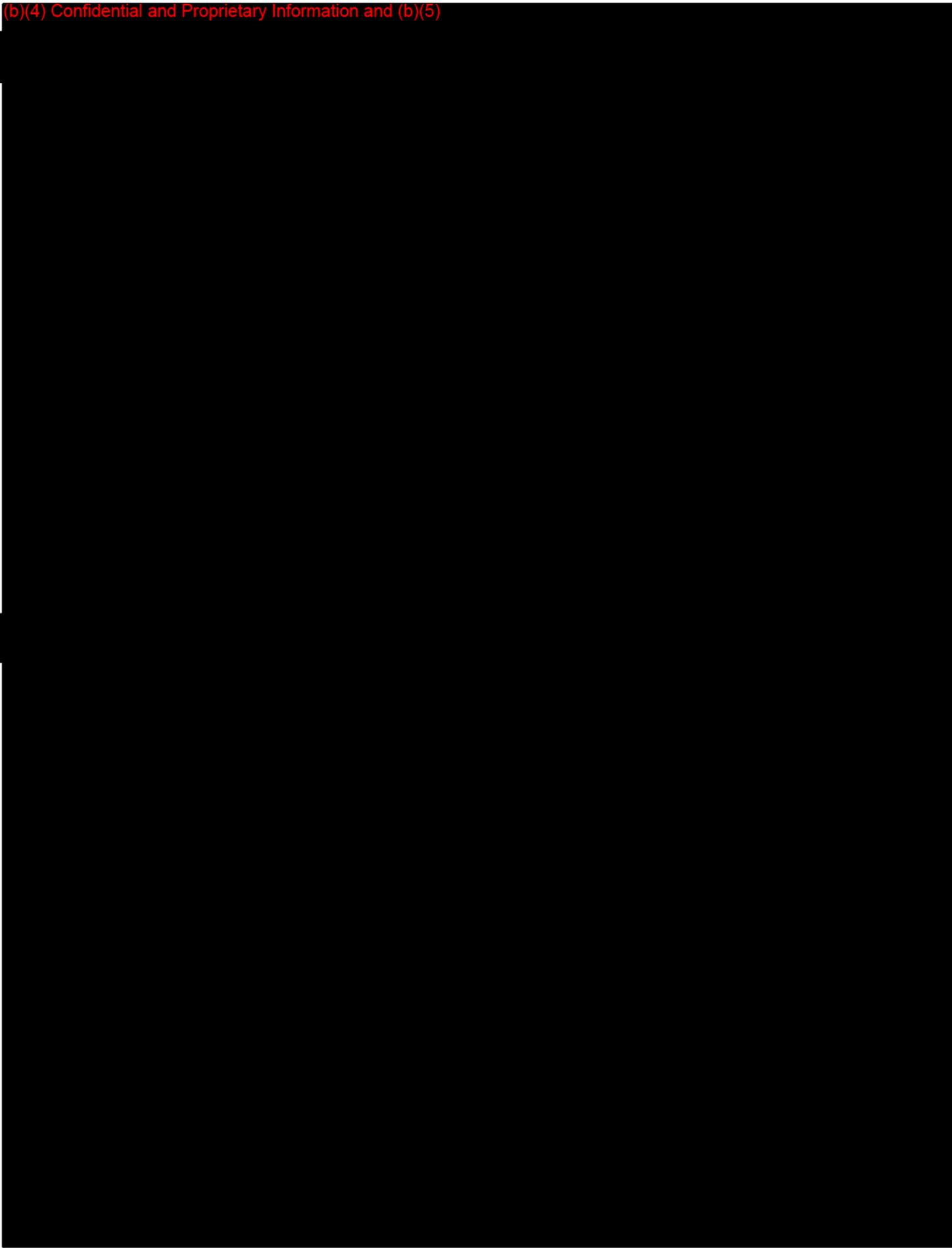
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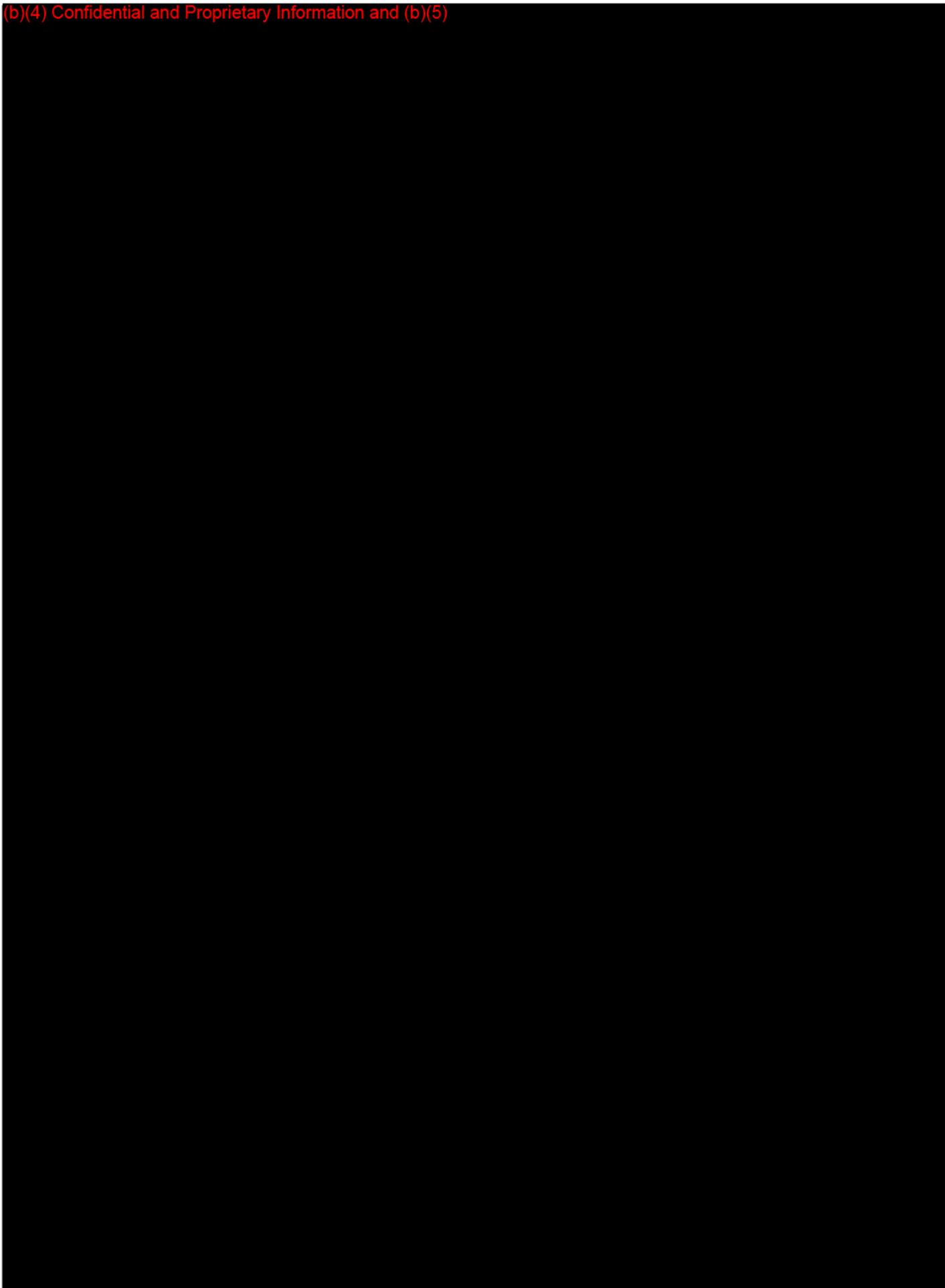
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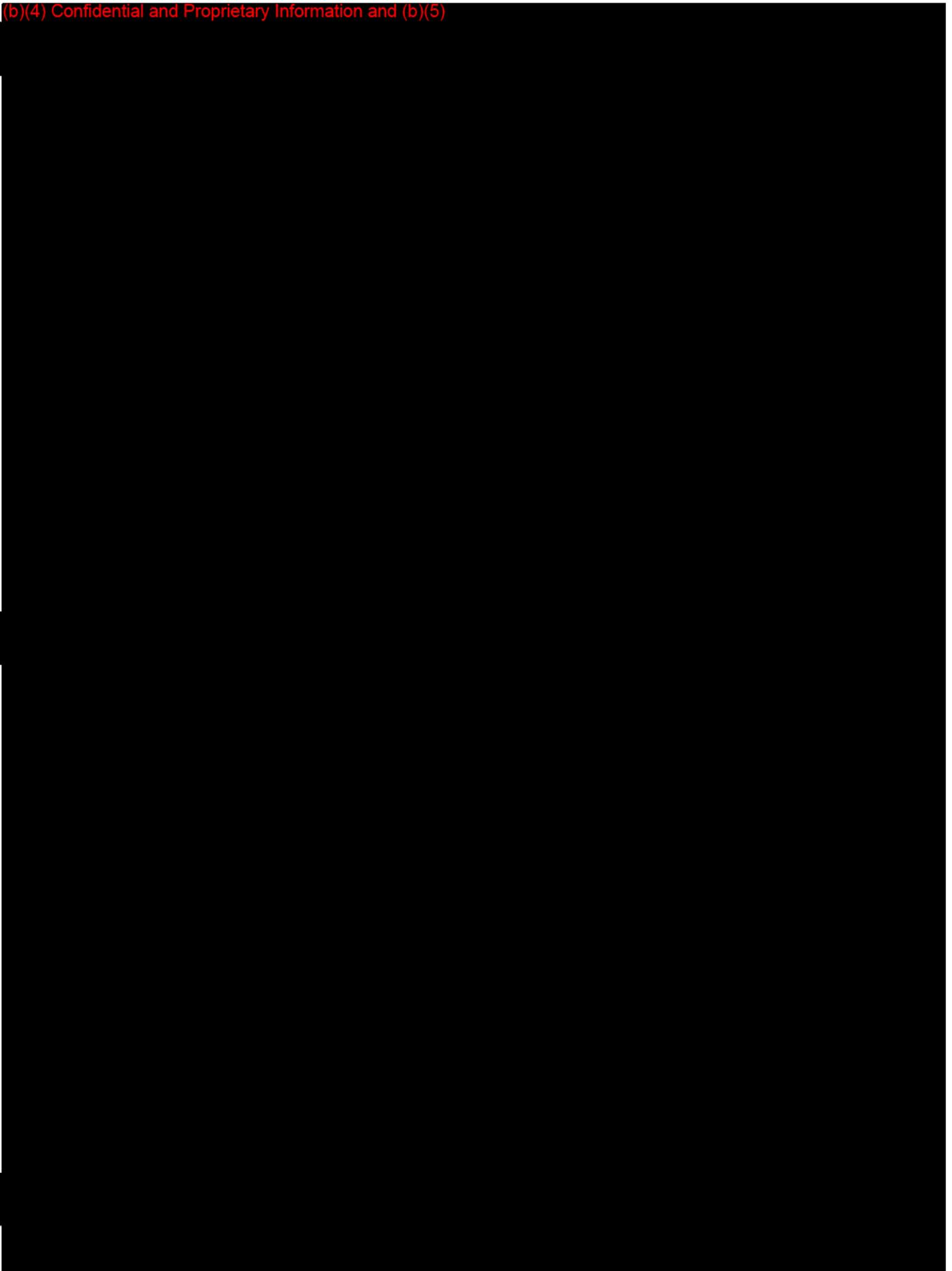
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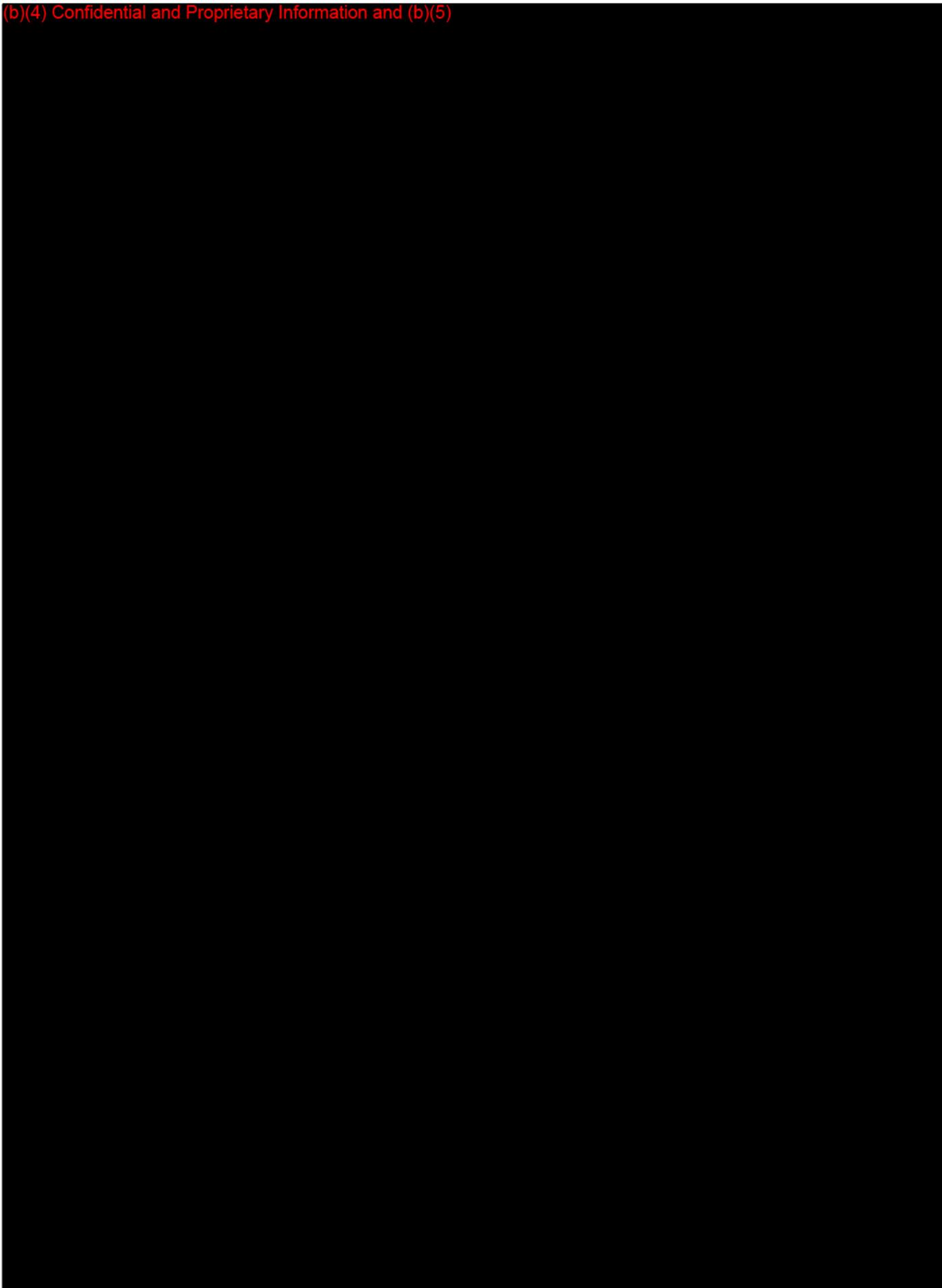
(b)(4) Confidential and Proprietary Information and (b)(5)



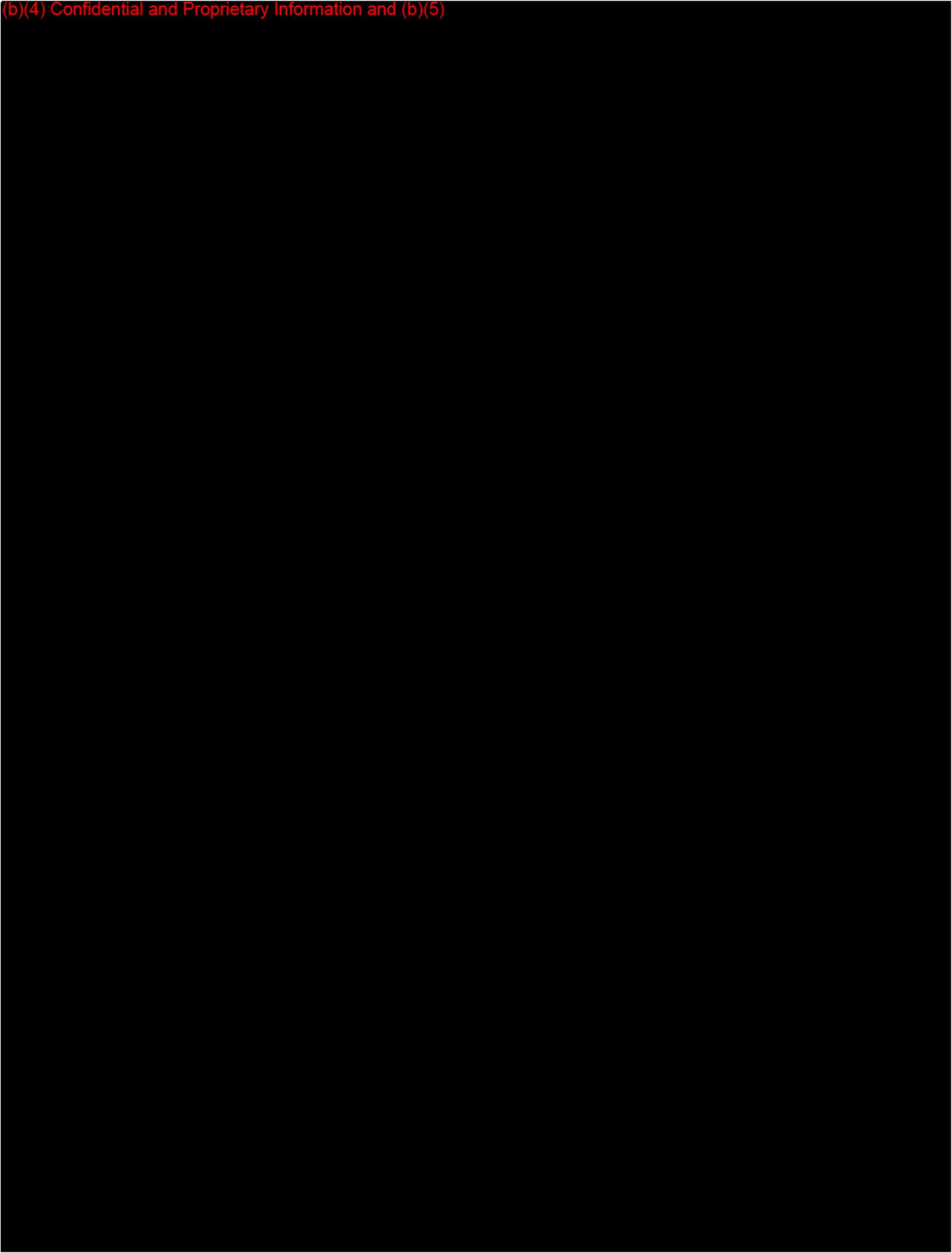
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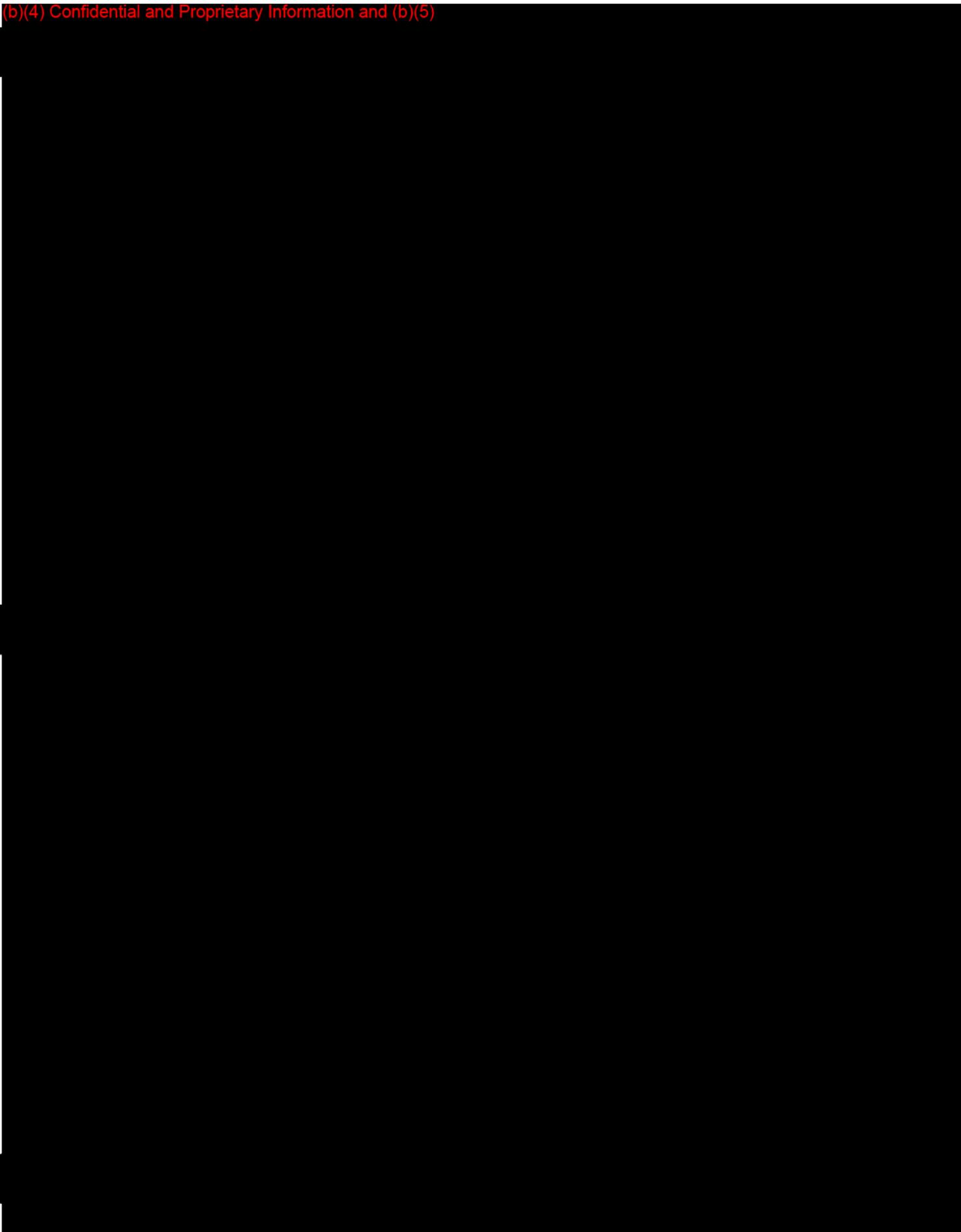
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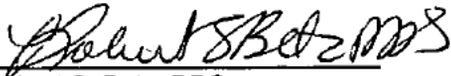
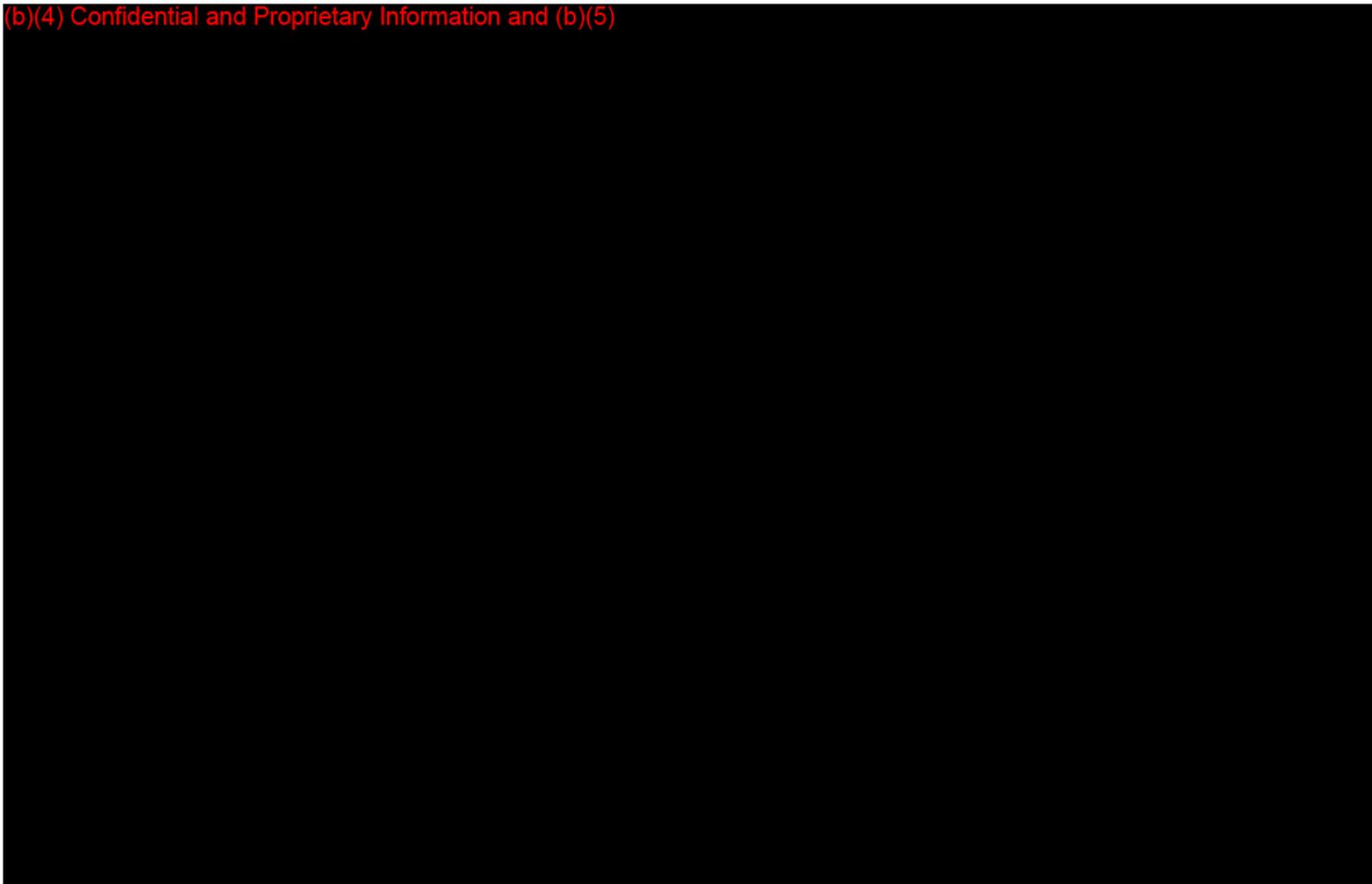
(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



Robert S. Betz, DDS
DAGID/DEDB

November 12, 2010

Dr. Susan Runner, Branch Chief
DAGID/DEDB

Date



COVER SHEET MEMORANDUM

From: Reviewer Name RS Betz DDS
Subject: 510(k) Number K100695
To: The Record

Please list CTS decision code T14

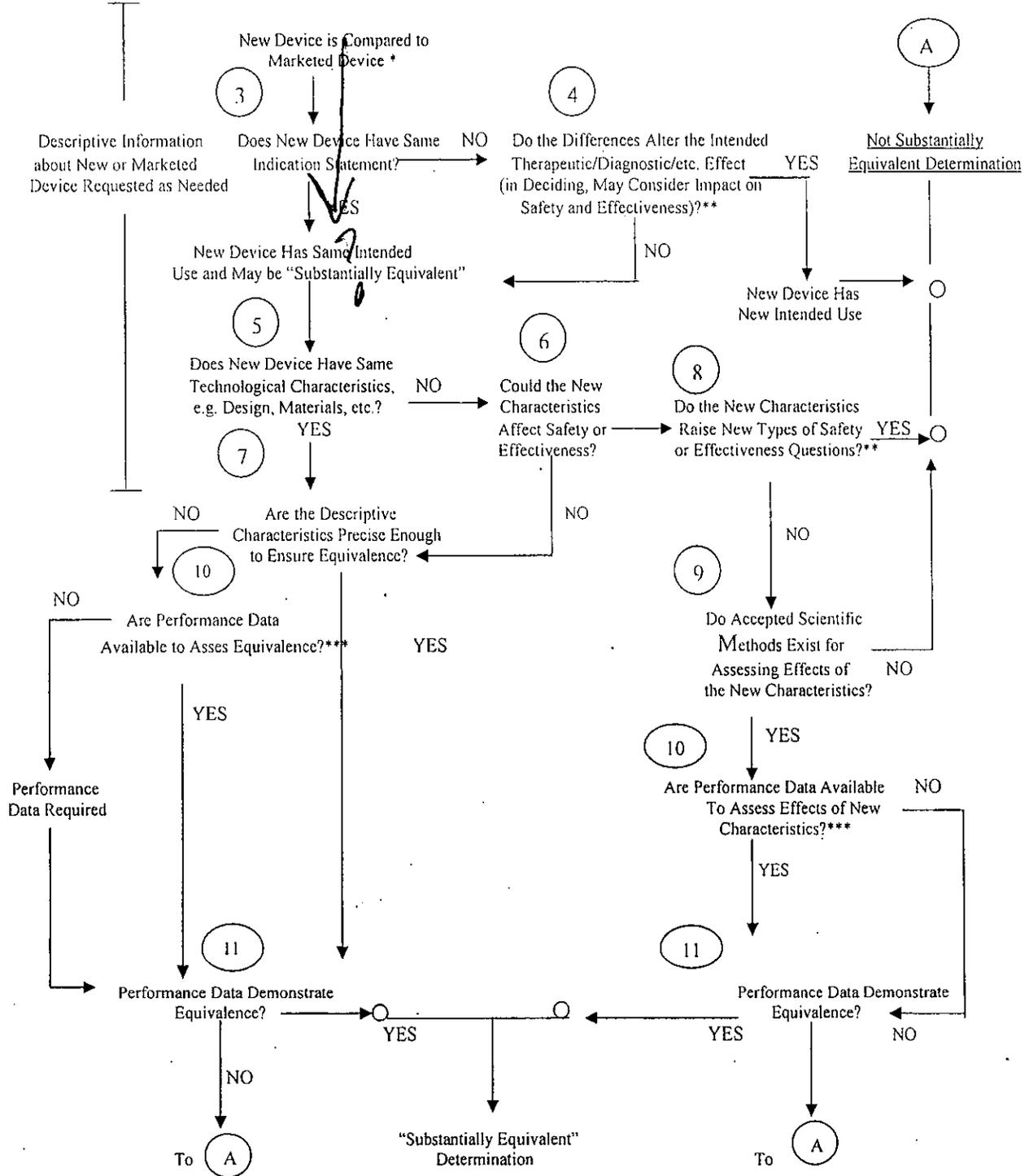
Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%20202%2007.doc)

Hold (Additional Information or Telephone Hold) E-mail sent 06-04-2010

Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	Attach IFU		
510(k) Summary /510(k) Statement	Attach Summary		
Truthful and Accurate Statement.	Must be present for a Final Decision		
Is the device Class III?			
If yes, does firm include Class III Summary?	Must be present for a Final Decision		
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)			
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC)			
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			
Is this device intended for pediatric use only?			
Is this a prescription device? (If both prescription & OTC, check both boxes.)			
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			
Is clinical data necessary to support the review of this 510(k)?			
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If not, then applicant must be contacted to obtain completed form.)			
Does this device include an Animal Tissue Source?			
All Pediatric Patients age<=21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days -< 2 years old)			
Child (2 years -< 12 years old)			
Adolescent (12 years -< 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



- ❖ 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 maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.



DEPARTMENT OF HEALTH AND HUMAN SERVICES

MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
Traditional/Abbreviated

K100695

Date: June 4, 2010
To: The Record
From: Robert S. Betz, D.D.S.

Office: ODE
Division: DAGID
Branch: DEDB

Device Name: CollaDental Barrier
510(k) Holder: Collamatrix, Inc.
Contact: Dennis J. N. Seah

Phone: 886-277-113299
Fax: 886-277-113599
E-mail: jnseah@collamatrix.com

- I. Purpose and Submission Summary - This product is a collagen dental barrier material. Barrier membranes are Class II devices that have a Product Code of NPL. They are accessories to dental bone grafting materials which are described in 21 CFR 872.3930. Substantial equivalence is claimed to Integra Life Science's BioMend Extend (K992216), and BioGide (K042197). Conformance is claimed to:
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3. ISO 10993 (Biological Evaluation of Medical Devices) Part 4 - Interaction with blood.
4. ISO 10993 (Biological Evaluation of Medical Devices) Part 5 - Cytotoxicity.
5. ISO 10993 (Biological Evaluation of Medical Devices) Part 10 - Irritation and sensitization.
6. ISO 10993 (Biological Evaluation of Medical Devices) Part 11 - Systemic toxicity.
7. ISO 2338 Package integrity using vacuum decay method.
8. USP 71 - Sterility test
9. USP 85 - Bacterial endotoxin testing

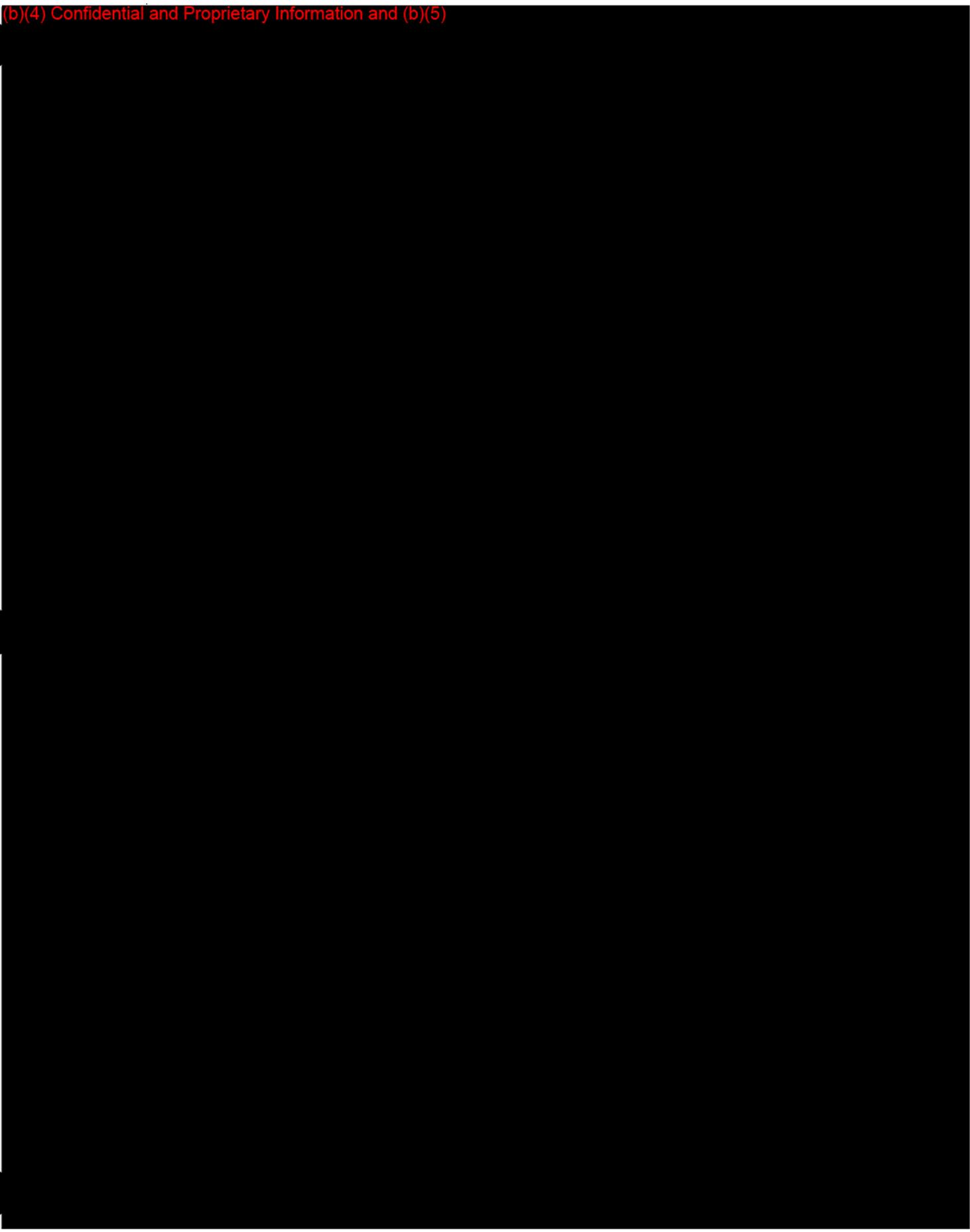
II. Administrative Requirements

Table with 4 columns: Requirement, Yes, No, N/A. Rows include: Indications for Use page (Indicate if: Prescription or OTC), Truthful and Accuracy Statement, 510(k) Summary or 510(k) Statement, Standards Forms.

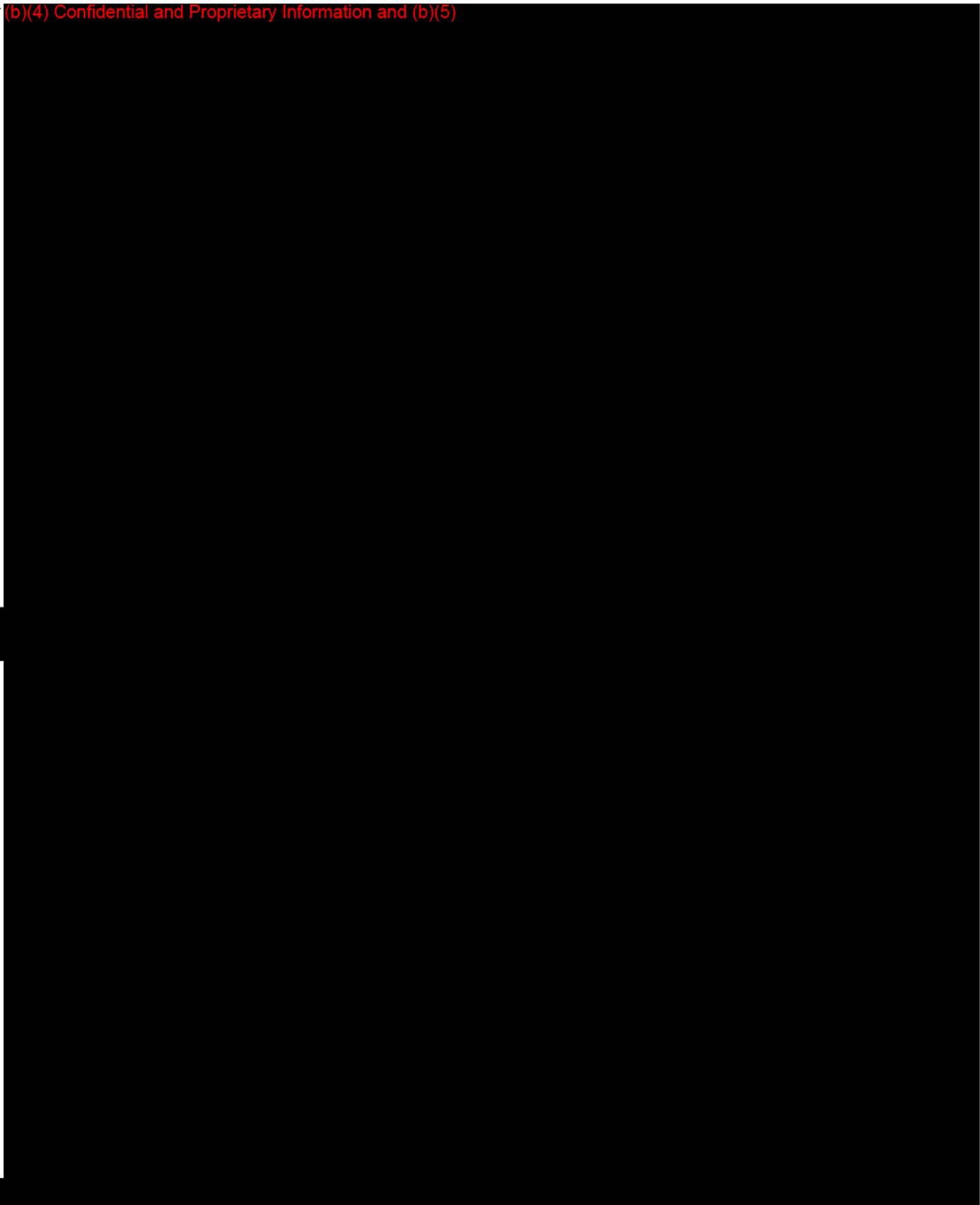
(b)(4) Confidential and Proprietary Information and (b)(5)

176

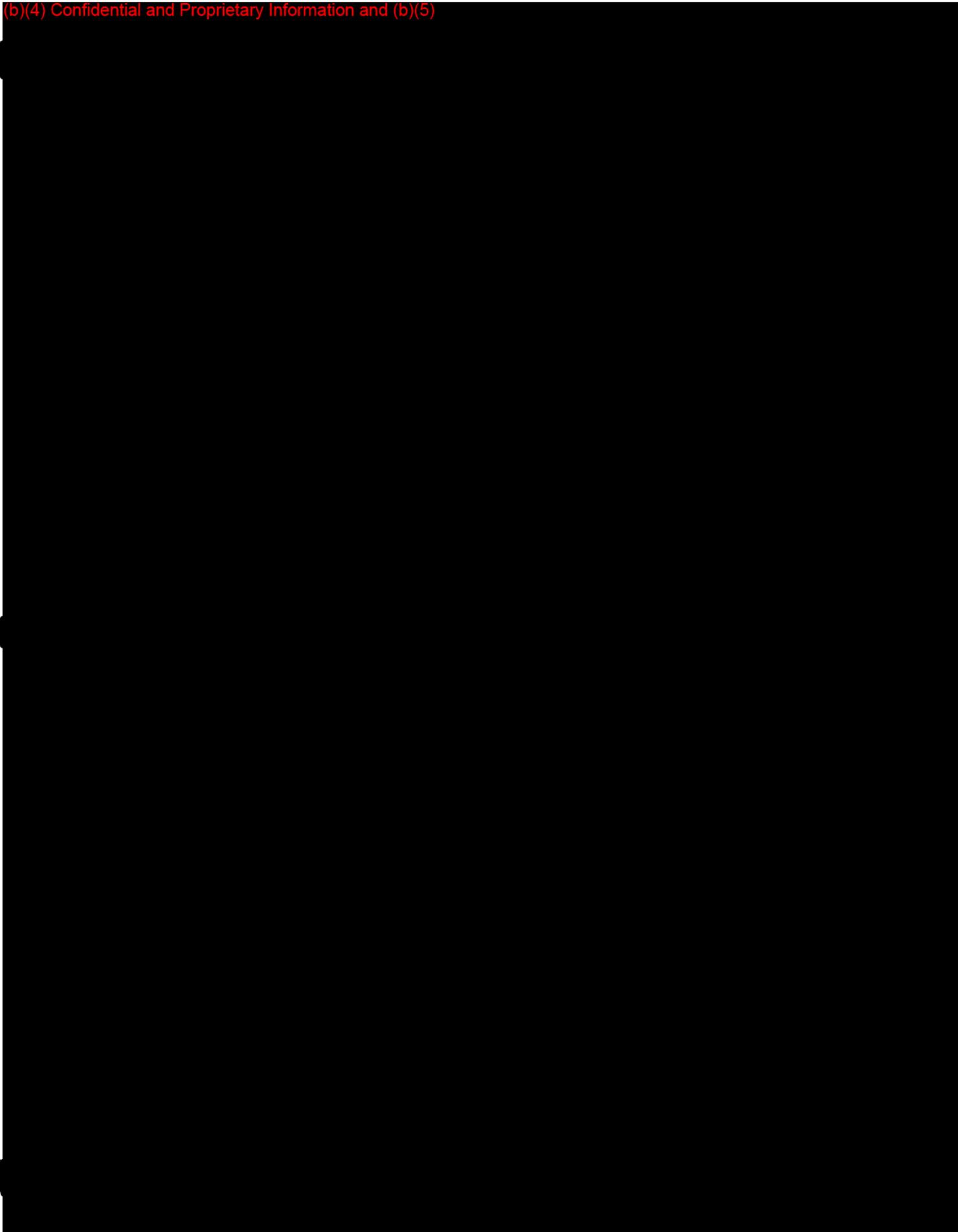
(b)(4) Confidential and Proprietary Information and (b)(5)



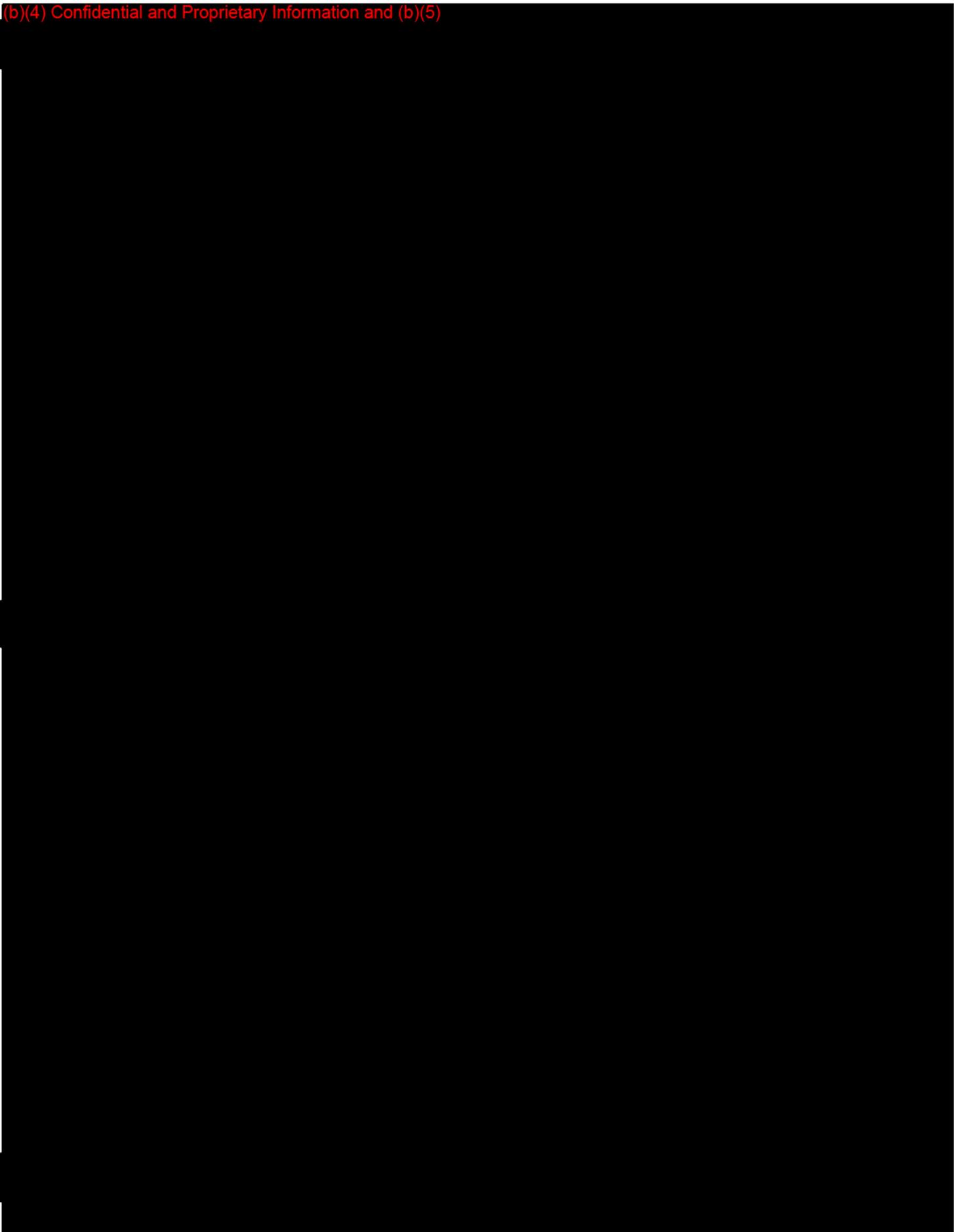
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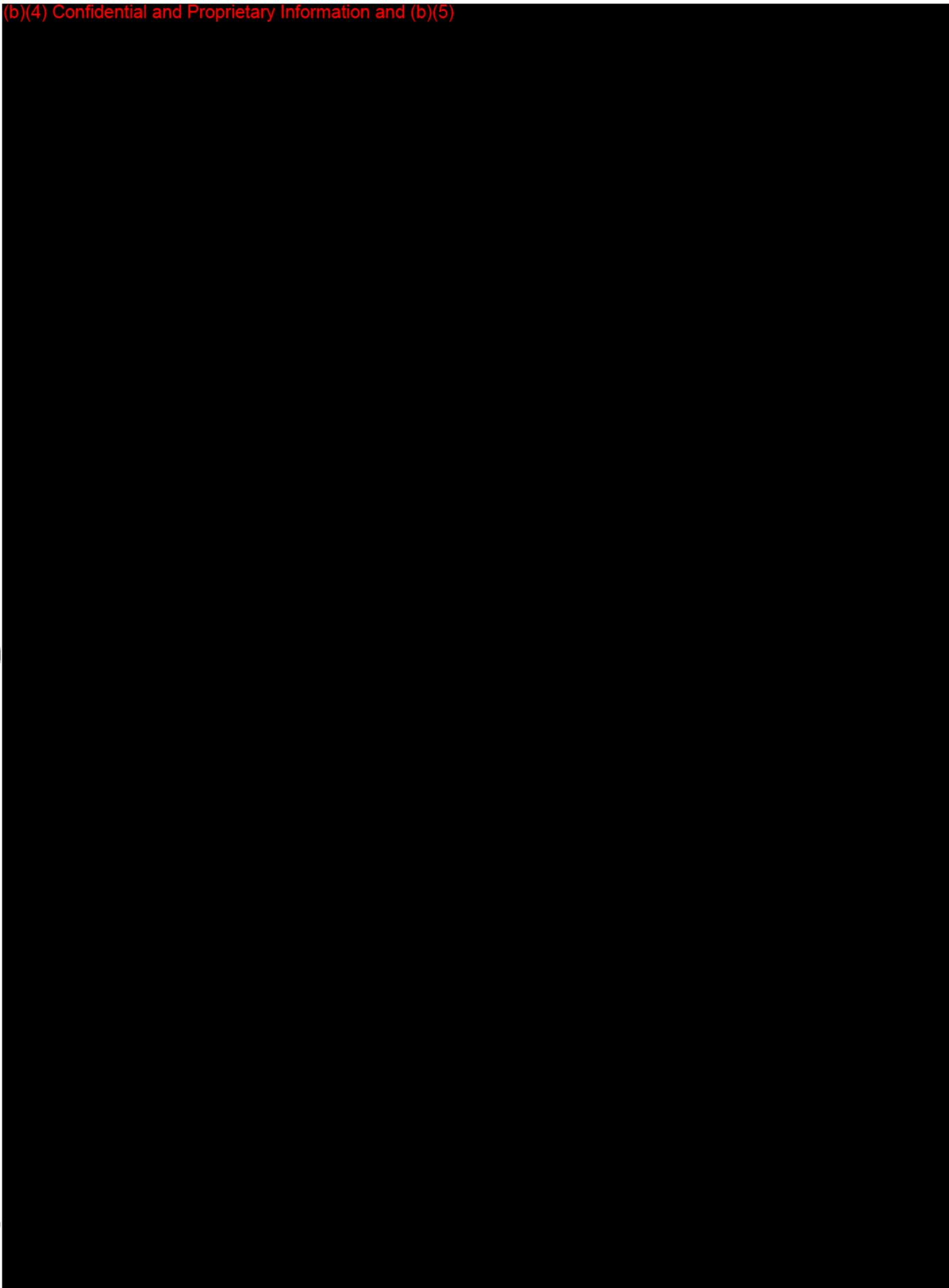
(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)

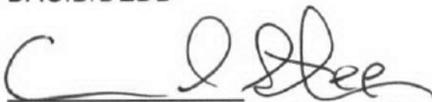


(b)(4) Confidential and Proprietary Information and (b)(5)



Robert S. Betz, DDS
DAGID/DEDB

June 4, 2010



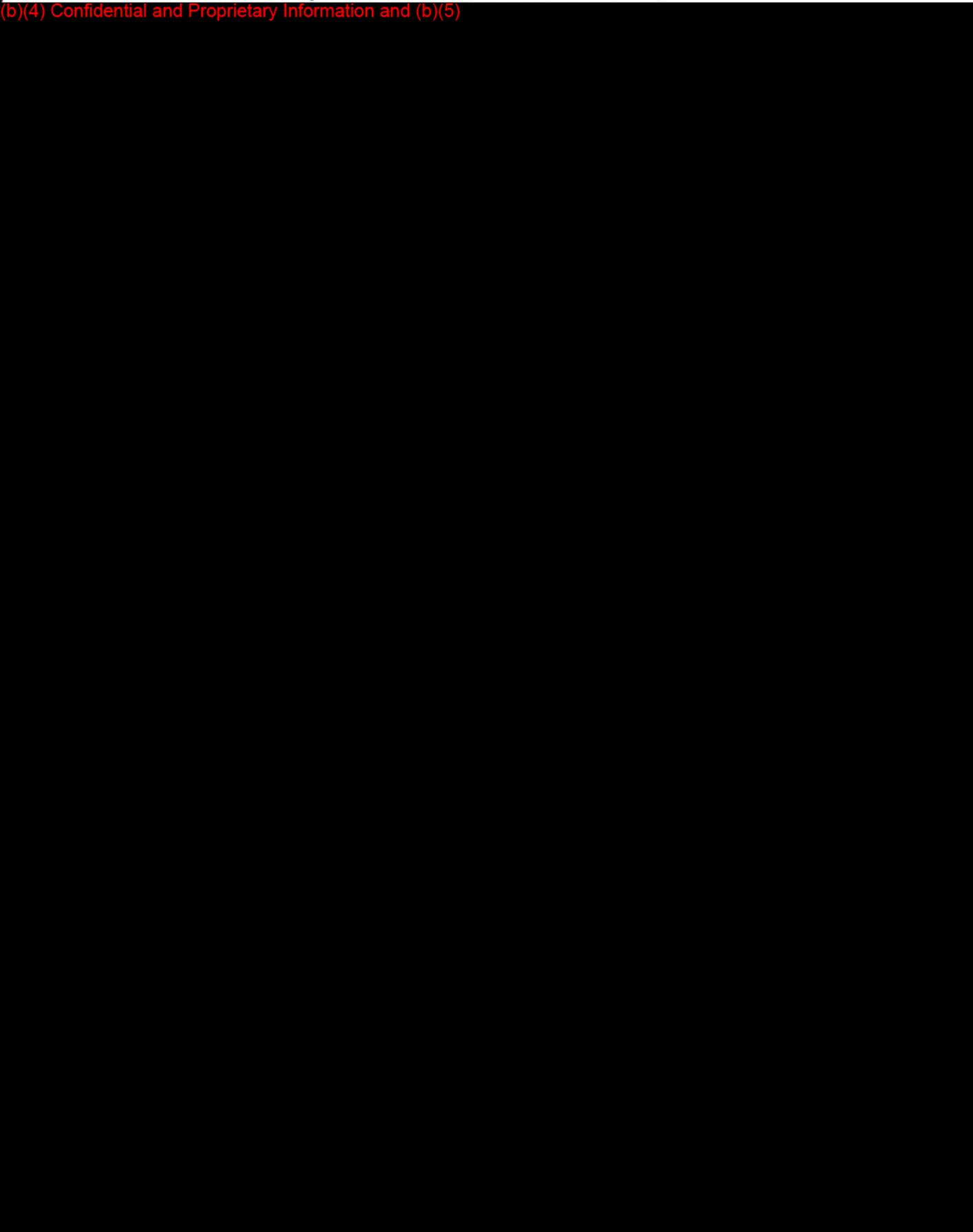
Dr. Kevin Mulry, Acting Branch Chief Date
DAGID/DEDB

AIS for
MSR

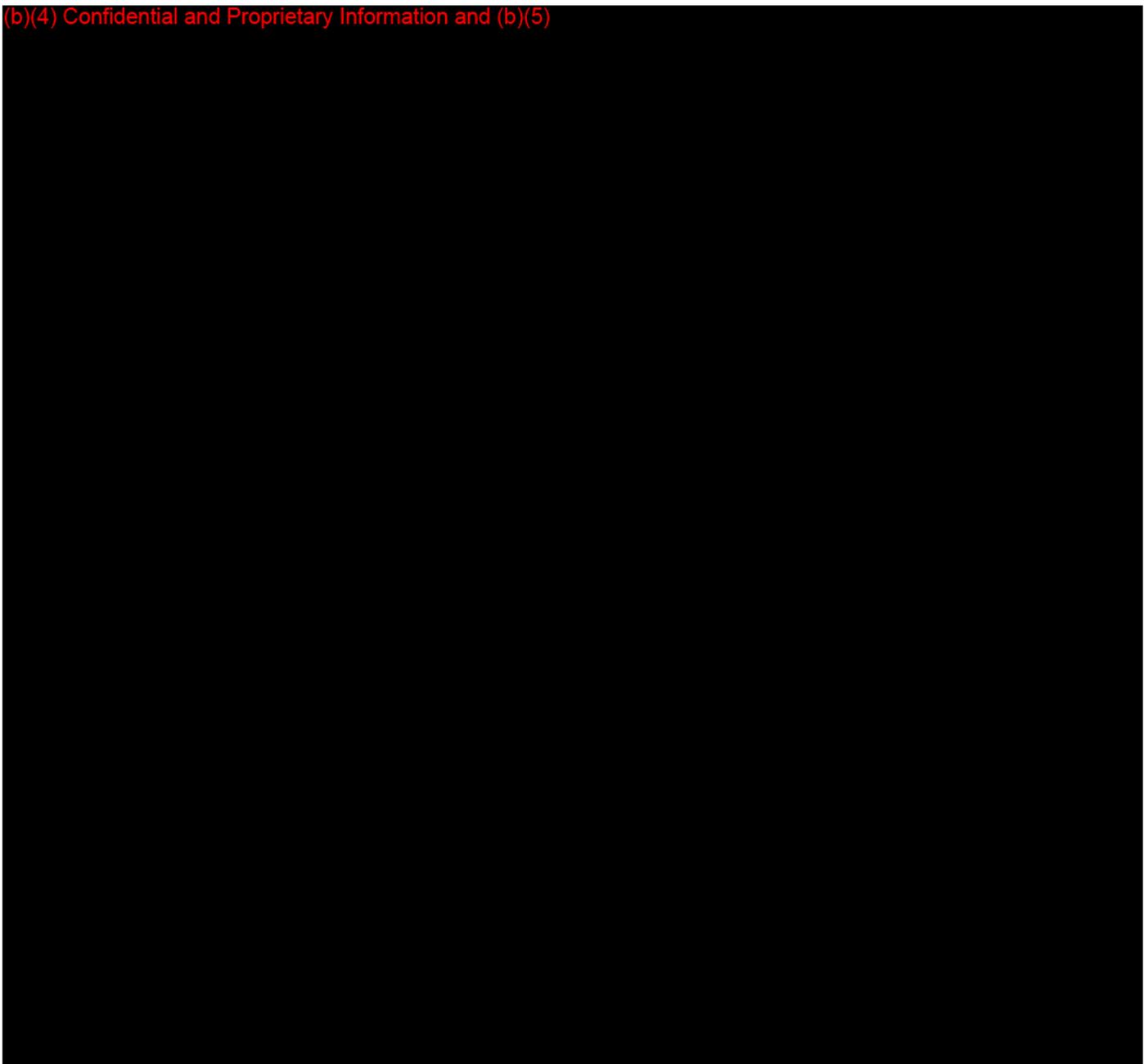
6/4/10

[Text of E-Mail to Sponsor on June 4, 2010]

(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



184

K100695/S1
V.1



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

January 3, 2013

Mr. Dennis J.N. Seah
Collamatrix, Incorporated
26F No. 105, Section 2 Dunhua
South Road, DA-AN Distric
Taipei, China 106

Re: K100695

Trade/Device Name: CollaDental Barrier
Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: II
Product Code: NPL
Dated: January 5, 2011
Received: December 14, 2012.

Dear Mr. Seah:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to 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.

Page 2 – Mr. Seah

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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to <http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Susan Runner DDS, MA

2013.01.03

08:32:49

-05'00'

Anthony D. Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Respiratory, Infection Control and
Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Concurrence & Template History Page
 [THIS PAGE IS INCLUDED IN IMAGE COPY ONLY]

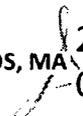
Full Submission Number: K100695

For Office of Compliance Contact Information:

http://insideportlets.fda.gov:9010/portal/page?_pageid=197,415881&_dad=portal&_schema=PORTAL&org=318

For Office of Surveillance and Biometrics Contact Information:

http://insideportlets.fda.gov:9010/portal/page?_pageid=197,415881&_dad=portal&_schema=PORTAL&org=423

Digital Signature Concurrence Table	
Reviewer Sign-Off	 Robert S. Betz 2013.01.03 08:36:48 -05'00'
Branch Chief Sign-Off	 Susan Runner DDS, MA 2013.01.03 08:33:27 -05'00'
Division Sign-Off	 Susan Runner DDS, MA 2013.01.03 08:33:44 -05'00'

Template Name: K1(A) – SE after 1996

Template History:

Date of Update	By	Description of Update
7/27/09	Brandi Stuart	Added Updates to Boiler Table
8/7/09	Brandi Stuart	Updated HFZ Table
1/11/10	Diane Garcia	Liability/Warranty sentence added at bottom of 1 st page
10/4/11	M. McCabe Janicki	Removed IFU sheet and placed in Forms
9/25/12	Edwena Jones	Added digital signature format
12/12/12	M. McCabe Janicki	Added an extra line between letter signature block and the word "Enclosure". Also, added a missing digit in 4-digit extension on letterhead zip code: "002" should be "0002".

271

K100695

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

Prescription Use (Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

2012.12.31

Susan Runner DDS, MA 10:48:45

-05'00'

**(Division Sign-Off)
Division of Anesthesiology, General Hospital
Infection Control, Dental Devices**

510(k) Number: K100695

* * * COMMUNICATION RESULT REPORT (JAN. 3. 2013 4:17PM.) * * *

TRANSMITTED/STORED FILE MODE	JAN. 3. 2013 OPTION	4:14PM	ADDRESS	RESULT	PAGE
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FAX HEADER 2:REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
E-3) NO ANSWERE-2) BUSY
E-4) NO FACSIMILE CONNECTION

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

January 3, 2013

Mr. Dennis J.N. Seah
Collamatrix, Incorporated
26F No. 105, Section 2 Dunhua
South Road, DA-AN Distric
Taipei, China 106

Re: K100695
Trade/Device Name: CollaDental Barrier
Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: II
Product Code: NPL
Dated: January 5, 2011
Received: December 14, 2012

Dear Mr. Seah:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to 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.



Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Robert S. Betz DDS
Subject: 510(k) Number K100695/S1
To: The Record

Please list CTS decision code SE

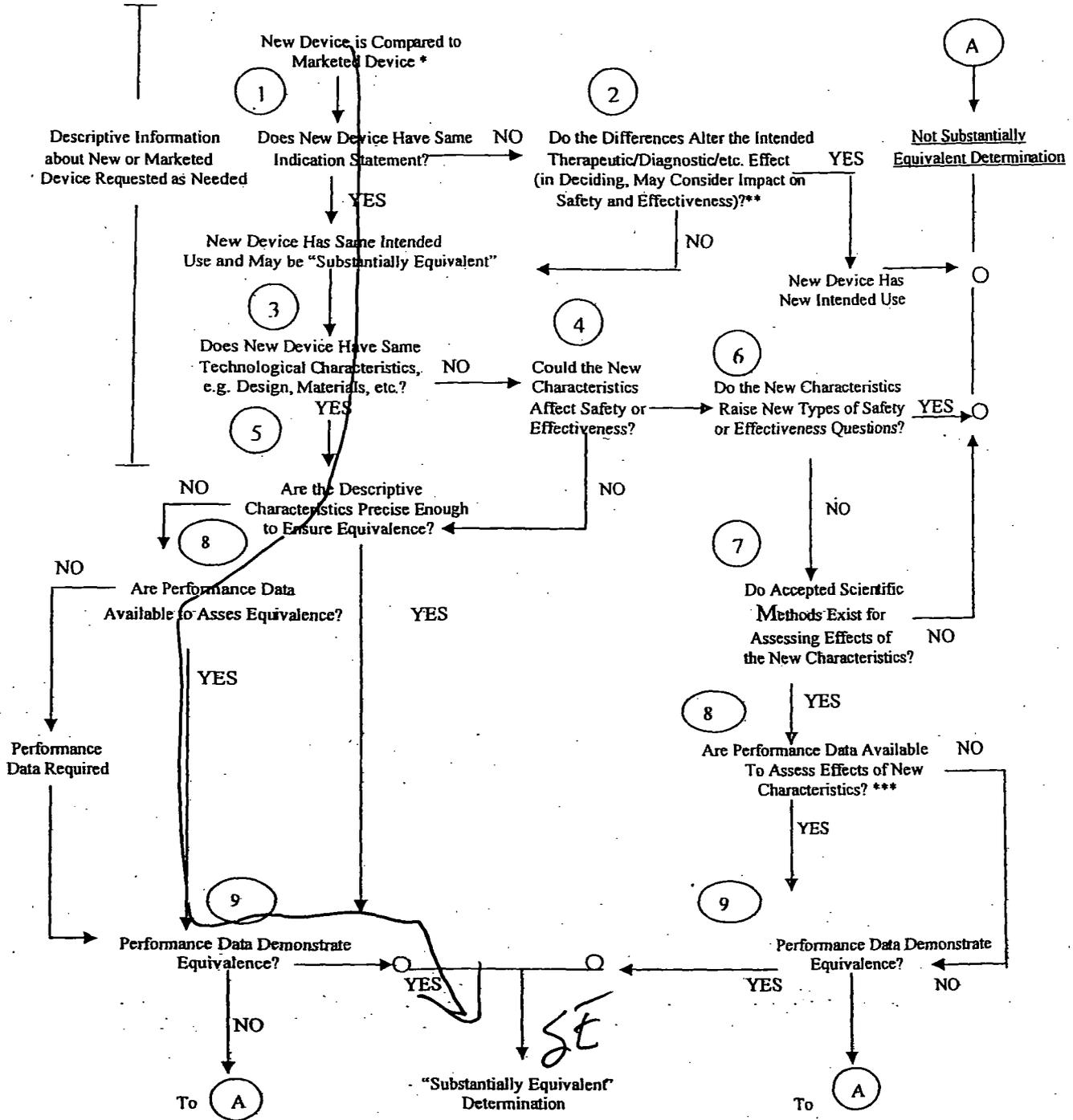
- Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPreMarketNotification510kProgram/0_5631/Screening%20Checklist%20202%2007.doc)
- Hold (Additional Information or Telephone Hold).
- Final Decision (SE) SE with Limitations, NSE (select code below), Withdrawn, etc.).

Not Substantially Equivalent (NSE) Codes

- NO NSE for lack of predicate
- NI NSE for new intended use
- NQ NSE for new technology that raises new questions of safety and effectiveness
- NU NSE for new intended use AND new technology raising new questions of safety and effectiveness
- NP NSE for lack of performance data
- NS NSE no response
- NL NSE for lack of performance data AND no response
- NM NSE pre-amendment device call for PMAs (515i)
- NC NSE post-amendment device requires PMAs
- NH NSE for new molecular entity requires PMA
- TR NSE for transitional device

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	Attach IFU	Rx	
510(k) Summary /510(k) Statement	Attach Summary	Sum	
Truthful and Accurate Statement.	Must be present for a Final Decision		
Is the device Class III?			X
If yes, does firm include Class III Summary?	Must be present for a Final Decision		X
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		X	
Is this a combination product? (Please specify category <u>N</u> see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPreMarketNotification510kProgram/0_413b/CO-MBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC)			X
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			X
Is this device intended for pediatric use only?			X
Is this a prescription device? (If both prescription & OTC, check both boxes.)		Rx only	X
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			X
Is clinical data necessary to support the review of this 510(k)?			X
For United States-based clinical studies only: Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If study was			X

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



* 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.

*** Questions: Contact FDA/CDRH, Office of Device Research and Evaluation, 1080 Willow Grove Road, Rockville, MD 20850, 796-8118.



DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

**Premarket Notification [510(k)] Review
Traditional/Abbreviated**

K100695/S001

Date: December 28, 2010
To: The Record
From: Robert S. Betz, D.D.S.

Office: ODE
Division: DAGID
Branch: DEDB

Device Name: CollaDental Barrier
510(k) Holder: Collamatrix, Inc.
Contact: Dennis J. N. Seah

Phone: 886-277-113299
Fax: 886-277-113599
E-mail: jnseah@collamatrix.com

- I. **Purpose and Submission Summary** – This product is a collagen dental barrier material. Barrier membranes are Class II devices that have a Product Code of NPL. They are accessories to dental bone grafting materials which are described in 21 CFR 872.3930. Substantial equivalence is claimed to Integra Life Science's BioMend Extend (K992216), and BioGide (K042197). Conformance is claimed to:
1. ISO 11137 (Sterilization – Radiation),
 2. ISO 10993 (Biological Evaluation of Medical Devices) Part 3 – Genotoxicity, carcinogenicity and reproductive toxicity.
 3. ISO 10993 (Biological Evaluation of Medical Devices) Part 4 – Interaction with blood.
 4. ISO 10993 (Biological Evaluation of Medical Devices) Part 5 – Cytotoxicity.
 5. ISO 10993 (Biological Evaluation of Medical Devices) Part 10 – Irritation and sensitization.
 6. ISO 10993 (Biological Evaluation of Medical Devices) Part 11 – Systemic toxicity.
 7. ISO 2338 Package integrity using vacuum decay method.
 8. USP 71 – Sterility test
 9. USP 85 – Bacterial endotoxin testing

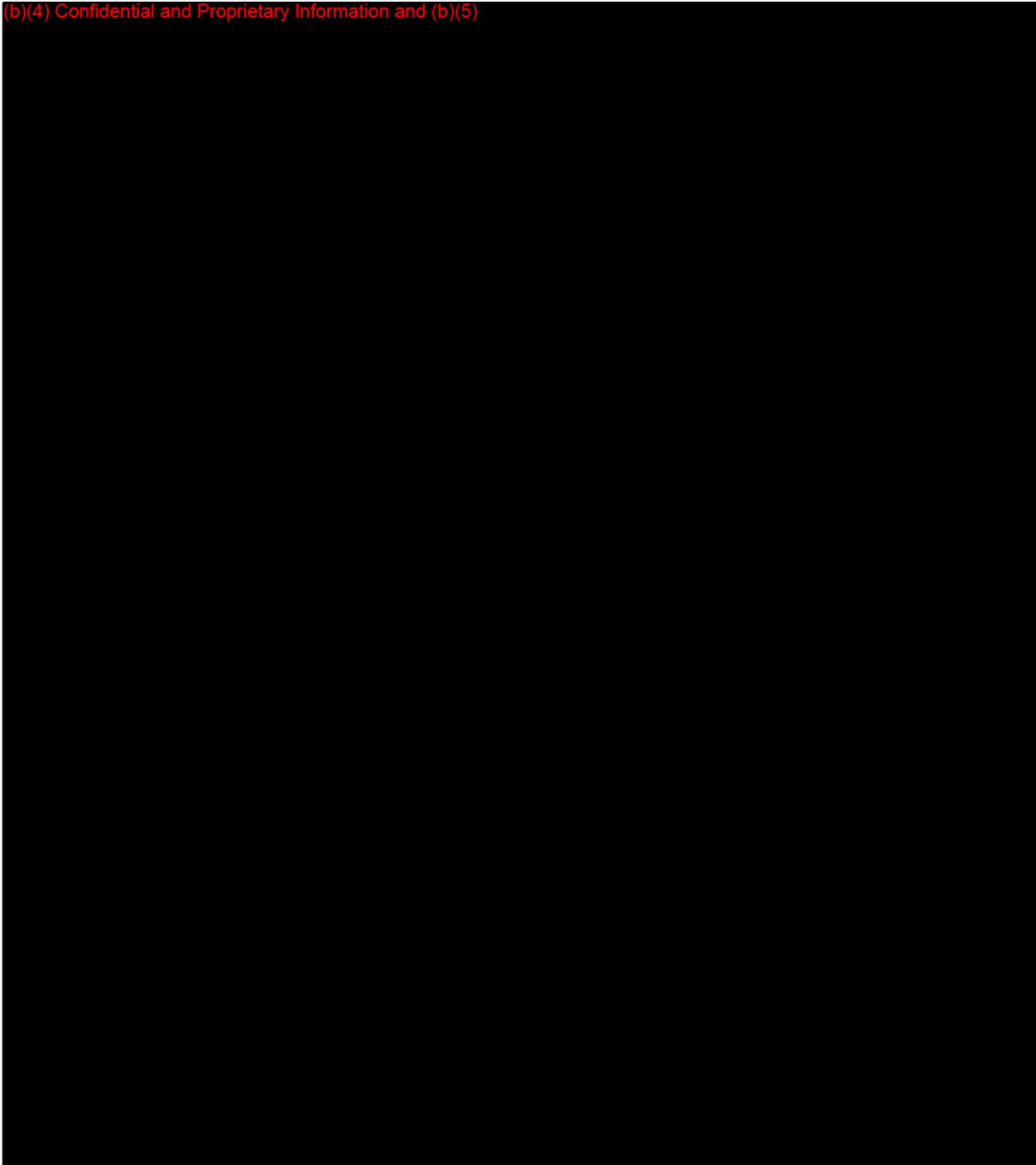
II. **Administrative Requirements**

	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or OTC)	Rx		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	SUM		
Standards Forms	X		

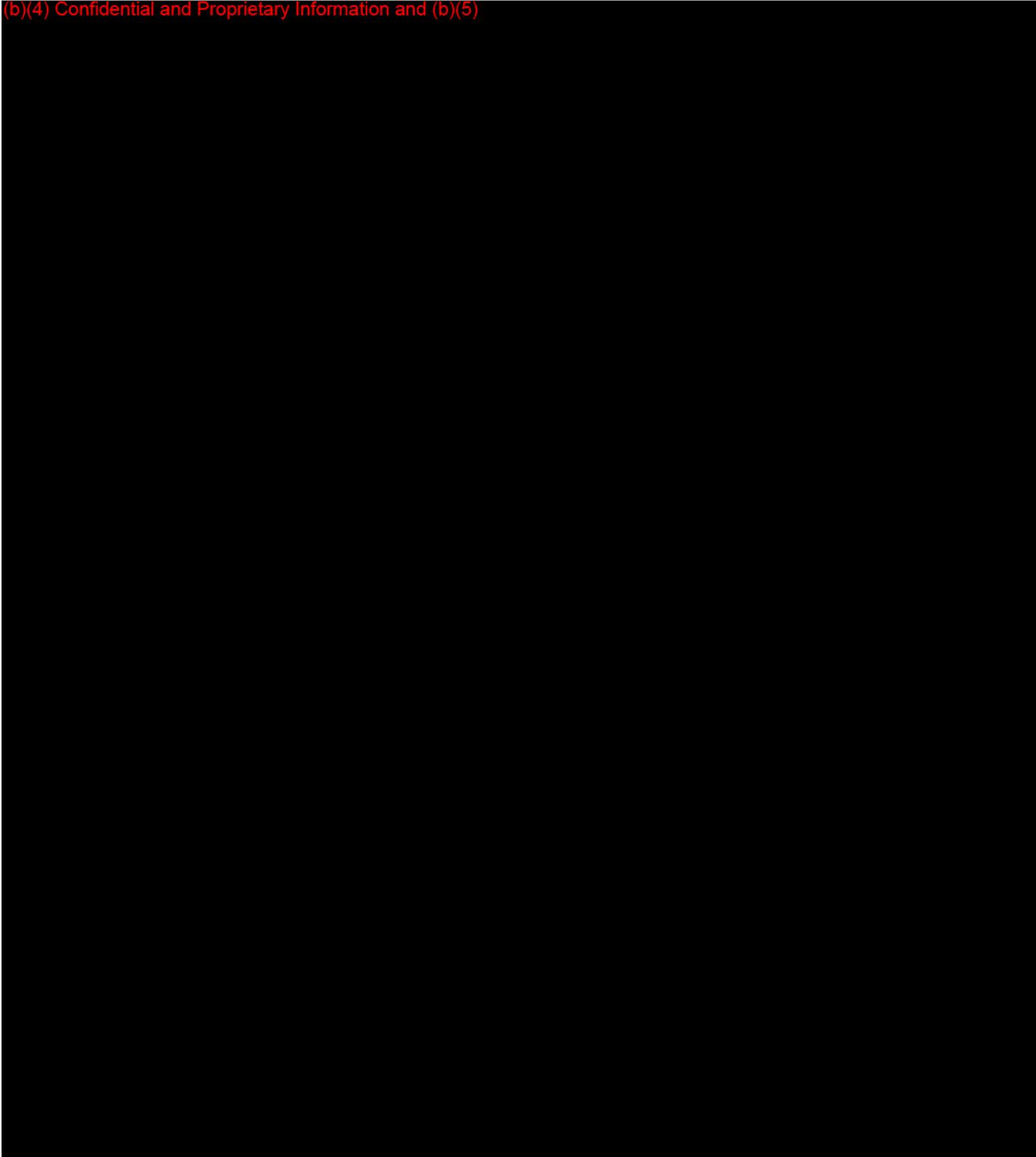
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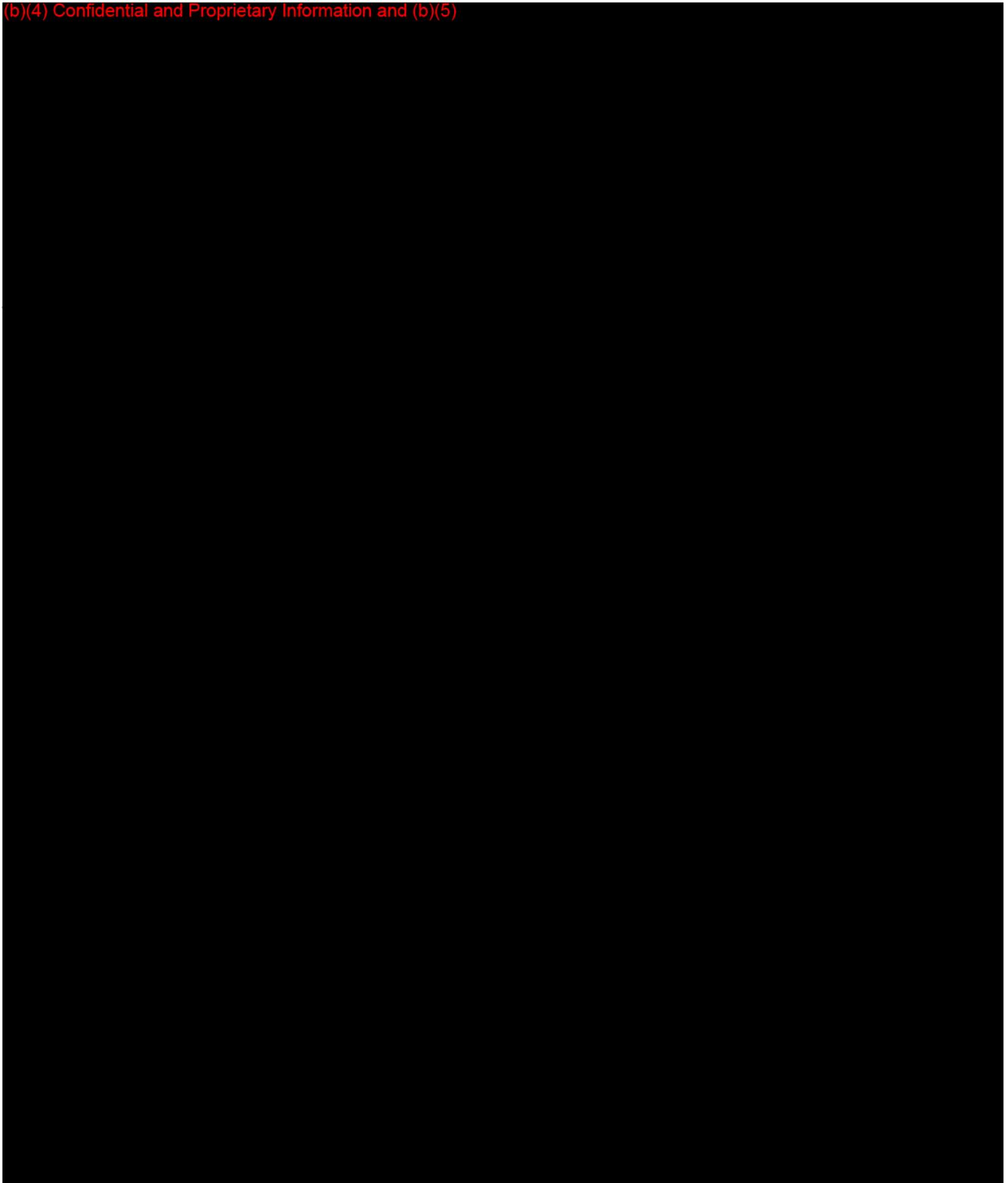
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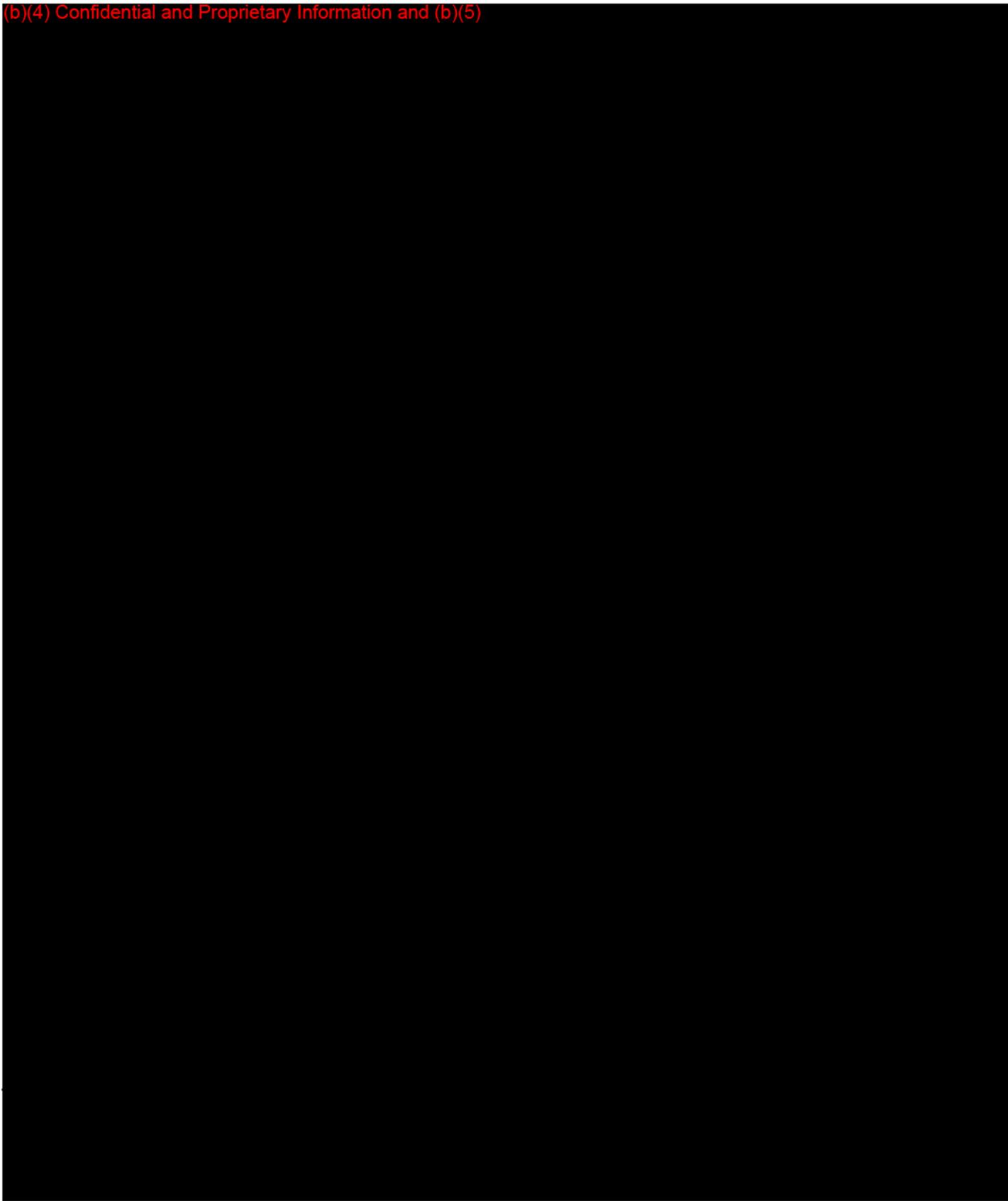
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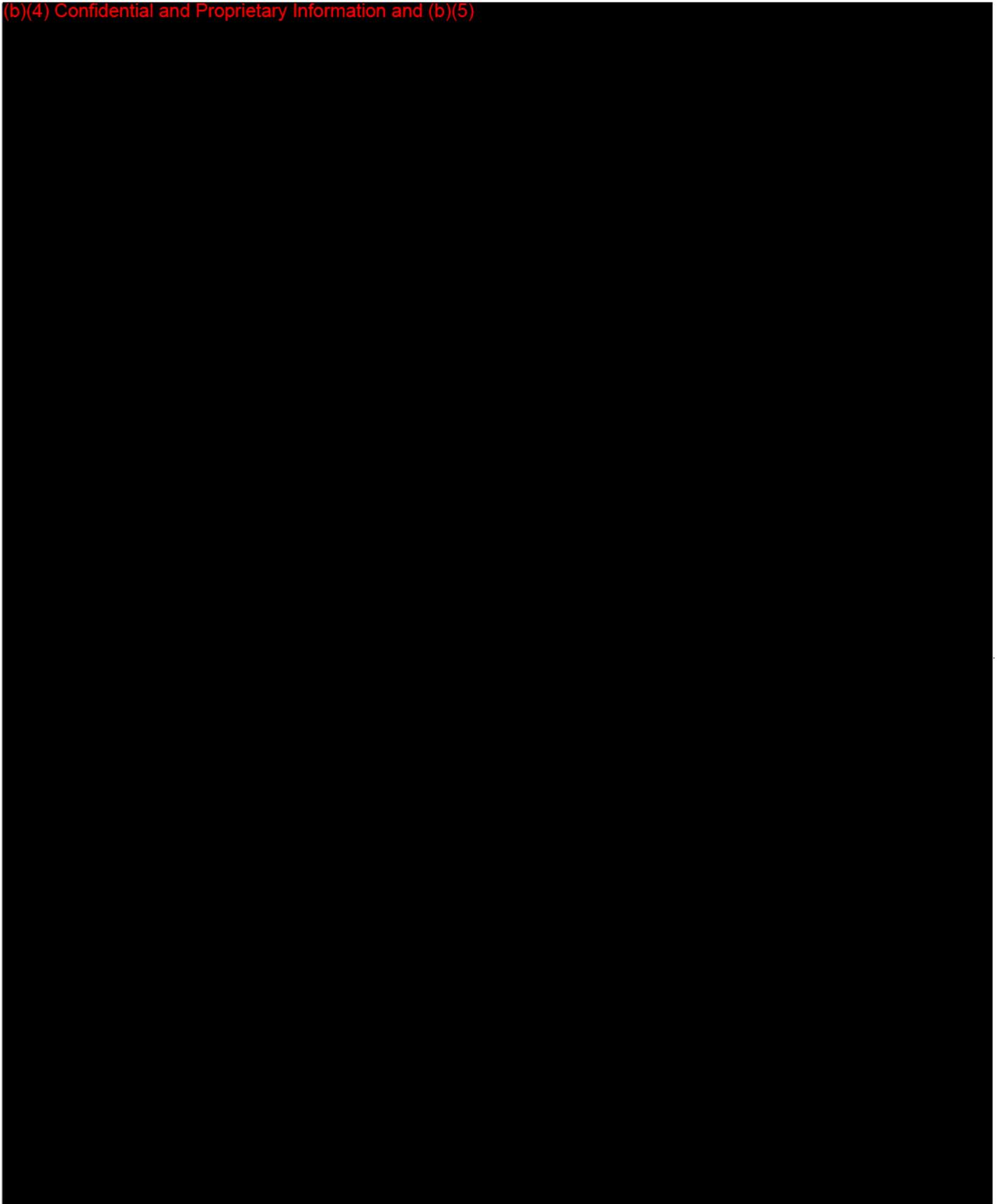
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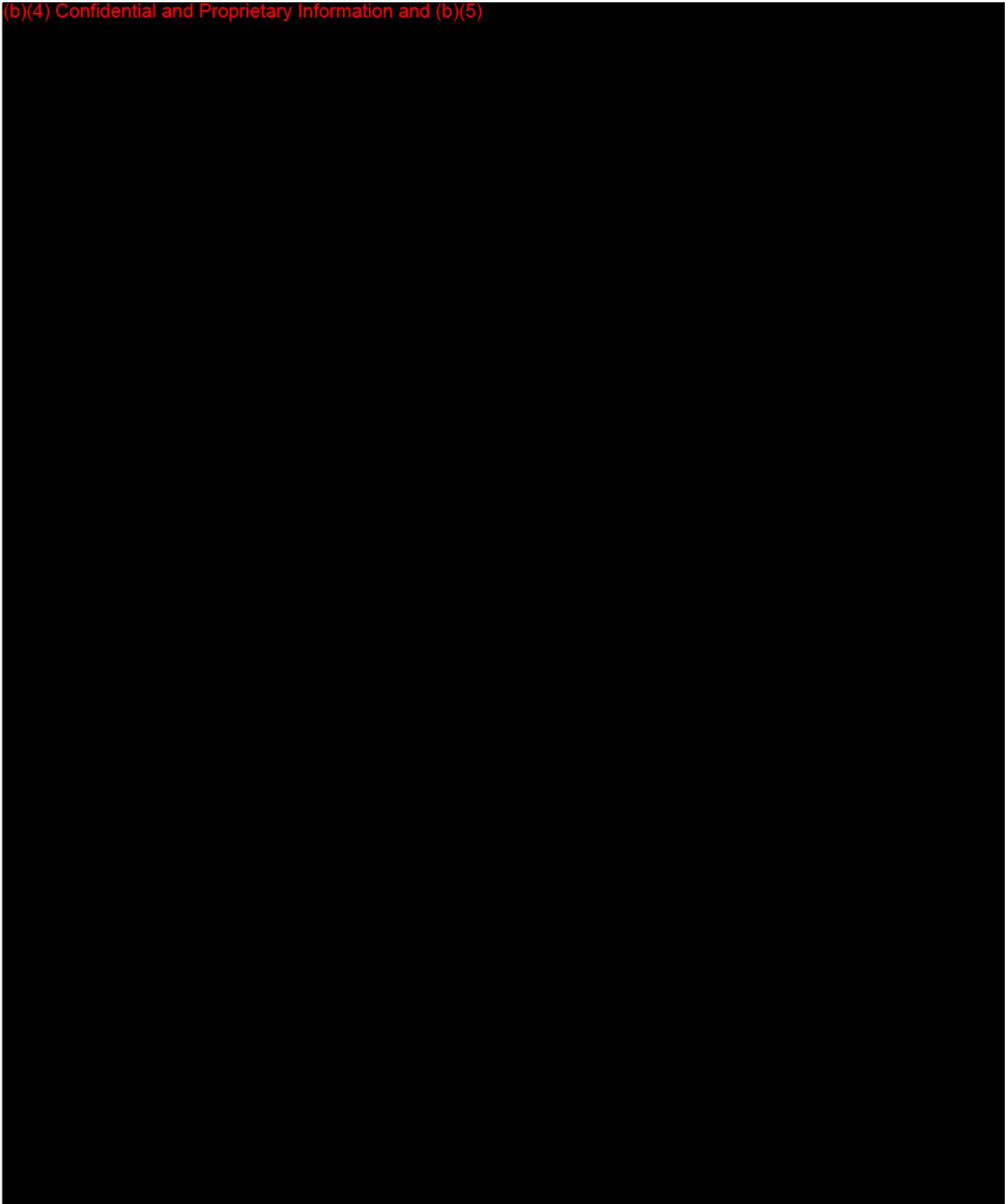
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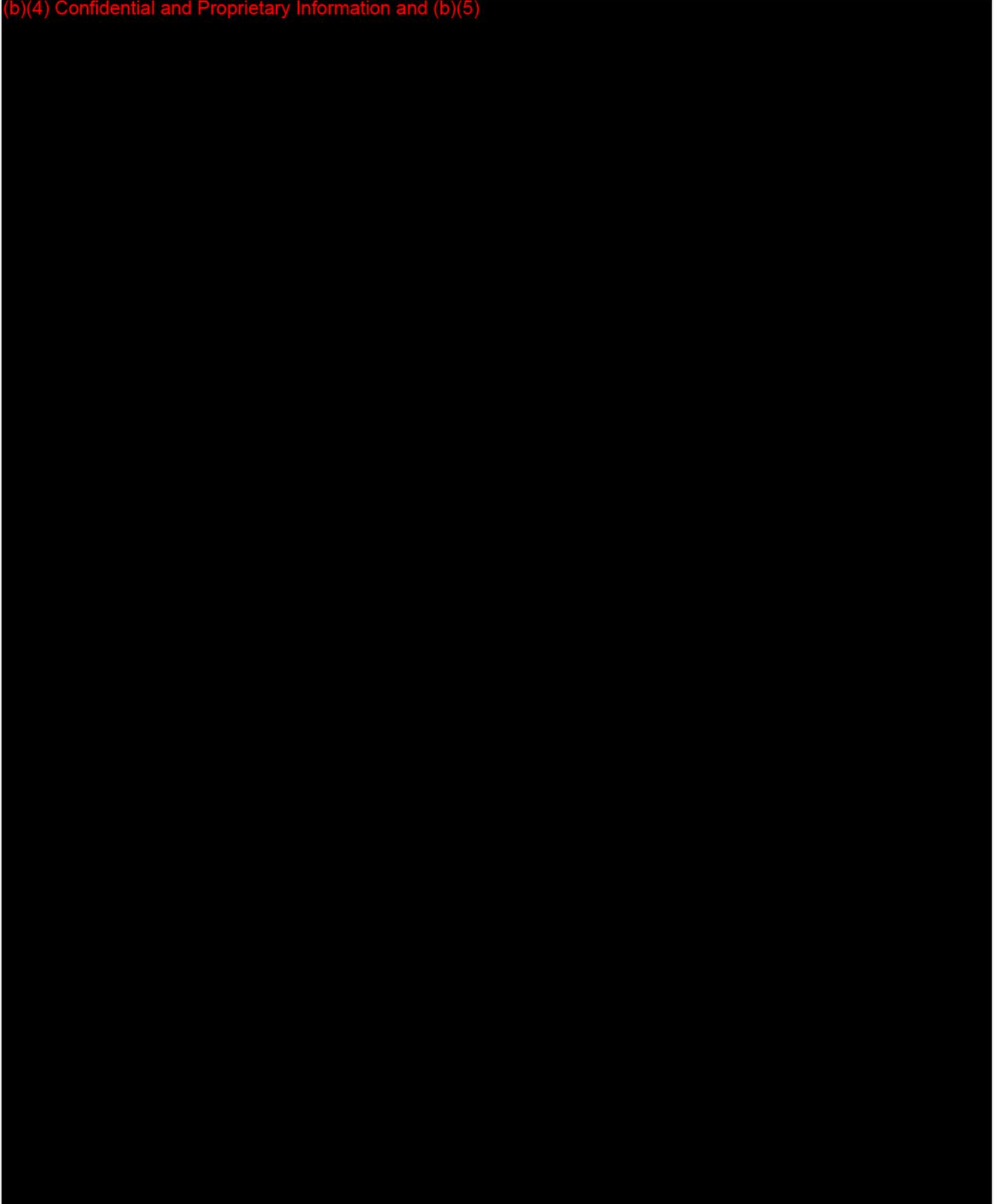
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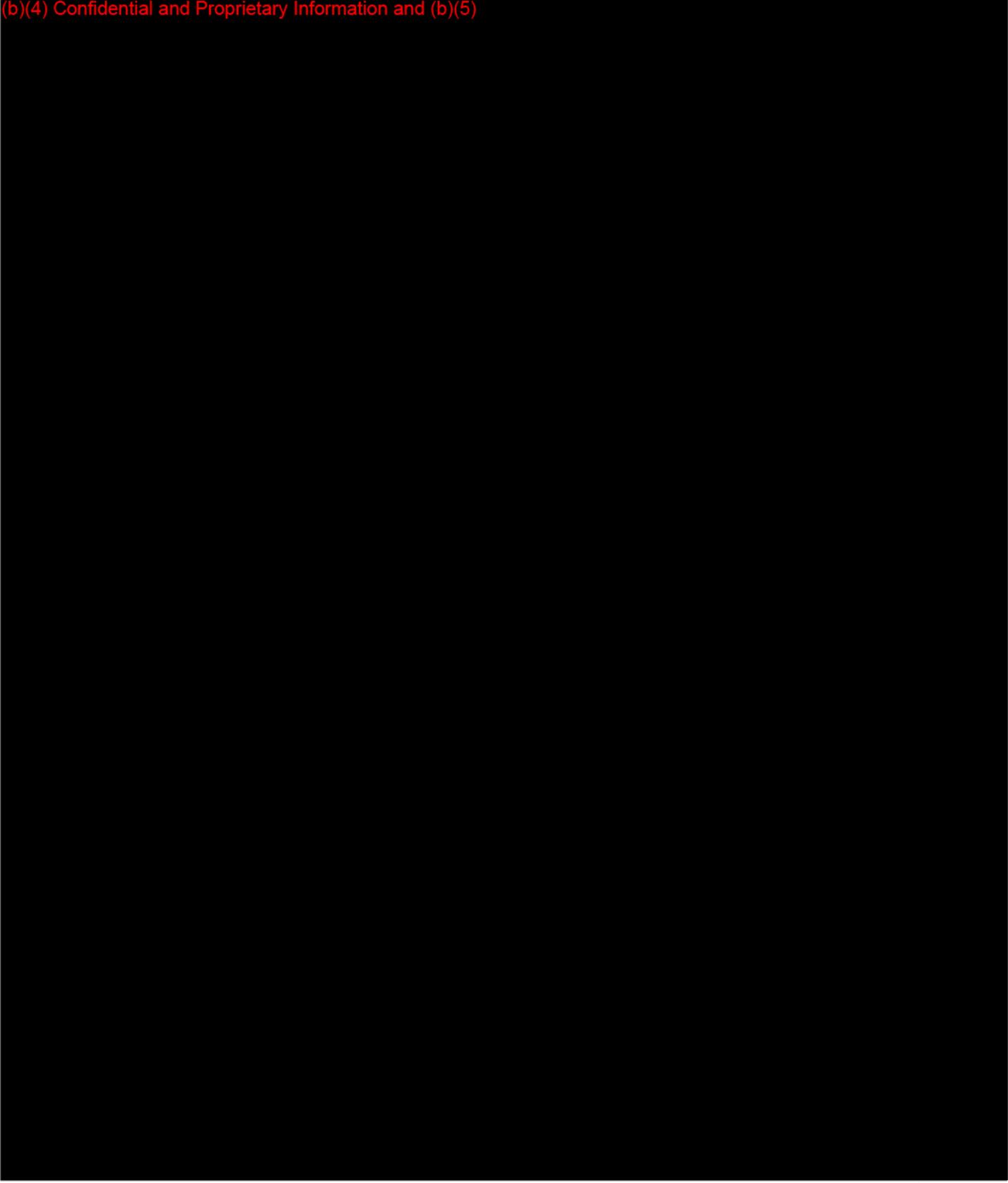
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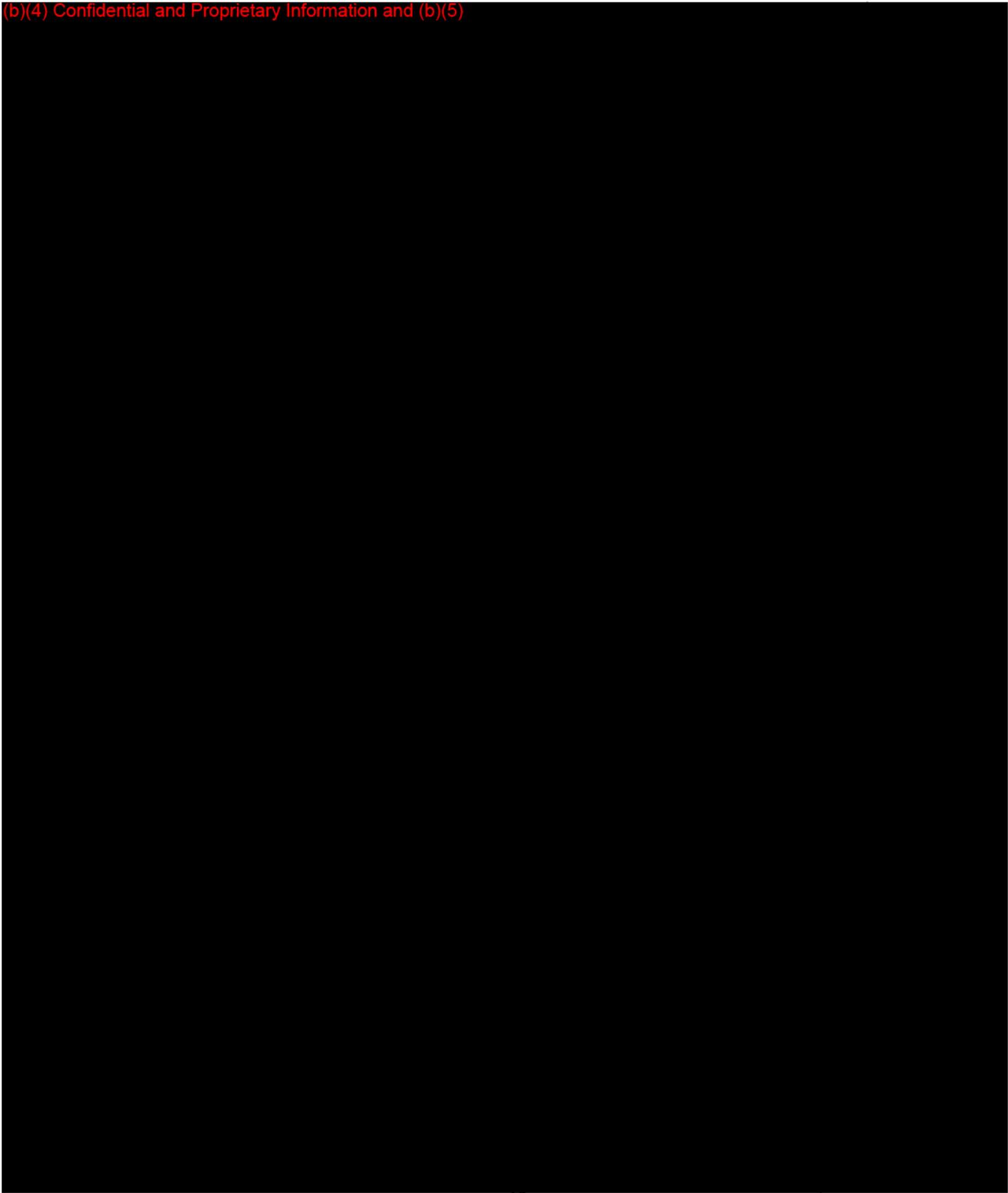
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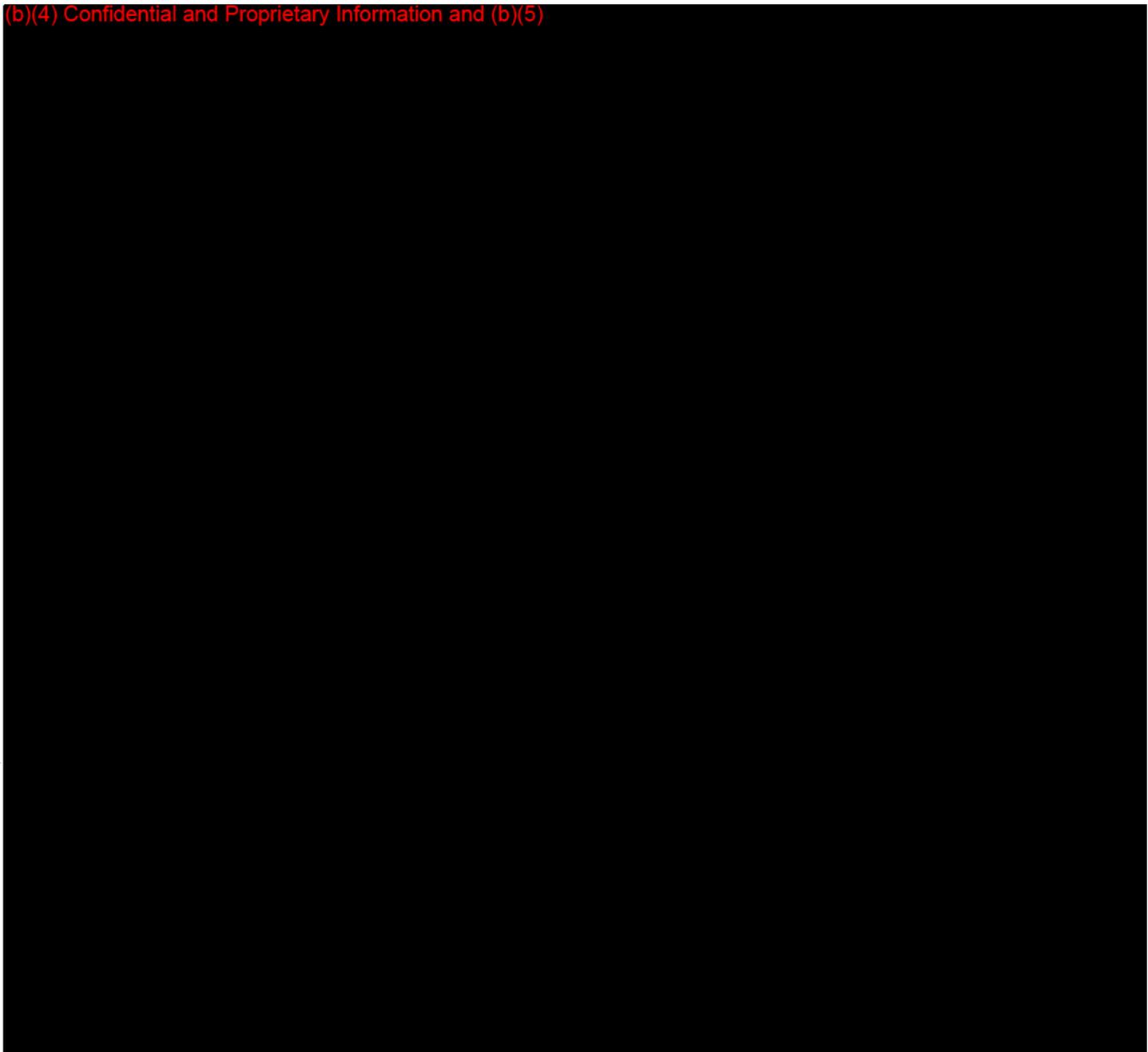
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(b)(4) Confidential and Proprietary Information and (b)(5)



(b)(4) Confidential and Proprietary Information and (b)(5)



XX. Recommendation – Substantially Equivalent (SE)

Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Graft Material (Accessory)
Regulatory Class: Class II
Product Code: NPL

Robert S. Betz

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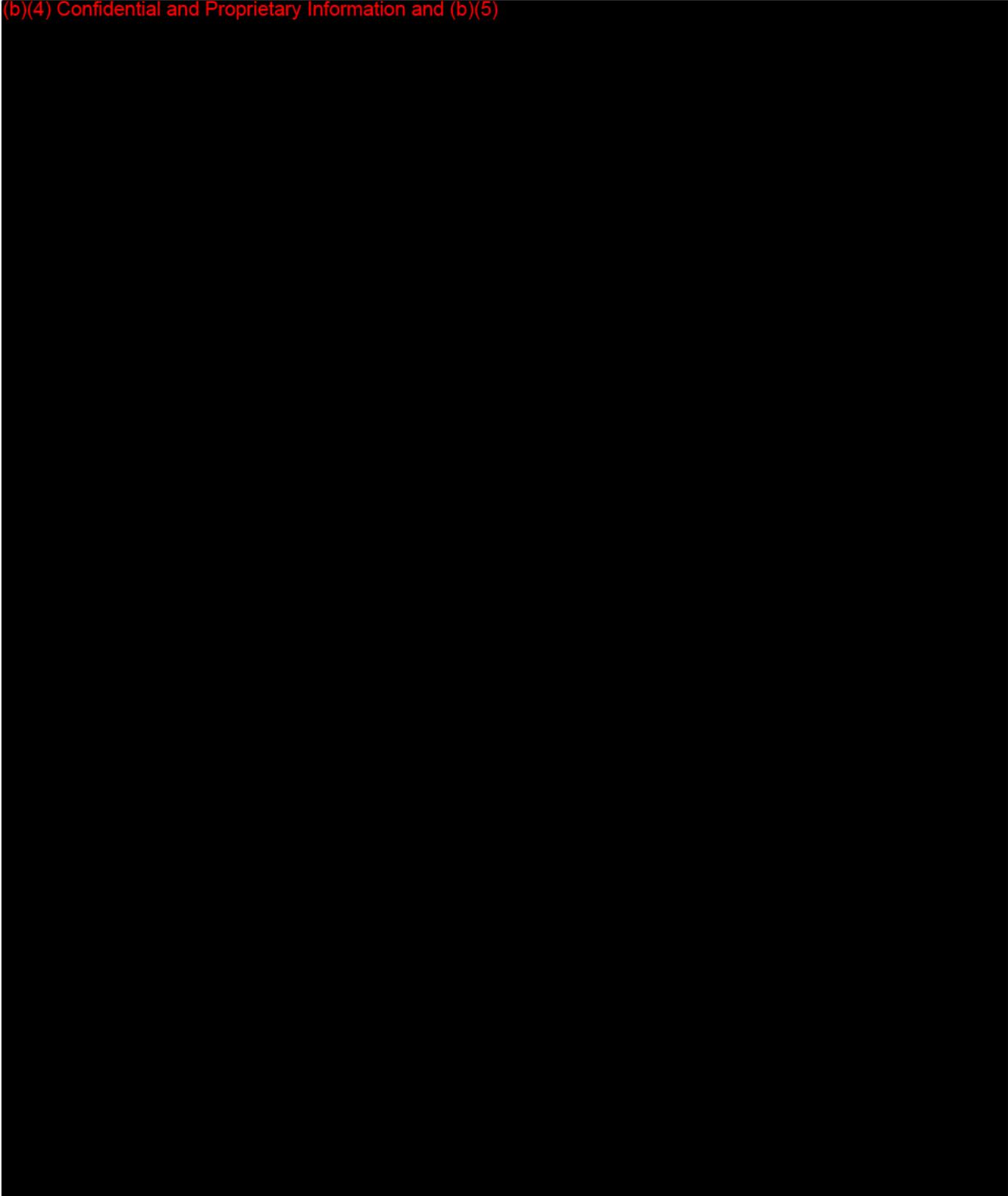
Robert S. Betz, DDS
DAGID/DEDB

December 28, 2012
Date

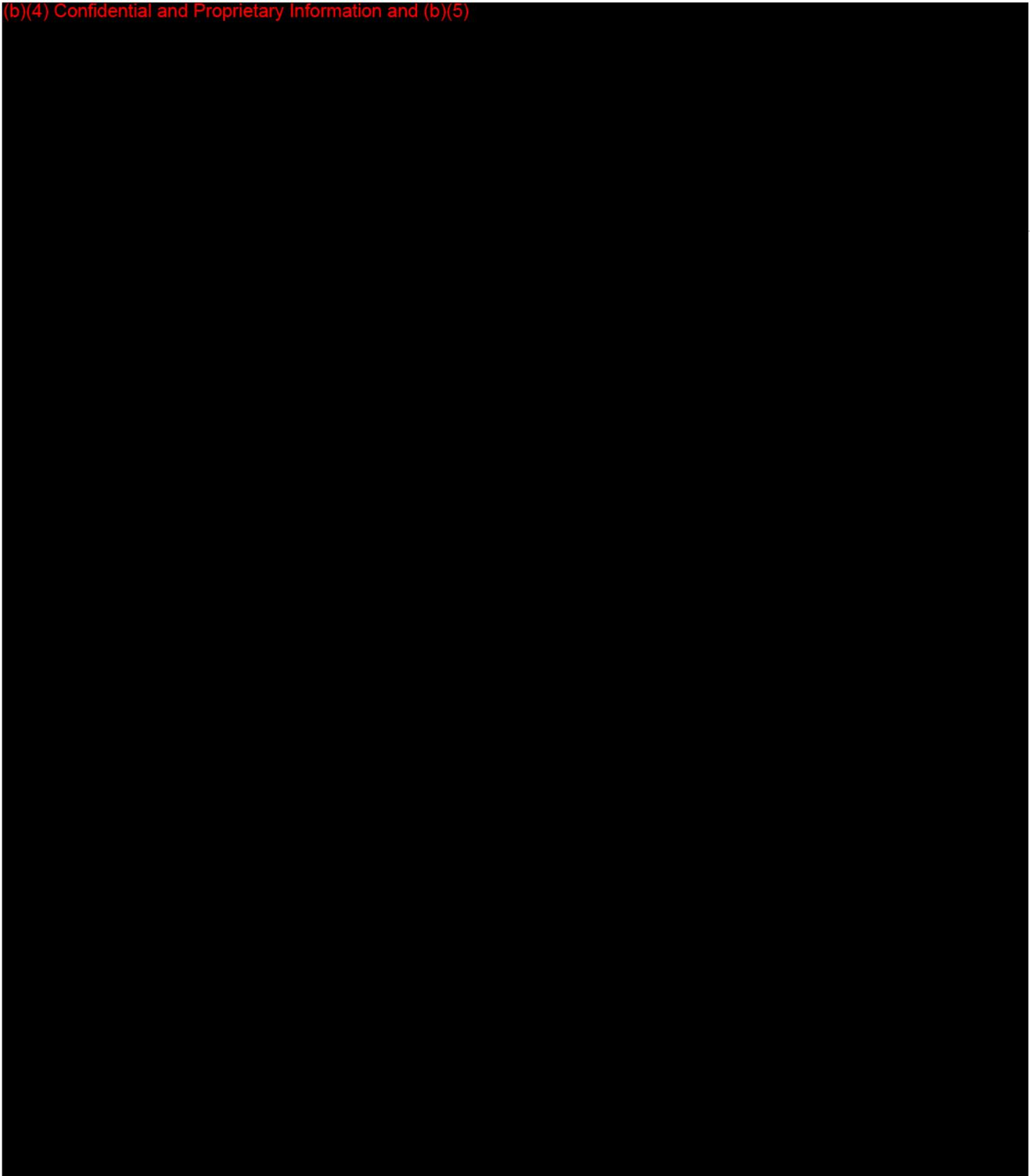
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[Text of E-Mail to Sponsor on June 4, 2010]

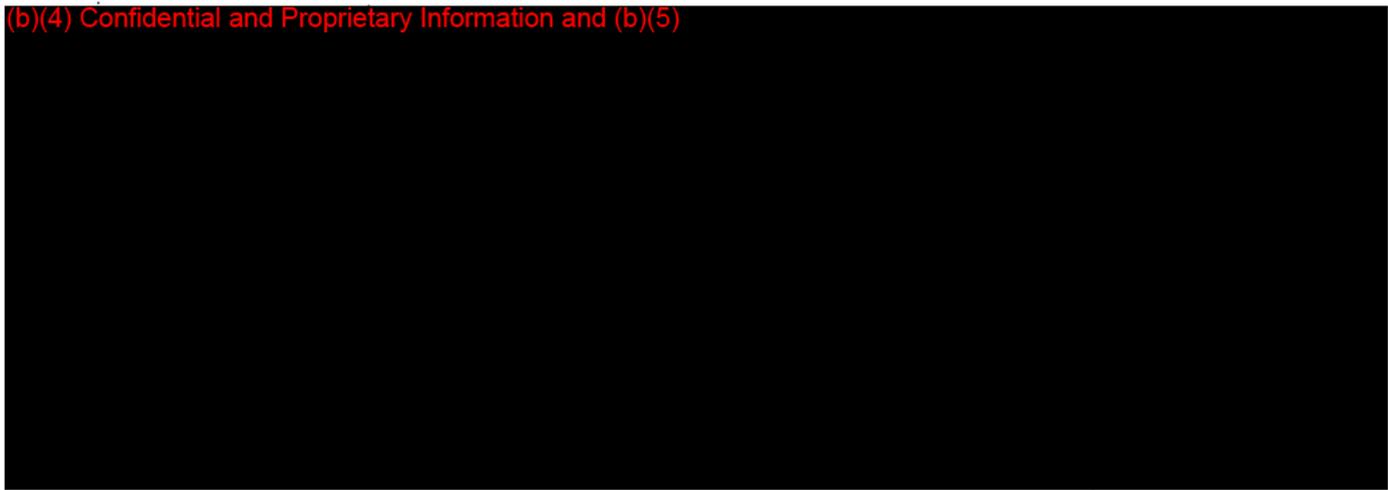
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(b)(4) Confidential and Proprietary Information and (b)(5)



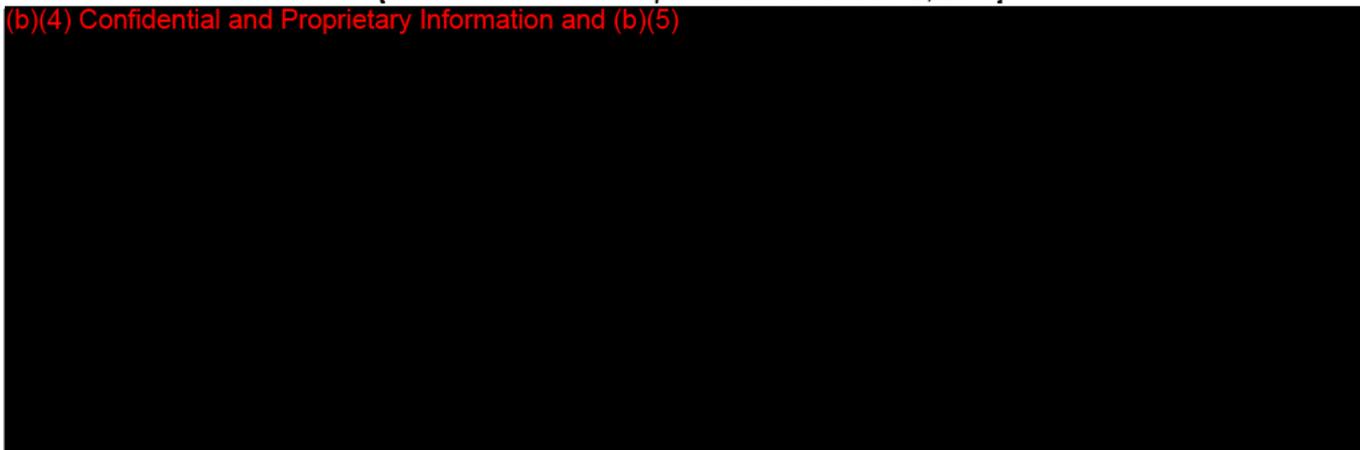
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Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

[Text of E-Mail Sent to Sponsor on November 12, 2010]

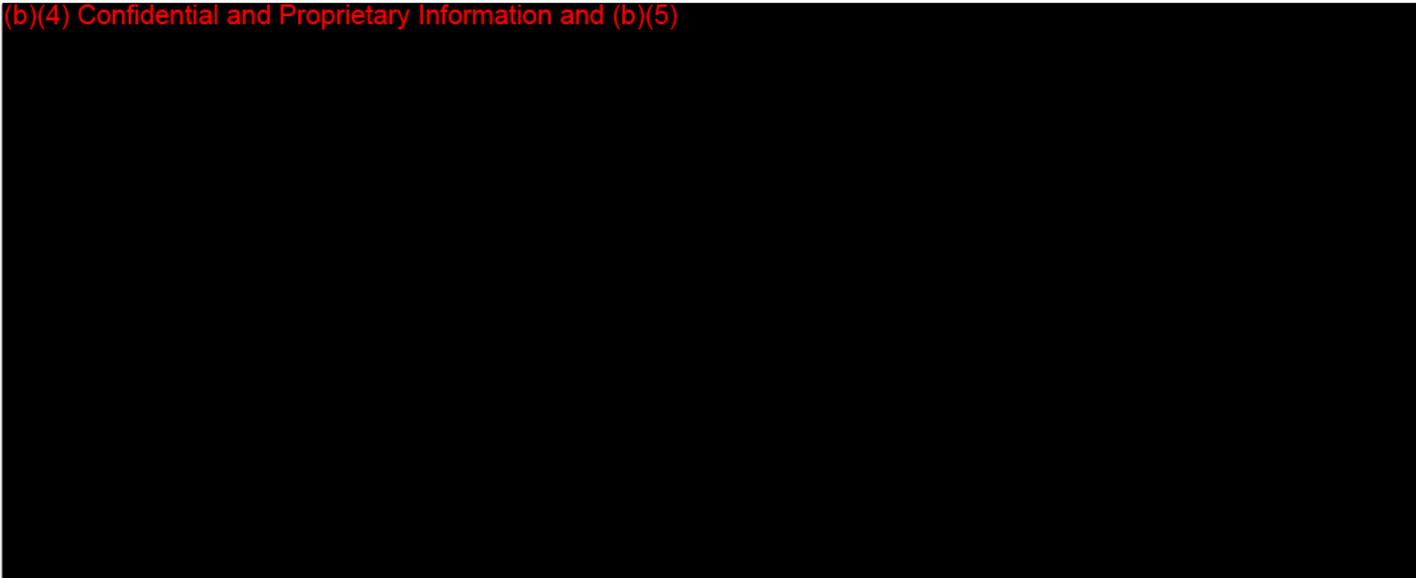
(b)(4) Confidential and Proprietary Information and (b)(5)



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FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov

[Text of E-mail Sent to Sponsor on December 1, 2010]

(b)(4) Confidential and Proprietary Information and (b)(5)



Thank you for your prompt response.

Robert S. Betz, DDS, Captain (Ret.) USPHS
Dental Devices Branch
FDA/CDRH/ODE/DAGID
10903 New Hampshire Avenue
Silver Spring, MD. 20993
301-796-6277
robert.betz@fda.hhs.gov



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

December 14, 2012

COLLAMATRIX, INC
QUALITY ASSURANCE
26F, NO. 105, SECTION 2 DUNHUA
SOUTH ROAD, DA-AN DISTRICT
TAIPEI
CHINA (TAIWAN) 106
ATTN: DENNIS J. N. SEAH

510k Number: K100695

Product: COLLADENTAL BARRIER

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 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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 in 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.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff

FAX HEADER 1:
FAX HEADER 2:

TRANSMITTED/STORED : FILE MODE	DEC. 14. 2012 4:05PM OPTION	ADDRESS	RESULT	PAGE
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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 Document Control Center WC66-G609
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December 14, 2012

COLLAMATRIX, INC
 QUALITY ASSURANCE
 26F, NO. 105, SECTION 2 DUNHUA
 SOUTH ROAD, DA-AN DISTRICT
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 ATTN: DENNIS J. N. SEAH

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Sincerely,

510(k) Staff

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

K100695/S1

FDA/CDRH/DCC

DEC 14 2012

RECEIVED

January 05, 2011

Re: Information for CollaDental Barrier (K100695)

~~FDA CDRH DMC~~

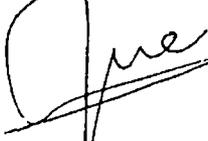
~~JAN 07 2011~~

Dear Dr. Betz,

Please find enclosed revised Indications for use statement and revised 510k summary required for the application of CollaDental Barrier.

Thank you.

Sincerely yours,


Dennis Seah

K-43

Statement of indications for use

510(K) Number (if known): K100695

Device Name: CollaDental Barrier

Indications for Use:

CollaDental barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

COLLAMATRIX Co. Ltd.

510(k) summary Summary information

1. **Date Prepared**

March 3, 2010

2. **Submitter name and address**

Collamatrix Inc.
1F, No.50-1, Keyan Road, Jhunan Science Park
Miaoli County, 350, Taiwan

3. **Contact person**

Name: Dennis J. N. Seah
Tel: + 886 2 7711 3299
Fax: + 886 2 7711 3599

4. **Device names**

Propriety name: CollaDental Barrier
Common name: Collagen dental matrix
Classification name: Dressing, Wound

5. **Device classification**

Regulatory class: Barrier, Animal Source, Intraoral, Class II
Product code: NPL

6. **Device description**

CollaDental Barrier is a nonfriable, resorbable membrane made of purified type I collagen derived from pig skin using standardized controlled manufacturing process. The collagen is obtained from veterinary certified pigs and purified to avoid its antigenicity. The manufacturing process complies with the standards for virus inactivation. The CollaDental

1F, No. 50-1, Keyan Road, Jhunan Science Park, Miaoli County, 350, Taiwan
Tel: +886 2 7711 3299 Fax: +886 2 7711 3599

Page 1 of 3

COLLAMATRIX Co. Ltd.

Barrier has been tested for purity using standard purity testing procedures, sterilized by gamma irradiation and for single use only. It is flexible and conforms to the contours of the defect site. When moistened with water, saline, serum or blood, the device is flexible and conforms to the contours of the defect site. CollaDental Barrier has not been tested on persons less than 18 years of age.

7. Intended use

CollaDental Barrier is intended for use in oral surgical procedures including use in augmentation around implants placed in immediate extraction sockets, delayed extraction sockets; filling of bone defects after roots resection, cystectomy, removal of retained teeth; guided bone regeneration in dental implant associated bony dehiscence defects and guided tissue regeneration procedures in bony dehiscence defects around teeth.

8. Statement of Substantial equivalence

CollaDental Barrier is a device similar to predicate devices that are previously approved by the agency. CollaDental Barrier is substantially equivalent in indications and design principles to predicate devices, BioMend Extend absorbable collagen membrane (K992216) and BIO-GIDE® (K042197), each of which has been determined by FDA to be substantially equivalent to preamendment devices. CollaDental Barrier has the following similarities to the predicate devices in terms of indication for use, technological characteristics, material use and the process for sterilization. In summary, CollaDental Barrier is substantially equivalent to the predicate devices under the 510(k) regulations.

9. Biocompatibility

CollaDental Barrier has been demonstrated to be safe. To support the biocompatibility of this product, safety tests were conducted in accordance with ISO 10993 Part 1 Biological Evaluation of Medical Devices.

All test results from tests conducted on CollaDental Barrier are taken together as a whole, CollaDental Barrier have been demonstrated to be a safe device in accordance with ISO 10993-1.

COLLAMATRIX Co. Ltd.

10. Conclusion

CollaDental Barrier is essentially equivalent in indication for use, technological characteristics and material to the commercially available predicate device, and therefore meets the requirements as defined in 21 CFR § 807.