Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

510k Summary

1 SUBMITTER/510K HOLDER

Address: Kerecis ltd.
Eyrargata 2
400 Isafjordur
Iceland

Contact Person: Gudmundur Fertram Sigurjonsson
Executive Chairman

Telephone: 011 354 562 2601

Date Prepared: October 1, 2013

OCT 2 3 2013

2 DEVICE NAME

Proprietary Name: MariGen Wound Dressing

Common/Usual Name: MariGen Wound

Classification Name: Collagen Wound Dressing

510k Number: K132343

3 PREDICATE DEVICES

- Mesynthes Endoform™ Dermal Template (K092096)
- ACell MatriStem™ (K092926)
- Integra™ Wound Matrix (Integra Life Sciences) (K021792)
- LifeCell Corporation's LTM Wound Dressing (K082103)
- TEI Biosciences Inc. PriMatrix (K083440)
- HemCon Chitoflex Surgical Dressing (K071519)
- Cook Biotech, Oasis (K061711)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

4 DEVICE DESCRIPTION

The Kerecis MariGen Wound Dressing is processed fish dermal matrix composed of fish collagen and is supplied as a sterile intact, or meshed sheet ranging in size from 3 x 3.5 cm (10.5 cm2), 3 x 7 cm (21 cm2) and 7 x 10 cm (70 cm2).

The device is intended for a single patient, one time use only.

5 INTENDED USE

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence).
- Draining wounds

6 TECHNOLOGICAL CHARACTERISTICS AND SUBSTANTIAL EQUIVALENCE

The Kerecis MariGen Wound Dressing is substantially equivalent to the predicate devices with respect to material composition, device characteristics and intended use.

7 MECHANICAL TESTS AND BIOCOMPATIBILITY TESTS

The Kerecis MariGen Wound Dressing has been subjected to extensive testing to assess the biocompatibility and the performance of the device. The Kerecis MariGen Wound Dressing was shown to be usable and biocompatible.

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

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All biocompatibility tests that are required according to ISO 10993-12 "Biological Evaluation of Medical Devices" where performed with favorable results. Tests were done in the following categories; cytotoxicity, sensitization, irritation, subchronic toxicity and genotoxicity.

8 ANIMAL TESTING

Several animal studies have been performed on the device.

The results of the tests support the safety of the device.

9 CLINICAL TESTING

MariGen Wound is CE marked and has been in commercial use since 2011

The product has been studied on a limited number of subjects and this use supports the safety of the device. No serious adverse events have been noted in limited clinical use.

10 CONCLUSIONS

The proposed and predicate devices have the same general intended use and principles of operation. The overall design of the proposed and predicate devices is similar in that they are all comprised of collagen. The differences between these devices are limited to the animal source of collagen. This difference is minor and does not raise new issues of safety or effectiveness.

The MariGen Wound Dressing meets all defined acceptance criteria for the non-clinical testing required by the risk analysis. The design validation activities confirmed that the device as designed functions to meet specified user requirements. The information provided confirms that the MariGen Wound Dressing device is safe and effective for its intended use and performs as intended.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

Kerecis LTD.
Gudmundur F. Sigurjonsson
Executive Chairman
Eyrargata 2
400 Isafjordur
Iceland

October 23, 2013

Re: K132343
Trade/Device Name: MeriGen Wound Dressing
Regulatory Class: Unclassified
Product Code: KGN
Dated: July 19, 2013
Received: August 7, 2013

Dear Sigurjonsson:

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.

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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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 contact 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. 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,

Mark N. Melkerson -S

Mark N. Melkerson
Acting Director
Division of Surgical Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K132343

Device Name
MariGen Wound Dressing

Indications for Use *(Describe)*

MariGen Wound Dressing is indicated for the management of wounds including:

- Partial- and full-thickness wounds
- Pressure ulcers
- venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), and
- Draining wounds.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

David Krause -S

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

Kerecis LTD.
Gudmundur F. Sigurjonsson
Executive Chairman
Eyrargata 2
400 Isafjordur
Iceland

October 23, 2013

Re: K132343
Trade/Device Name: MeriGen Wound Dressing
Regulatory Class: Unclassified
Product Code: KGN
Dated: July 19, 2013
Received: August 7, 2013

Dear Sigurjonsson:

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.

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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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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 contact 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. 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.

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Sincerely yours,

Mark N. Melkerson -S

Mark N. Melkerson
Acting Director
Division of Surgical Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Concurrence & Template History Page
[THIS PAGE IS INCLUDED IN IMAGE COPY ONLY]

Full Submission Number:

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	Stephen Curtis
Branch Chief Sign-Off	David Krause
Division Sign-Off	Mark N. Melkerson -S 2013.10.23 08:20:45 -04'00'

f/t:SKC:dlm:10/22/13

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 1st 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".
4/2/2013	M. McCabe Janicki	Edited sentence that starts "If you desire specific advice for your device on our labeling regulation (21 CFR Part 801)…" Replaced broken Compliance link with general link to DSMICA.
4/12/2013	Margaret McCabe Janicki	Fixed a typo: Paragraph 1, final sentence, "We remind you, however; that device labeling must be truthful…" Replaced incorrect semicolon with a comma.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K132343

Device Name
MariGen Wound Dressing

Indications for Use *(Describe)*

MariGen Wound Dressing is indicated for the management of wounds including:

- Partial- and full-thickness wounds
- Pressure ulcers
- venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), and
- Draining wounds.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

David Krause -S

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

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KERECIS

K132343

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

FDA CDRH DMC
AUG 07 2013
Received

Isafjordur, Iceland, August 5, 2013

Subject: eCopy replacement K132343

Dear Sir / Madam:

We are in receipt of your hold letter dated August 5, 2013 regarding the eCopy of the dossier for K132343 (Pending).

Please find enclosed a new CD with the requested file reformatted.

Please contact me on gfsigurjonsson@kerecis.com should there be any further complications.

Sincerely,

Gudmundur Fertram Sigurjonsson
Executive Chairman
Kerecis Limited

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

K132343

KERECIS

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
United States of America

FDA CDRH DMC
AUG 05 2013
Received

Isafjordur, Iceland, August 1, 2013

Subject: eCopy replacement for K132343 (Kerecis MariGen Wound Dressings)

Dear Sir / Madam:

Enclosed is a replacement eCopy for our traditional 510k Premarket Notification for the Kerecis MariGen Wound Dressing. For further information please see Chapter 2 – "CDRH Premarket Review and Submission Cover Sheet and 510k" in the enclosed paper dossier (three folders). An electronic version is enclosed on the CD. Also attached is a second CD with a backup copy should the first CD fail.

The eCopy is an exact duplicate of the paper copy;

Sincerely,

Gudmundur Fertram Sigurjonsson
Executive Chairman
Kerecis Limited

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

K132343

FDA CDRH DMC
JUL 30 2013
Received

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
United States of America

Isafjordur, Iceland, July 19, 2013

Subject: TRADITIONAL 510k Premarket Notification for the Kerecis MariGen Wound Dressings

Dear Sir / Madam:

Enclosed is our traditional 510k Premarket Notification for the Kerecis MariGen Wound Dressing. This is (b)(4)

This submission relates to a collagen based wound dressing. Collagen wound dressings are unclassified, but have been assigned the product code KGN. This device was classified by the General and Plastic Surgery Panel.

The MariGen Wound Dressing is manufactured from (b)(4)
The dressing material is derived (b)(4)

Kerecis ehf • Box 151, 400 Isafjordur, Iceland • Skolavordustigur 16, 101 Reykjavík, Iceland
Phone +354 5622601 • www.kerecis.is

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

(b)(4)

The (revised) indications for use are as follows:

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence).
- Draining wounds

The MariGen Wound dressing is supplied sterile in a peel-open packages and is intended for one-time use.

Administrative information for this premarket notification is summarized below.

Applicant / Sponsor
Kerecis limited
Eyrargata 2
400 Isafjordur
Iceland

Contact Person: G. Fertram Sigurjonsson, Executive Chairman Telephone: +354 562 2601

Manufacturer
Kerecis limited
Eyrargata 2
400 Isafjordur
Iceland

Device Classification:

Classification Name:	Collagen Wound Dressings
Classification Regulation:	Unclassified
Product code:	KGN

The information provided in the table below is provided in accordance with table 3 of "Guidance for Industry and FDA Staff – Format for Traditional and Abbreviated 510k's"

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

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KERECIS

Question	Yes	No
Is the device intended for prescription use (21 CFR 801 Subpart D)?	X	
Is the device intended for over-the-counter use (21 CFR 807 Subpart C)?		X
Does the device contain components derived from a tissue or other biological source?	X	
Is the device provided sterile?	X	
Is the device intended for single use?	X	
Is the device a reprocessed single use device?		X
- If yes, does this device type require reprocessed validation data?		
Does the device contain a drug?		X
Does the device contain a biologic?		X
Does the device use software?		X
Does the submission contain clinical information?	X	
Is the device implanted?		X

In accordance with the Safe Medical Devices Act of 1990 and 21 CFR 807.92, a 510k Summary is included in SECTION 5 of this premarket notification. In addition, a 510k Screening Checklist (See SECTION 2), Indications for Use Statement (See SECTION 4), and Truthful and Accurate Statement (See SECTION 6) are included.

As required by the new FDA Safety and Innovation Act (FDASIA) and the publication of the revised Title 21 CFR, Part 807 on August 2, 2012, we have paid the Medical Device Establishment Registration and Listing Fee, USD (b)(4) through pay.gov as follows:

Application Name: FDA User Fees
Pay.gov Tracking ID: (b)(4)
Agency Tracking ID: (b)(4)
Transaction Type: Sale
Transaction Date: Jul 9, 2013 1:48:50 PM

A copy of the Medical Device User Fee Cover Sheet is provided in SECTION 1 of this premarket notification.

This premarket notification includes trade secret and commercial information that is privileged or confidential and, in accordance with 21 CFR 20.61, is not available for public disclosure.

If you have any questions regarding this notification or require additional information, please contact G. Fertram Sigurjonsson on email gfsigurjonsson@kerecis.com or direct phone 011 354 8494960

Sincerely,

Gudmundur Fertram Sigurjonsson
Executive Chairman
Kerecis Limited

Kerecis ehf • Box 151, 400 Isafjordur, Iceland • Skolavordustigur 16, 101 Reykjavík, Iceland
Phone +354 5622601 • www.kerecis.is

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

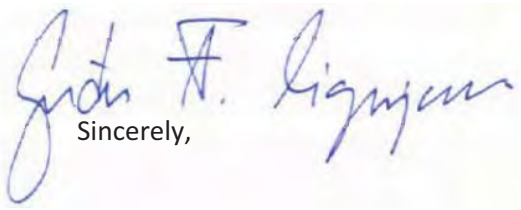
Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
United States of America

Isafjordur, Iceland, July 19, 2013

Subject: e-copy statement

This eCopy is an exact duplicate of the paper copy.



Sincerely,

Gudmundur Fertram Sigurjonsson
Executive Chairman
Kerecis Limited

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Traditional 510k Premarket Notification

for

Kerecis ltd

MariGen Wound Dressing

July 19, 2013-07-23

Kerecis ltd

Isafjordur, Iceland

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Traditional 510k Premarket Notification
for
Kerecis ltd
MariGen Wound Dressing

Section	Contents
	Table of Contents
1	MDUFMA Cover Sheet
2	CDRH Premarket Review and Submission Cover Sheet and 510(k)
3	Cover letter
4	Indications for Use Statement
5	510(k) Summary
6	Truthful and Accurate Statement
7	Class III Summary and Certification Not Applicable
8	Financial Certification or Disclosure Statement
9	Declarations of Conformity and Summary Reports Not applicable
10	Executive Summary
11	Device Description
12	Substantial Equivalence Discussion
13	Proposed Labeling
14	Sterilization and Shelf Life
15	Biocompatibility
16	Software Information Not applicable
17	Electromagnetic Compatibility Electrical Safety Not Applicable
18	Performance Testing Bench
19	Performance Testing Animal
20	Performance Testing Clinical
21	Certification of Compliance with Requirements of ClinicalTrials.gov

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Traditional 510k Premarket Notification
for
Kerecis ltd
MariGen Wound Dressing

Table of Contents

Item			Page
Section 1	MDUFMA Cover Sheet		1-1
	1-1 MDUFA Establishment Registration Cover Sheet		1-1
	1-2 MDUFA 510k Cover Sheet		1-1
Section 2	CDRH Premarket Review and Submission Cover Sheet and 510(k)		2-1
Section 3	Cover letter		3-1
Section 4	Indications for Use Statement		4-1
Section 5	510(k) Summary		5-1
	5-1	510k Holder	5-1
	5-2	Device Name	5-1
	5-3	Predicate Devices	5-1
	5-4	Device Description	5-2
	5-5	Intended Use	5-2
	5-6	Technological Characteristics	5-2
	5-7	Mechanical test and biocompatibility tests	5-2
	5-8	Animal Testing	5-3
	5-9	Clinical Testing	5-3
	5-10	Conclusion	5-4
Section 6	Truthful and Accurate Statement		6-1
Section 7	Class III Summary and Certification Not Applicable		7-1
Section 8	Financial Certification or Disclosure Statement		8-1
Section 9	Declarations of Conformity and Summary Reports Not applicable		9-1
Section 10	Executive Summary		10-1
	10-1	Executive Summary	10-1
	10-2	Comparison to predicates	10-3
Section 11	Device Description		11-1
	11-1	Intended use	11-1

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

	11-2	Performance standards	11-1
	11-3	Principles of operation	11-1
	11-4	Evidence of conformity with special controls	11-3
	11-5	Device description	11-4
	11-6	Risk management	11-22
	11-7	Manufacturing	11-23
	11-8	(b)(4)	11-30
	11-9	(b)(4)	11-30
	11-10	Packaging design and material	11-36
	11-11	Design release	11-36
	11-12	Appendixes	11-36
	11-13	References	11-37
Section 12	Substantial Equivalence Discussion		12-1
	12-1	Substantial equivalence	12-1
	12-2	Intended use / Indications for use	12-1
	12-3	List of proposed predicated	12-2
	12-4	Design	12-3
	12-5	Operational characteristics	12-4
	12-6	Technological characteristics	12-4
	12-7	Substantial equivalence pathway	12-5
	12-8	Conclusion	12-6
	12-9	Selected comparative tests	12-7
Section 13	Proposed Labeling		13-1
Section 14	Sterilization and Shelf Life		14-1
	14-1	Sterilization Information	14-1
	14-2	Packaging validation	14-1
	14-3	Product shelf life	14-3
	14-4	Appendixes	14-3
Section 15	Biocompatibility		15-1
	15-1	Introduction	15-1
	15-2	Biocompatibility-test overview	15-2
	15-2-1	(b)(4) Cytotoxicity Test(b)(4))	15-3
	15-2-2	Cytotoxicity (b)(4)	15-3

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4) Testing 15-3
15-4
15-4
15-4
15-5
15-6
15-6
15-6
15-7
15-7
15-9
15-9
15-9

Section 16 Software Information Not applicable 16-1

Section 17 Electromagnetic Compatibility Electrical Safety Not Applicable 17-1

Section 18 Performance Testing Bench 18-1

18-1 Introduction 18-1

(b)(4) Testing 18-3
18-4
18-5
18-6
18-6

18-7 Appendixes 18-6

Section 19 Performance Testing Animal 19-1

19-1 Introduction 19-1

19-2 Summary (b)(4) studies 19-2

19-3 (b)(4) Testing 19-2

19-4 (b)(4) Testing 19-3

(b)(4) Testing

Section 20 Performance Testing Clinical 20-1

20-1 Introduction 20-1

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4) Testing 20-2
20-2
20-3
20-4
Section 21 Certification of Compliance with Requirements of ClinicalTrials.gov 21-2

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 1: MDUFMA Cover Sheet

1 MDUFMA Cover Sheet

1.1 MDUFA Establishment Registration User Fee 2013

Enclosed in Appendix 1.1 please find the cover sheet for the MDUFA Establishment Registration User Fee for the year 2013. A receipt is enclosed in Appendix 1.2.

Erroneously we have two Organization Numbers in the FDA system. The Organization Number used for this submission was (b)(4)

1.2 MDUFA Cover Sheets

Enclosed in Appendix 1.3 please find the cover sheet for the 510k cover sheet. A receipt is enclosed in Appendix 1.4.

Erroneously we have two Organization Numbers in the FDA system. The Organization Number used for this submission was (b)(4)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 1.1 - Device Facility User Fee Cover Sheet

Form Approved OMB No 0910 0625 Expiration Date June 30, 2015 See Instructions for OMB Statement

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **DEVICE FACILITY USER FEE**	PAYMENT IDENTIFICATION NUMBER: (b)(4) Include the Payment Identification Number (PIN) with payment.

The following actions must be taken to properly submit your payment:

1. To submit payment, please select one of the following options:

A. To pay electronically using ACH (electronic check from a US bank) or a credit card, please select the "Pay Now" option.

B. To pay using a check drawn on a US bank in US dollars, please follow these instructions:

- Make check payable to the Food and Drug Administration
- Write the payment identification number (PIN) on the check
- Mail check and a printed copy of the order to:

Food and Drug Administration
P.O. Box 979108
St. Louis, MO 63197-9000

OR

- For checks sent by courier, mail the check and printed copy of the order to:

Attn: ATTN: Government Lockbox 979108
1005 Convention Plaza
St. Louis, MO 63101

Note: This U.S. Bank address is for courier delivery only; do not send mail to this address.

C. To pay by wire transfer, please read the following:

You are responsible to pay any administrative costs associated with the processing of a wire transfer. Contact your bank or financial institution regarding the additional fees.

US Department of Treasury
TREAS NYC
33 Liberty Street
New York, NY 10045

FDA Deposit Account Number: 75060099
Beneficiary: Food and Drug Administration, 1350 Piccard Drive, Suite 200A, Rockville, MD 20850
US Department of Treasury routing/transit number: 021030004
SWIFT Number: FRNYUS33

You must include the user fee payment identification number (PIN), and ensure that the fee that your bank will charge for the wire transfer is added to your fee payment.

2. Company Name and Address	3. Contact Name
KERECIS EHF Eyrargata 2 Isafjordur 400 IS 2.1 Employer Identification Number (EIN)	Fertram Sigurjonsson 3.1 E-mail Address gfsigurjonsson@kerecis.com 3.2 Telephone Number 5622601 3.3 Fax Number

4. PIN-PCN (*Payment Identification Number-Payment Confirmation Number*):

(b)(4) Testing

5. Amount Due:

(b)(4) 09-Jul-2013

Close Print Order

Form FDA 3601 (01/2007)

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 1.2 - Receipt for payment of Device Facility User Fee

Pay.gov Payment Confirmation: FDA User Fees
paygovadmin to: gfsigurjonsson@kerecis.com 09.07.2013 17:49

From: paygovadmin@mail.doc.twai.gov
To: "gfsigurjonsson@kerecis.com" <gfsigurjonsson@kerecis.com>

Your payment has been submitted to Pay.gov and the details are below. If you have any questions or you wish to cancel this payment, please contact FDA User Fees at (301) 796-7200.

Application Name: FDA User Fees
Pay.gov Tracking ID: (b)(4)
Agency Tracking ID: (b)(4)
Transaction Type: Sale
Transaction Date: Jul 9, 2013 1:48:50 PM

Account Holder Name: Gudmundur F Sigurjonsson
Transaction Amount: (b)(4)
Billing Address: Bergstadastraeti 62
City: Reykjavik
Zip/Postal Code: 101
Country: ICE
Card Type: (b)(4)
Card Number: (b)(4)

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 1.3 - 510k User Fee Cover Sheet (small business)

Form Approved: OMB No. 0910-0511 Expiration Date: April 30, 2016 See Instructions for OMB Statement

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **MEDICAL DEVICE USER FEE COVER SHEET**	PAYMENT IDENTIFICATION NUMBER: (b)(4) 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/coversheet.html	
1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code) KERECIS LIMITED EYRARGATA 2 400 ISAFIJORDUR ICELAND IS 1.1 EMPLOYER IDENTIFICATION NUMBER (EIN) (b)(4)	2. CONTACT NAME Gudmundur Sigurjonsson 2.1 E-MAIL ADDRESS gfsigurjonsson@kerecis.com 2.2 TELEPHONE NUMBER (include Area code) 354-5622601 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/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345263.htm

Select an application type:	3.1 Select a center
[X] Premarket notification(510(k)); except for third party	[X] CDRH
[ ] 513(g) Request for Information	[ ] CBER
[ ] Biologics License Application (BLA)	3.2 Select one of the types below
[ ] Premarket Approval Application (PMA)	[X] Original Application
[ ] Modular PMA	Supplement Types:
[ ] Product Development Protocol (PDP)	[ ] Efficacy (BLA)
[ ] Premarket Report (PMR)	[ ] Panel Track (PMA, PMR, PDP)
[ ] 30-Day Notice	[ ] 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)

[X] 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 (b)(4)

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?

[X] 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/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053165.htm 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 PREMARKET 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 [X] NO

PAPERWORK REDUCTION ACT STATEMENT

Public reporting burden for this collection of information is estimated to average 18 minutes 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 the address below.

Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, 1350 Piccard Drive, 4th Floor Rockville, MD 20850

[Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]

8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

(b)(4) 26-Jul-2013

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 1.4 - Receipt for payment of 510k fee (small business)

Pay.gov Payment Confirmation : FDA User Fees
paygovadmin to: gfsigurjonsson@kerecis.com 26.07.2013 21:24

From: paygovadmin@mail.doc.twai.gov
To: "gfsigurjonsson@kerecis.com" <gfsigurjonsson@kerecis.com>

Your payment has been submitted to Pay.gov and the details are below. If you have any questions or you wish to cancel this payment, please contact FDA User Fees at (301) 796-7200.

Application Name: FDA User Fees
Pay.gov Tracking ID: (b)(4)
Agency Tracking ID: (b)(4)
Transaction Type: Sale
Transaction Date: Jul 26, 2013 5:24:19 PM

Account Holder Name: Gudmundur F Sigurjonsson
Transaction Amount: (b)(4)
Billing Address: Eyrargata 2
City: Isafjordur
Zip/Postal Code: 400
Country: ICE
Card Type: (b)(4)
Card Number: (b)(4)

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 2: Submission Cover Sheet

2 Submission cover sheet

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
10/07/2013	Agency Tracking ID (b)(4)	Not yet assigned

SECTION A — TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Request for Feedback
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	☒ Original Submission	☐ Pre-Submission
☐ Premarket Report	☐ Special	☐ Notice of Completion	☐ Traditional	☐ Informational Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Submision Issue Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Day 100 Meeting
☐ Report	☐ 30-day Notice		☐ Additional Information	☐ Agreement Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Determination Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Study Risk Determination
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify)*:
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other *(describe submission)*:
☐ Supplement	☐ Supplement			
	☐ Report			
	☐ Report Amendment			

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	Establishment Registration Number *(if known)*		
Kerecis ltd			
Division Name *(if applicable)*	**Phone Number *(including area code)***		
	+354 562 2601		
Street Address	**FAX Number *(including area code)***		
Eyrargata 2	+354 4564117		
City	**State / Province**	**ZIP/Postal Code**	**Country**
Isafjordur		400	Iceland
Contact Name			
Gudmundur F.Sigurjonsson			
Contact Title	**Contact E-mail Address**		
Executive Chairman	gfsigurjonsson@kerecis.com		

SECTION C — APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name *(if applicable)*	**Phone Number *(including area code)***		
Street Address	**FAX Number *(including area code)***		
City	**State / Province**	**ZIP Code**	**Country**
Contact Name			
Contact Title	**Contact E-mail Address**		

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

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SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ New Device
- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Process change:
  - ☐ Manufacturing ☐ Packaging
  - ☐ Sterilization
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Response to FDA correspondence:

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify)*:

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Response to FDA Letter Concerning:
  - ☐ Conditional Approval
  - ☐ Deemed Approved
  - ☐ Deficient Final Report
  - ☐ Deficient Progress Report
  - ☐ Deficient Investigator Report
  - ☐ Disapproval
  - ☐ Request Extension of Time to Respond to FDA
  - ☐ Request Meeting
  - ☐ Request Hearing

- ☐ Other Reason *(specify)*:

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☒ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☒ Other Reason *(specify)*:

(b)(4) [redacted]

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	KGN	2	FRO	3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☒ 510 (k) summary attached
☐ 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	K092926	1	MatriStem Wound Sheet	1	ACell, Inc.
2	K021792	2	IntegraTM Wound Matrix	2	Integra Life Sciences
3	K082103	3	LTM Wound Dressing	3	LifeCell Corporation
4	K083440	4	PriMatrix	4	TEI Biosciences Inc.
5	K071519	5	Chitoflex Surgical Dressing	5	HemCon
6	K061711	6	Oasis Wound Matrix	6	Cook Biotech

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Collagen Wound Dressing

	Trade or Proprietary or Model Name for This Device		Model Number
1	Collagen Wound Dressing	1	
2		2	
3		3	
4		4	
5		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	C.F.R. Section *(if applicable)*	Device Class
KGN		☐ Class I ☐ Class II ☐ Class III ☐ Unclassified

Classification Panel

General and Plastic Surgery

Indications *(from labeling)*

ManGen Wound is indicated for the management of wounds including: Partial and full-thickness wounds, Pressure ulcers, Venous ulcers, Chronic vascular ulcers, Diabetic ulcers, Trauma wounds (abrasions, lacerations, second-degree burns, skin tears), Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), Draining wounds

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Note: Submission of the information entered in Section H does not affect the need to submit device establishment registration.	FDA Document Number *(if known)*

SECTION H — MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☒ Manufacturer ☐ Contract Manufacturer ☐ Contract Sterilizer ☐ Repackager / Relabeler

Company / Institution Name	Establishment Registration Number
Kerecis ltd	
Division Name *(if applicable)*	**Phone Number** *(including area code)*
	+354 5622601
Street Address	**FAX Number** *(including area code)*
Eyrargata 2	+354 4564117

City	State / Province	ZIP Code	Country
Isafjordur		400	Iceland

Contact Name	Contact Title	Contact E-mail Address
Gudmundur F Sigurjonsson	Executive Chairman	gfsigurjonsson@kerecis.com

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Manufacturer ☒ Contract Sterilizer ☐ Repackager / Relabeler

(b)(4)

[redacted]

☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Manufacturer ☐ Contract Sterilizer ☐ 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	ZIP Code	Country

Contact Name	Contact Title	Contact E-mail Address

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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	ISO13485	ISO	Medical Devices - Quality management systems - requirements for regulatory purposes		1/1/2003
2	(b)(4)	ISO	(b)(4)		15/07/2006
3	(b)(4)	ISO	(b)(4)		01/09/2012
4	ISO 10993-1	ISO	Biological evaluation of medical devices - Part 1: Evaluation and testing		15/02/2010
5	ISO 14971	ISO	Medical devices - Application of Risk Management to Medical Devices		20/10/2012
6	ISO 22442-1	ISO	Medical Devices Utilizing Animal Tissues and Their Derivatives - Part 1 Application of Risk Management		15/03/2008
7	ISO 11607-1	ISO	Packaging for Terminally Sterilized Medical Devices Part 1, Requirements for materials, sterile barrier systems and packaging systems		15/10/2009

Please include any additional standards to be cited on a separate page.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

"DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF ADDRESS BELOW."

The burden time for this collection of information is estimated to average 0.5 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
1350 Piccard Drive, Room 400
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 number.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 3: Cover Letter

3 Cover letter

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
United States of America

Isafjordur, Iceland, July 19, 2013

Subject: TRADITIONAL 510k Premarket Notification for the Kerecis MariGen Wound Dressings

Dear Sir / Madam:

Enclosed is our traditional 510k Premarket Notification for the Kerecis MariGen Wound Dressing. This is (b)(4)

This submission relates to a collagen based wound dressing. Collagen wound dressings are unclassified, but have been assigned the product code KGN. This device was classified by the General and Plastic Surgery Panel.

The MariGen Wound Dressing is manufactured from (b)(4)
The dressing material is derived (b)(4)

Kerecis ehf • Box 151, 400 Isafjordur, Iceland • Skolavordustigur 16, 101 Reykjavík, Iceland
Phone +354 5622601 • www.kerecis.is

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

(b)(4)

The (revised) indications for use are as follows:

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence).
- Draining wounds

The MariGen Wound dressing is supplied sterile in a peel-open packages and is intended for one-time use.

Administrative information for this premarket notification is summarized below.

Applicant / Sponsor
Kerecis limited
Eyrargata 2
400 Isafjordur
Iceland

Contact Person: G. Fertram Sigurjonsson, Executive Chairman Telephone: +354 562 2601

Manufacturer
Kerecis limited
Eyrargata 2
400 Isafjordur
Iceland

Device Classification:

Classification Name:	Collagen Wound Dressings
Classification Regulation:	Unclassified
Product code:	KGN

The information provided in the table below is provided in accordance with table 3 of "Guidance for Industry and FDA Staff – Format for Traditional and Abbreviated 510k's"

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

Question	Yes	No
Is the device intended for prescription use (21 CFR 801 Subpart D)?	X	
Is the device intended for over-the-counter use (21 CFR 807 Subpart C)?		X
Does the device contain components derived from a tissue or other biological source?	X	
Is the device provided sterile?	X	
Is the device intended for single use?	X	
Is the device a reprocessed single use device?		X
- If yes, does this device type require reprocessed validation data?		
Does the device contain a drug?		X
Does the device contain a biologic?		X
Does the device use software?		X
Does the submission contain clinical information?	X	
Is the device implanted?		X

In accordance with the Safe Medical Devices Act of 1990 and 21 CFR 807.92, a 510k Summary is included in SECTION 5 of this premarket notification. In addition, a 510k Screening Checklist (See SECTION 2), Indications for Use Statement (See SECTION 4), and Truthful and Accurate Statement (See SECTION 6) are included.

As required by the new FDA Safety and Innovation Act (FDASIA) and the publication of the revised Title 21 CFR, Part 807 on August 2, 2012, we have paid the Medical Device Establishment Registration and Listing Fee, USD (b)(4) through pay.gov as follows:

Application Name: FDA User Fees
Pay.gov Tracking ID: (b)(4)
Agency Tracking ID: (b)
Transaction Type: Sale
Transaction Date: Jul 9, 2013 1:48:50 PM

A copy of the Medical Device User Fee Cover Sheet is provided in SECTION 1 of this premarket notification.

This premarket notification includes trade secret and commercial information that is privileged or confidential and, in accordance with 21 CFR 20.61, is not available for public disclosure.

If you have any questions regarding this notification or require additional information, please contact G. Fertram Sigurjonsson on email (b)(4) or direct phone (b)(4)

Sincerely,

Gudmundur Fertram Sigurjonsson
Executive Chairman
Kerecis Limited

Kerecis ehf • Box 151, 400 Isafjordur, Iceland • Skolavordustigur 16, 101 Reykjavík, Iceland
Phone +354 5622601 • www.kerecis.is

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 4: Indications for Use

4 Indications for use

510(k) Number (if known):

Device Name: MariGen Wound Dressing

Intended Use:

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence).
- Draining wounds

Prescription Use _X_ AND/OR Over-The-Counter Use___
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

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

(b)(4) Draft Document

(b)(4) Draft Document

(b)(4) Draft Document

(b)(4) Draft Document

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 6: Truthful and Accurate Statement

6 Premarket Notification Truthful and Accurate Statement for the Kerecis MariGen Wound Dressing

I certify that in my capacity as Executive Chairman of Kerecis ltd, I believe to the best of my knowledge, that all data and information submitted in this premarket notification for the Kerecis MariGen Wound Dressing are truthful and accurate and that no material fact has been omitted.

Signature

21 July 2013
Date

Gudmundur Fertram Sigurjonsson
Executive Chairman

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 7: Class III Summary and Certification

7 Class III Summary and Certification

This section is not applicable

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 8: Financial Certification or Disclosure Statement

8 Financial Certification and Disclosure Statement

8.1 Declaration

None of the investigators in any clinical studies submitted with this notification have any financial interest and arrangements as specified in 21 CFR, apart from Dr. Baldursson and Dr. Kjartansson, which both are part time employees of the sponsor (Kerecis ltd) and are owners of shares in the company (less than 5%).

8.2 Appendixes

Appendix	Description
8.1	No-financial interests
8.2	Financial interests Dr. Baldursson
8.3	Financial interests Dr. Kjartansson

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable check box.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators

(b)(6) [redacted]

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Gudmundur Fertram Sigurjonsson	Executive Chairman
FIRM/ORGANIZATION: Kerecis ltd	
SIGNATURE	DATE *(mm/dd/yyyy)*: 07/22/2013

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right.

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
PRAStaff@fda.hhs.gov

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FORM FDA 3454 (4/13)

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning (b)(6) [redacted], who participated as a clinical investigator in the submitted study (b)(4) [redacted] (Name of clinical study) is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest, as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Gudmundur Fertram Sigurjonsson	Executive Chairman
FIRM/ORGANIZATION: Kerecis ltd	
SIGNATURE	Date *(mm/dd/yyyy)*: 07/22/2013

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

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. Public reporting burden for this collection of information is estimated to average 5 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

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Food and Drug Administration
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FORM FDA 3455 (4/13)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Details of the individual's disclosable financial arrangements

(b)(4), (b)(6)

[redacted]

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 8.3

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning (b)(6) _____, who participated
Name of clinical investigator

as a clinical investigator in the submitted study (b)(4) _____

(b)(4) _____ is submitted in accordance with 21 CFR part 54. The
clinical study

named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest, as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Gudmundur Fertram Sigurjonsson	Executive Chairman
FIRM/ORGANIZATION: Kerecis Ltd	
SIGNATURE	Date *(mm/dd/yyyy)*: 07/22/2013

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

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. Public reporting burden for this collection of information is estimated to average 3 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

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Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
PRAStaff@fda.hhs.gov

"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 number."

FORM FDA 3455 (4/13)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Details of the individual's disclosable financial arrangements

(b)(4), (b)(6)

[redacted]

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 9: Declaration of Conformity and Summary Reports

9 DECLARATIONS OF CONFORMITY AND SUMMARY REPORTS

This Section is not applicable.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 10: Executive Summary

10 510(k) Premarket Notification for the Kerecis MariGen Wound Dressing

10.1 EXECUTIVE SUMMARY

The Kerecis MariGen Wound Dressing is supplied sterile and is intended for single use in the treatment of the following wounds:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence).
- Draining wounds

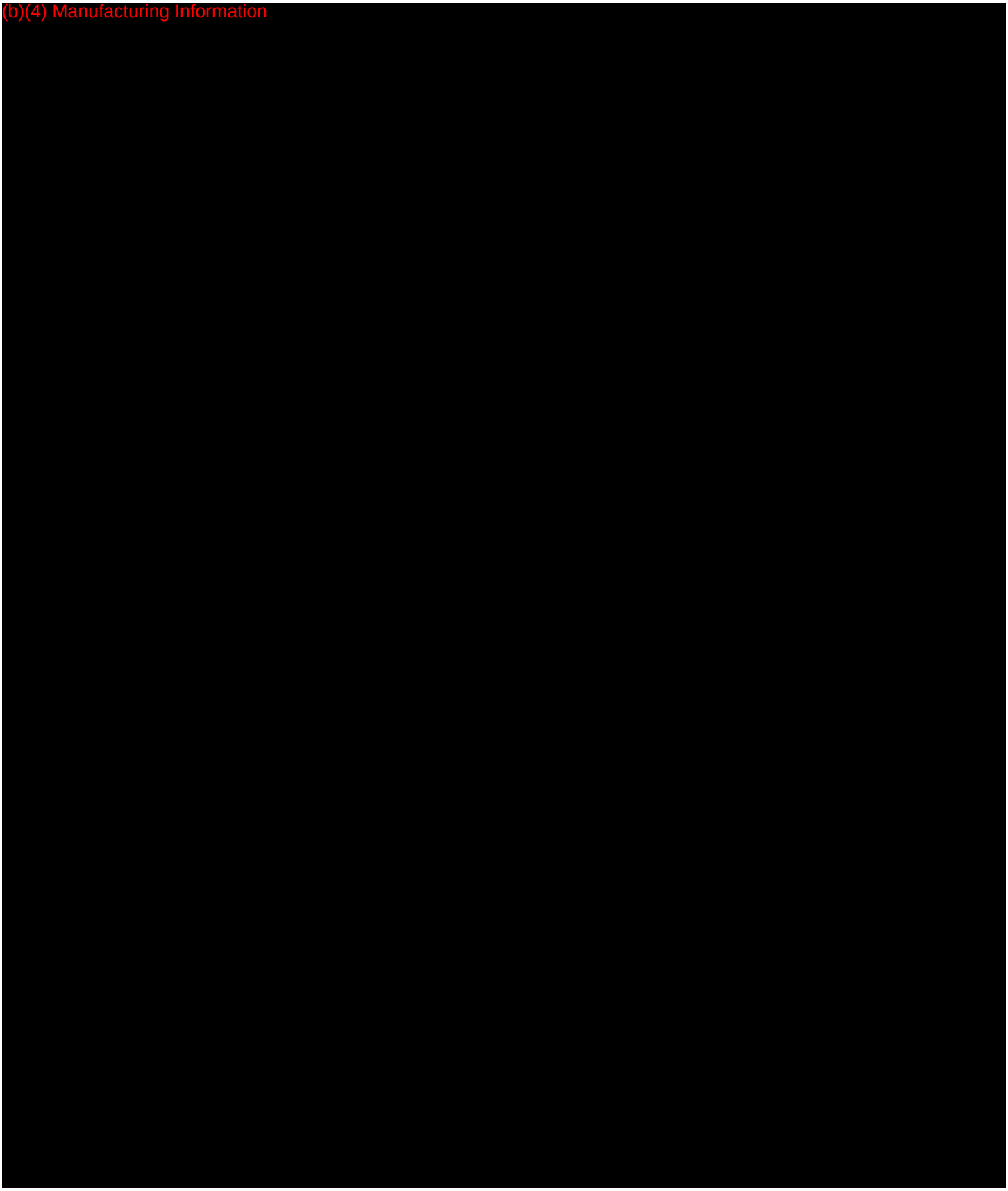
(b)(4) Manufacturing Information

[redacted]

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4) Manufacturing Information



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

10.2 Comparison to predicates

	Kerecis	Mesynthes	Cook Biotech (New)	ACell, Inc
510K		K092096	K061711	K092926
Device name	MariGen Dressing	Endoform™ Dermal Template	Oasis Wound Matrix	MatriStem® Wound Sheet
Product Codes	KGN	KGN	KGN	KGN
Intend. use	Wound dressing	Wound dressing	Wound dressing	Wound dressing
Indications	(b)(4) Draft - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds	Partial and full-thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - tunneled/undermined wounds - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds	Partial and full thickness wounds: - Pressure ulcers; - Venous ulcers; - Diabetic ulcers; - Chronic vascular ulcers; -Tunneled/ undermined wounds; - Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence); - Trauma wounds (abrasions, lacerations, second-degree burns and skin tears); - Draining wounds	Partial and full-thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - tunneled/undermined wounds - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds
Animal origin	(b)(4)	(b)	(b)(4)	(b)(4)
Tissue type	(b)(4)			
Nominal sizes	3 x 3.5 cm (10.5 cm^2) 3 x 7 cm (21 cm^2) 7 x 20 cm (140 cm^2)	Sizes ranging from 9 cm^2 to 400 cm^2, fenestrated, meshed	3 x 3.5cm 7x20cm	3 x 3.5 cm (10.5 cm^2) 3 x 7 cm (21 cm^2)
Presentation	(b)(4)			
Components	(b)(4) (b)(4)	(b)(4)	(b)(4)	(b)(4)

Table 10-2 Comparison to predicates (Table continued below)

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

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	Integra Life Sciences	LifeCell Corporation's	HemCon, Inc (New)	TEI Biosciences Inc.
510K	K021792	K082103	K071519	K083440
Device name	Integra™ Wound Matrix	LTM Wound Dressing	Hemcon Chitoflex-Surgical Dressing	PriMatrix
Product Codes	FRO	KGN	FRO	KGN
Intend. use	Wound dressing	Wound dressing	Wound dressing	Wound dressing
Indications	Partial and full thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence) - trauma wounds (abrasions, lacerations, second-degree bums, and skin tears) - draining wounds.	Partial and full thickness wounds: - Pressure ulcers; - Venous ulcers; - Diabetic ulcers; - Chronic vascular ulcers; - Tunneled/ undermined wounds; - Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence); - Trauma wounds (abrasions, lacerations, second-degree burns and skin tears); - Draining wounds - And other bleeding surface wounds. -supports wound healing and control of minor bleeding	Intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations and abrasions. May also be used for temporary treatment of severely bleeding wounds such as surgical wounds (operative, postoperative, dermatological, etc.) and traumatic injuries.	Partial and full thickness wounds: · Pressure, diabetic, and venous ulcers · Second-degree burns * Surgical wounds-donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence * Trauma wounds-abrasions, lacerations, and skin tears · Tunneled/undermined wounds * Draining wounds
Animal origin	(b)(4)			
Tissue type				
Nominal sizes	5 x 5cm 10 x 12.5cm 10 x 25cm 20 x 25cm	8cm x 16cm 5cm x 16cm 20cm x 25cm 10cm x 16cm	1 x 3 in 3x 9 in 3x 28 in	4 x 4 cm 6 x 6cm 8 x 12 10 x 12 20 x 25cm
Presentation	(b)(4)			
Components				

Table 10-3 Comparison to predicates continued

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 11: Device Description

11 DEVICE DESCRIPTION

11.1 Intended Use

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence)
- Draining wounds

11.2 Performance Standards

No performance standards applicable to this device have been adopted under Section 514 of the Act.

11.3 Principles of Operation

(b)(4)

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

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(b)(4)

[redacted]

11.3.2 The Device Development

(b)(4)

[redacted]

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4)

11.4 Evidence of Conformity with Special Controls

The following standards have been used in the characterization, design and manufacturing of the MariGen device.

Standard	Name
ISO-13485	Medical devices-Quality management systems - Requirements for regulatory purposes (2003).
(b)(4)	
ISO-10993-1	Biological evaluation of medical devices - Part 1: Evaluation and testing (2009).
ISO 10993-5	Biological Evaluation of Medical Devices - Part 5: Tests for In Vitro Cytotoxicity (2009).
ISO 10993-6	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation (2006).
(b)(4)	
ISO 10993-10	Biological Evaluation of Medical Devices - Part 10; Tests for Irritation and Delayed-Type Hypersensitivity (2010).
ISO 10993-11	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (2009).
ISO 10993-12	Biological Evaluation of Medical Devices - Part 12: Sample Preparation and Reference Materials (2012).
ISO 14971	Medical devices Application of Risk Management to Medical Devices (2012).
ISO 22442-1	Medical Devices Utilizing Animal Tissues and Their Derivatives - Part 1:

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

	Application of Risk Management (2007).
ISO 22442-2	Medical Devices Utilizing Animal Tissues and Their Derivatives - Part 2: Controls on Sourcing, Collection and Handling (2007).
ISO 22442-3	Medical Devices Utilizing Animal Tissues and Their Derivatives - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents (2007).
(b)(4)	(b)(4)
	(2008).
EN 980	Symbols for use in the labeling medical devices (2008).
ISO 11607-1	Packaging for Terminally Sterilized Medical Devices Part 1, Requirements for materials, sterile barrier systems and packaging systems (2009)
ISO 11607-2	Packaging for Terminally Sterilized Medical Devices Part 2, Validation requirements for forming, sealing and assembly processes. (2006)
EN 868-5	Packaging materials for terminally sterilized medical devices –Part 5: Sealable pouches and reels of porousmaterials and plastic film construction – Requirements and test methods (2009).
ISO11607:2009	Packaging for Terminally Sterilized Medical Devices

Table 11-2 - Conformity with Special Controls

The FDA standards forms (FDA Form 3654) are included in APPENDIX 11-1.

MariGen Wound dressing is manufactured in compliance with the Guidance for FDA Reviewers and Industry Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices), issued 11/6/98.

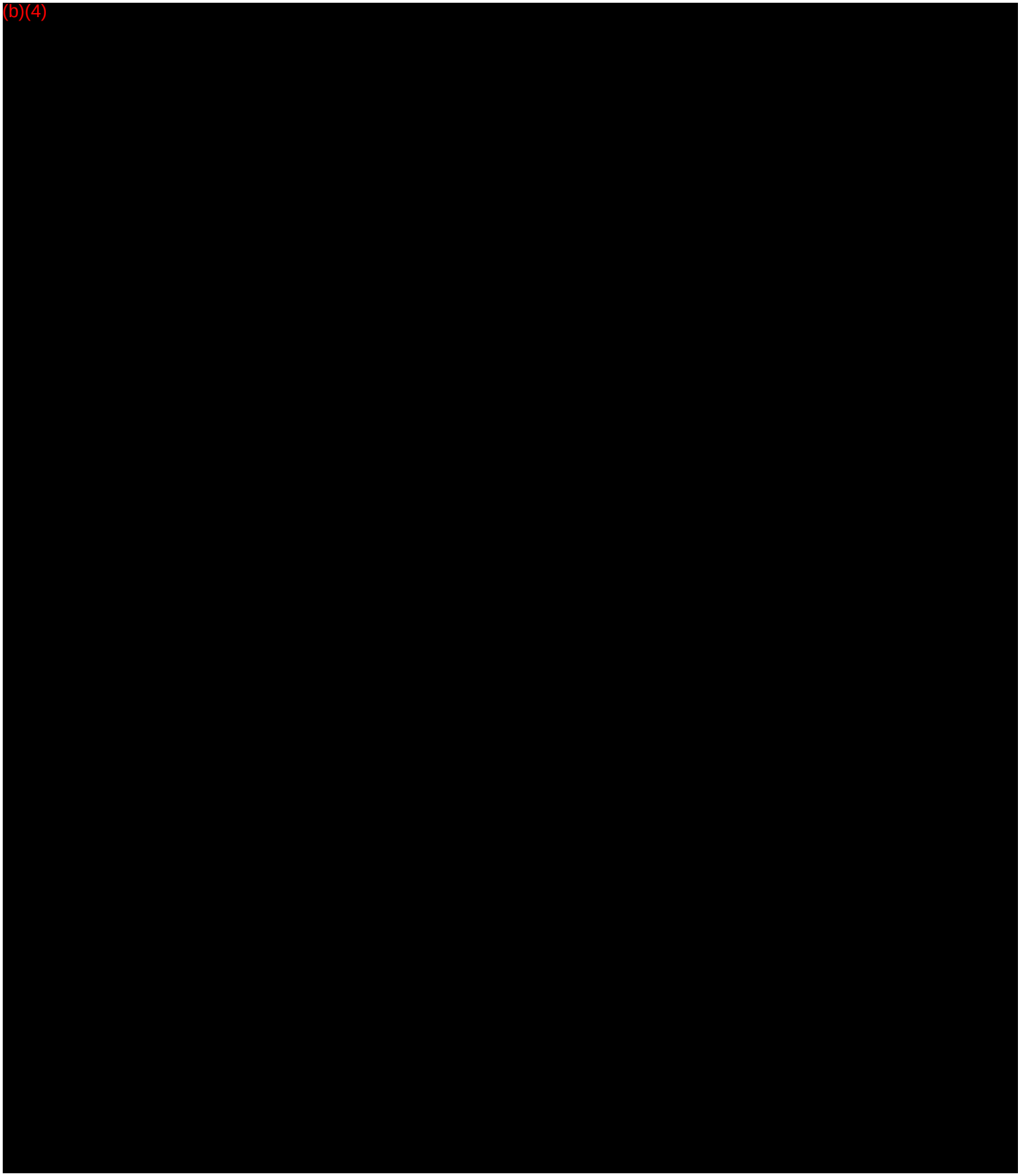
11.5 Device Description

(b)(4)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4)



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4)

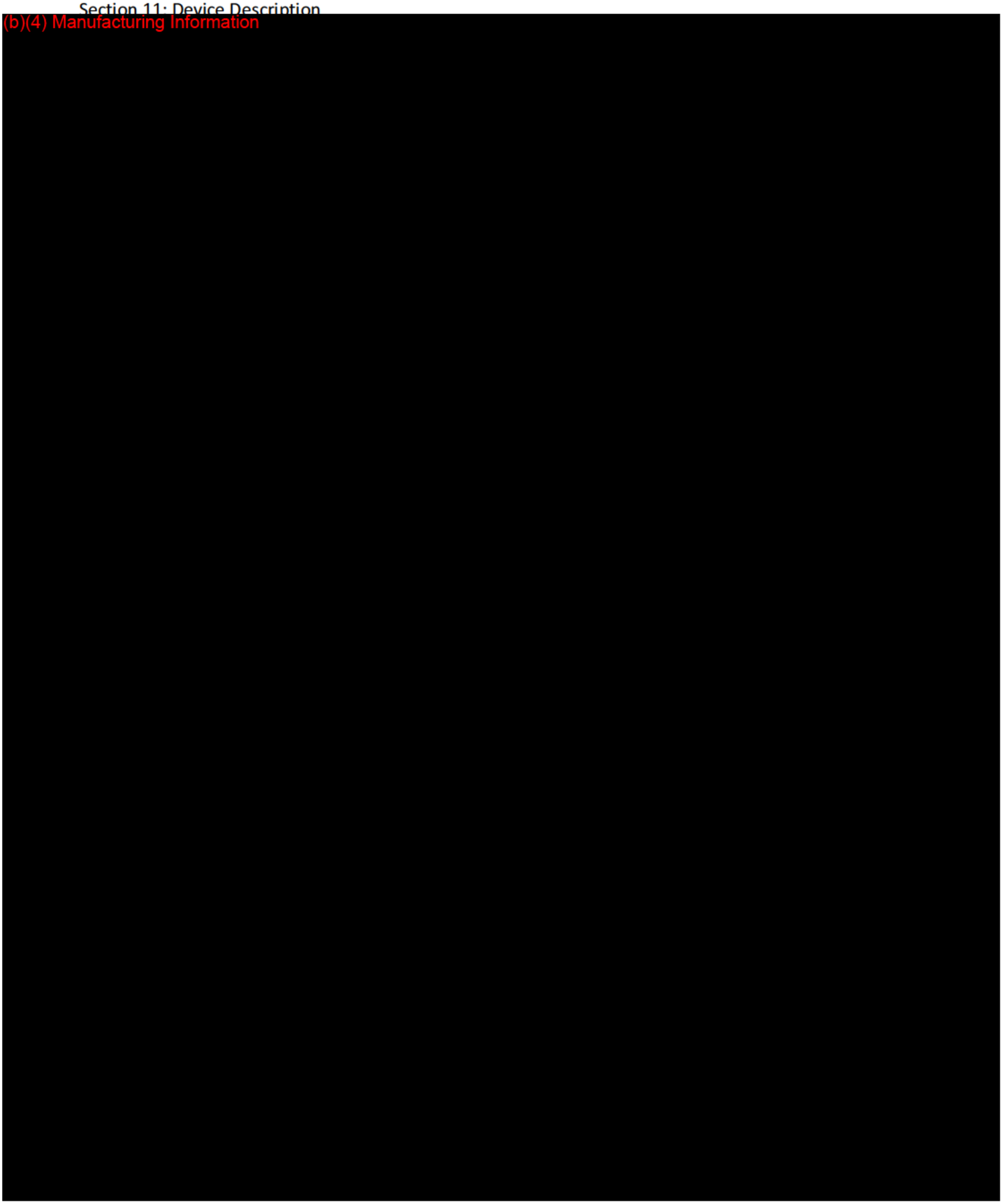
(b)(4)

(b)(4)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

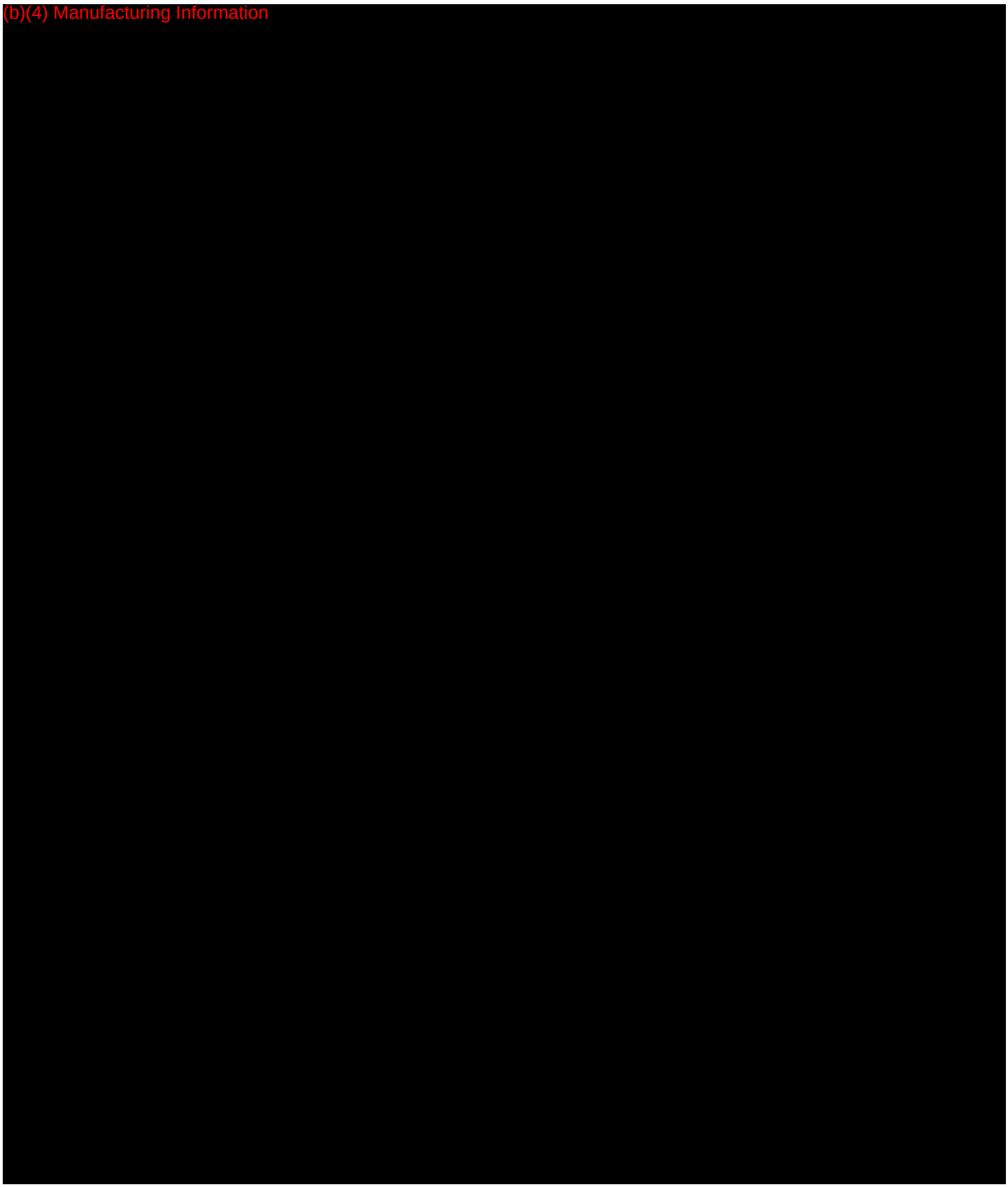
(b)(4) Manufacturing Information



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

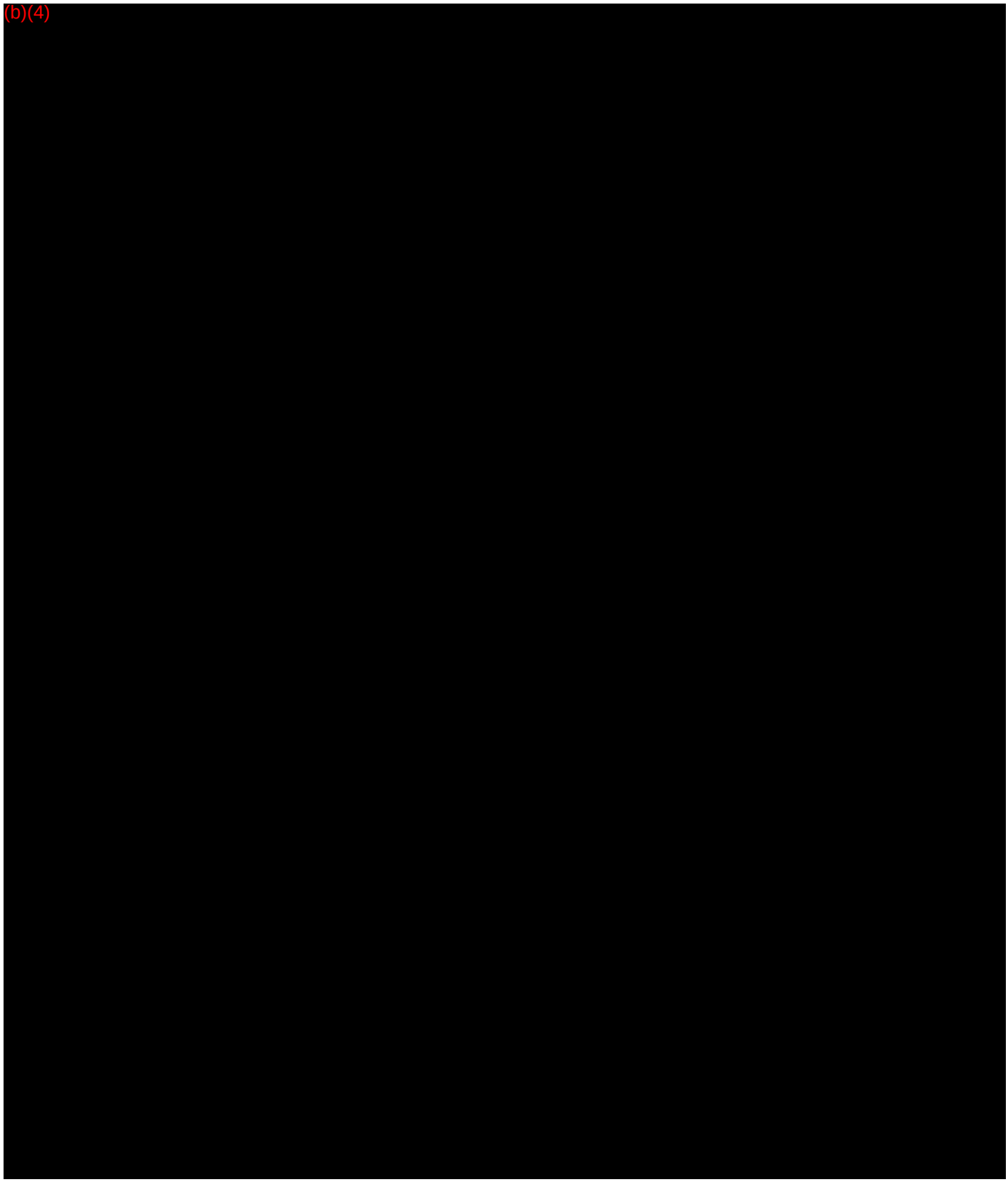
(b)(4) Manufacturing Information



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

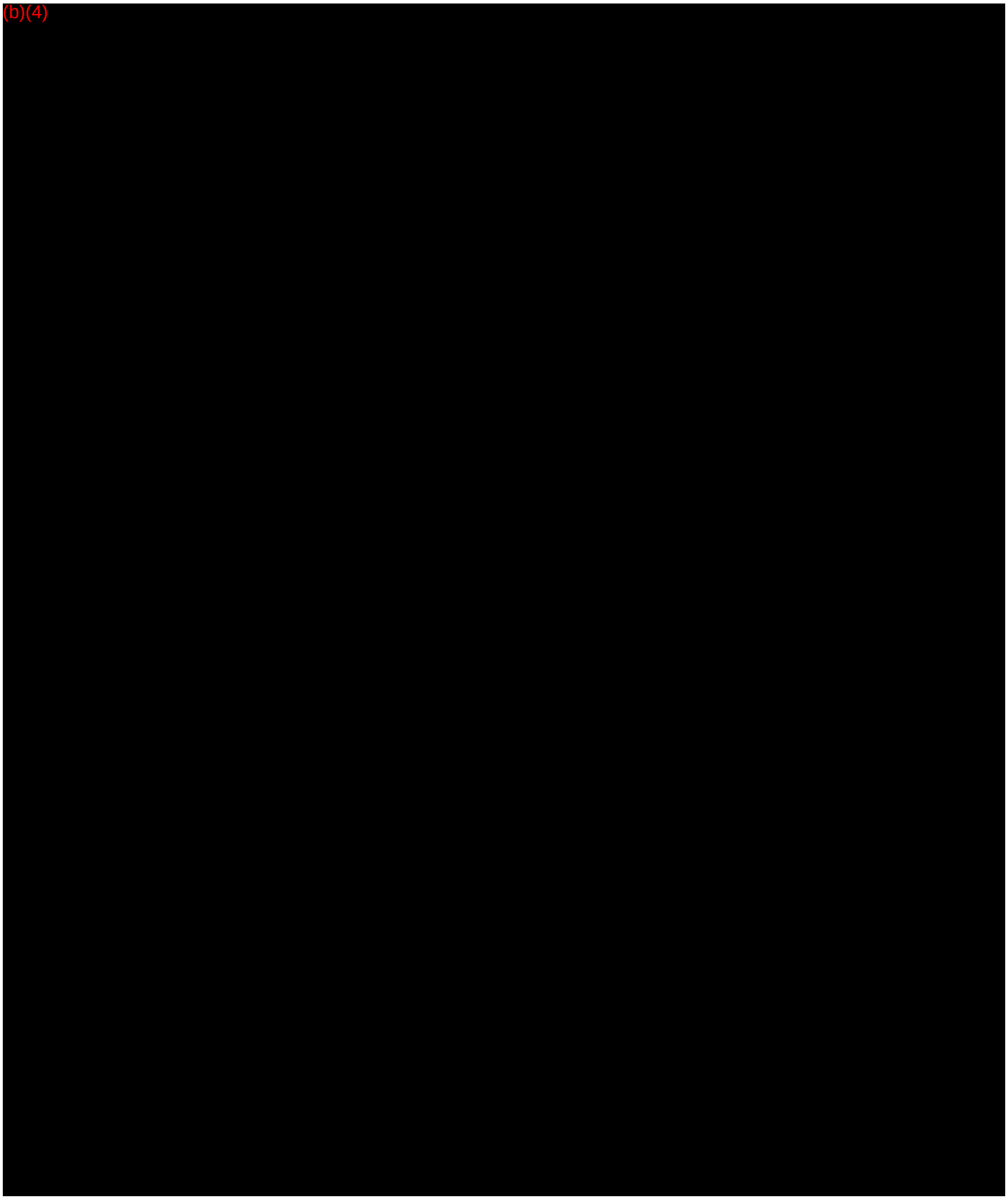
(b)(4)



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4)



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

(b)(4)

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

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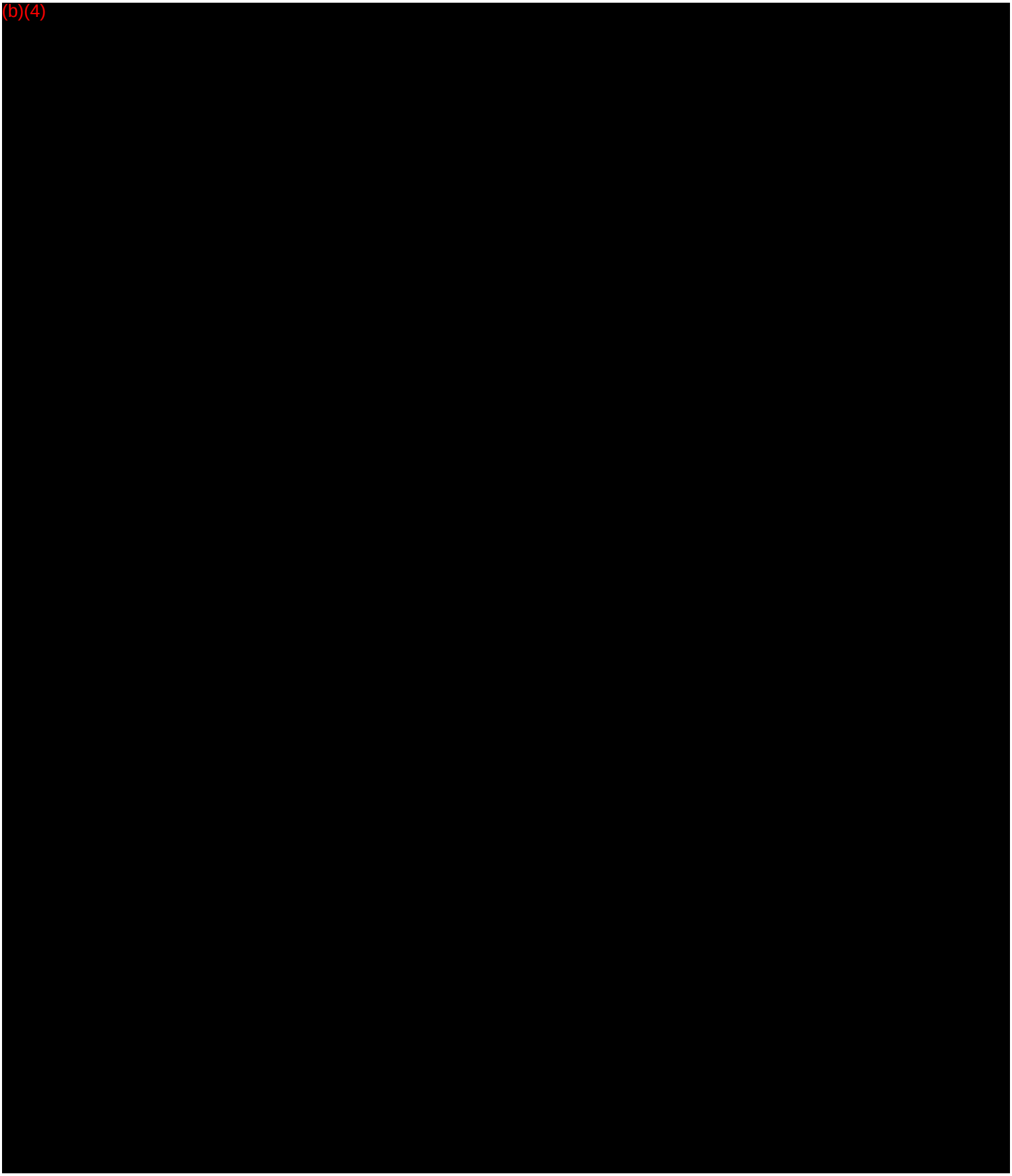
(b)(4)



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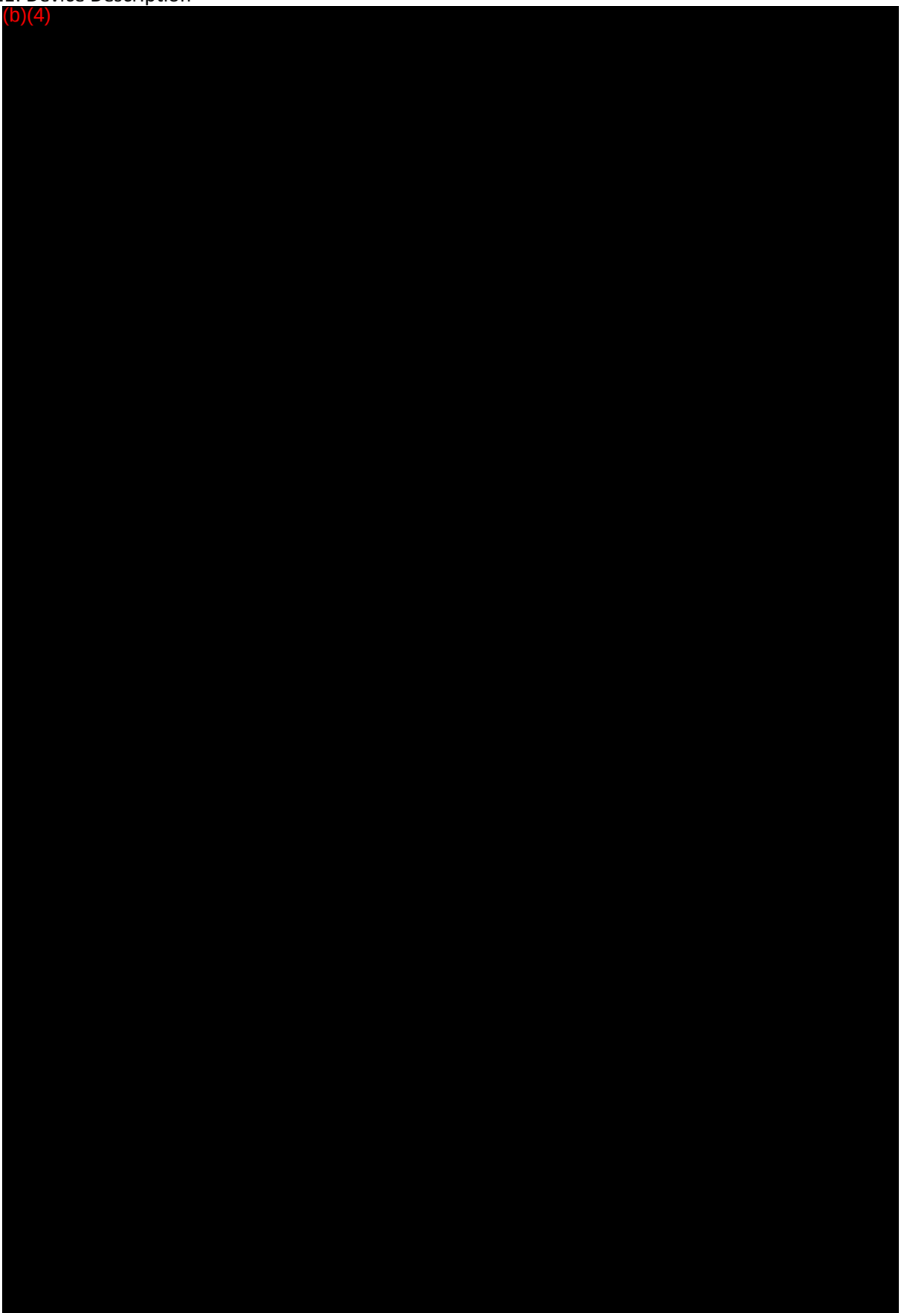

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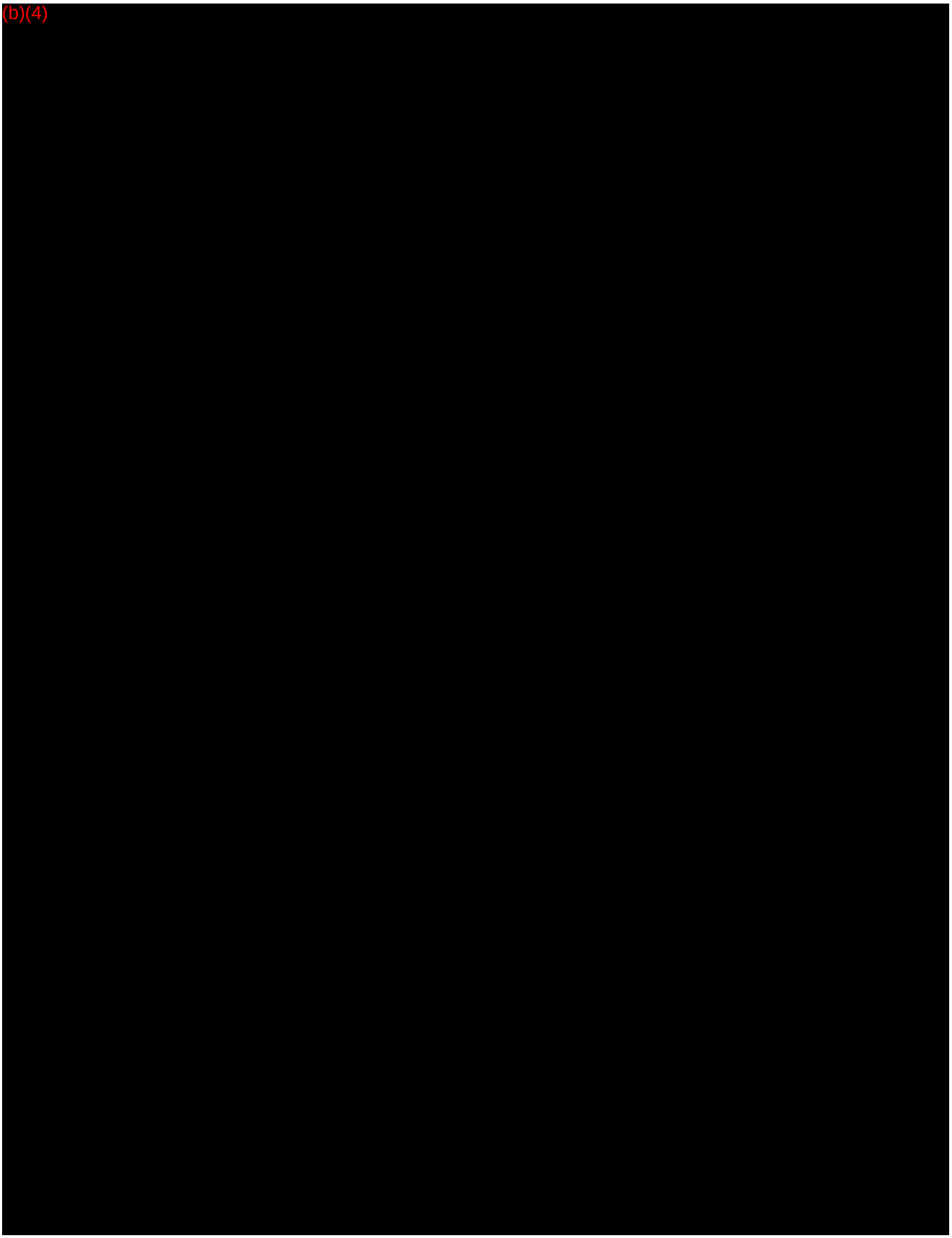

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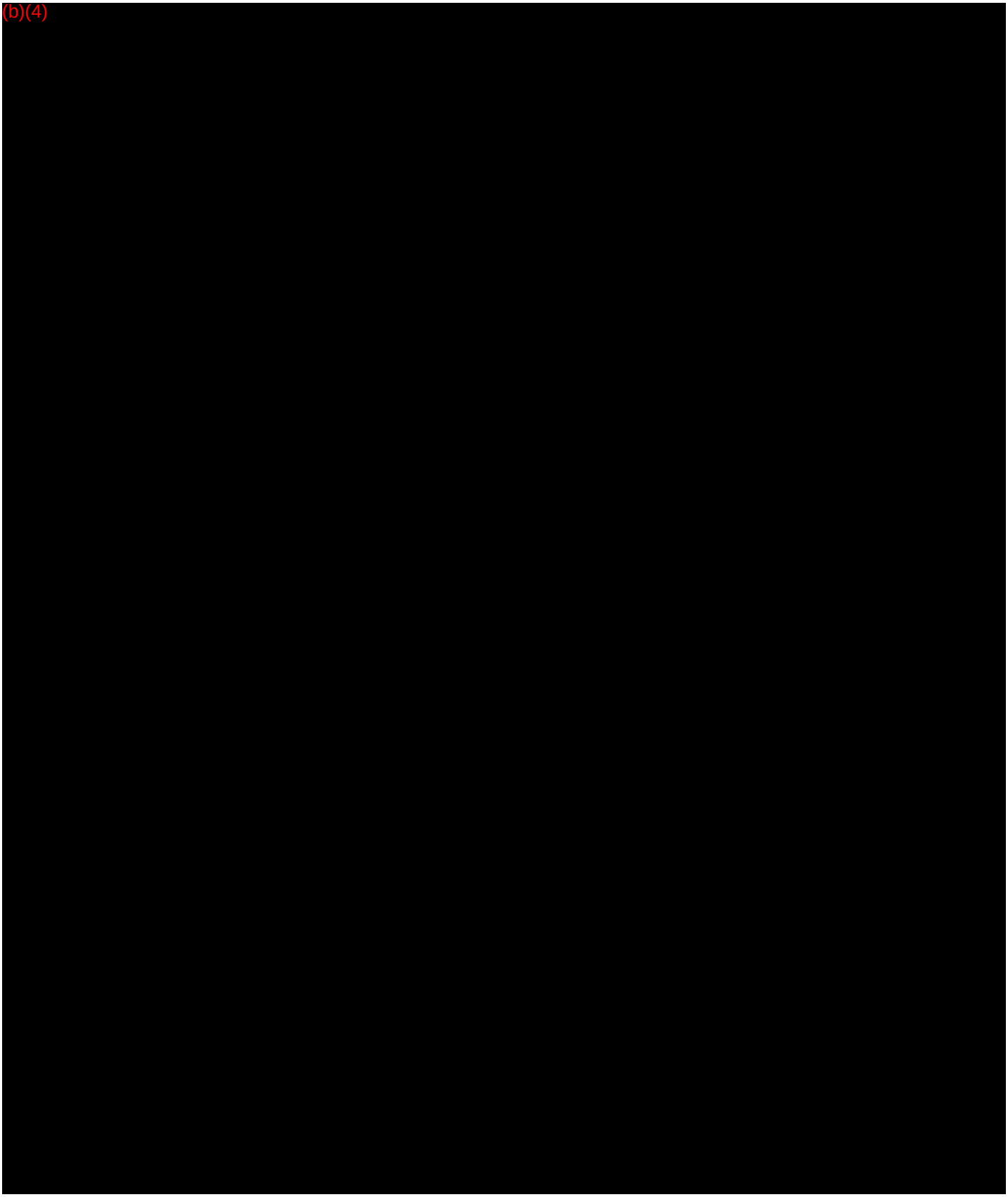

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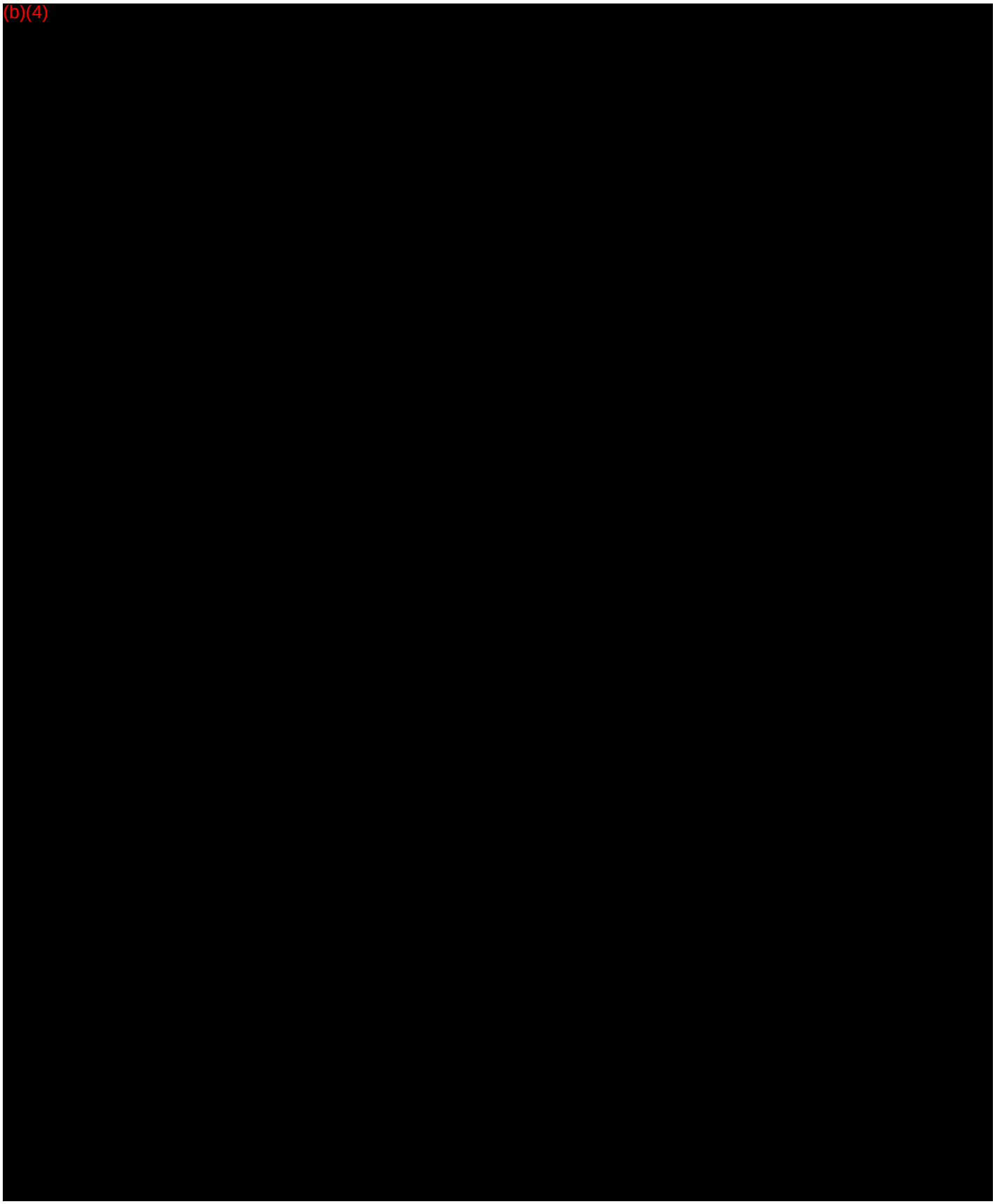

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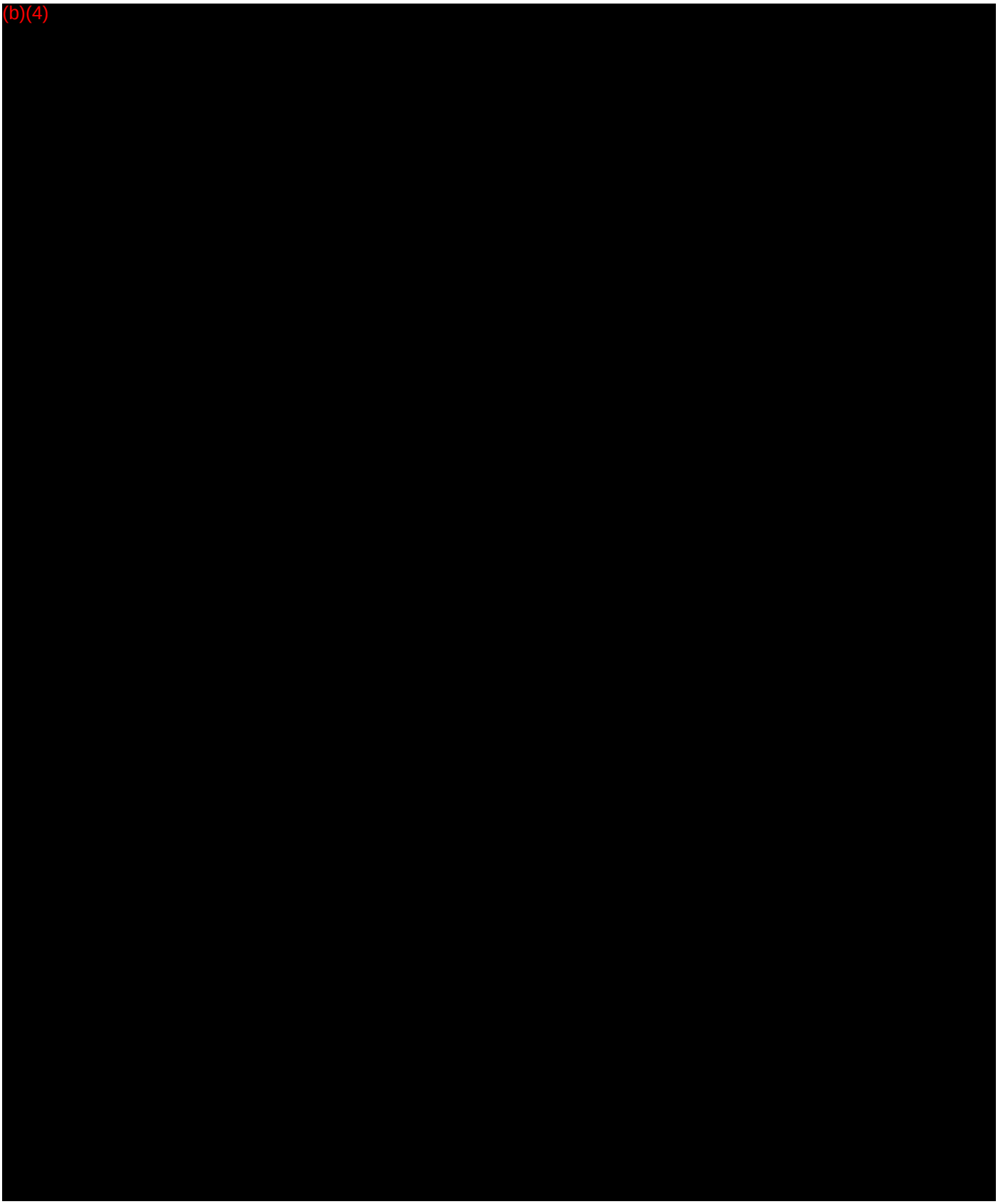

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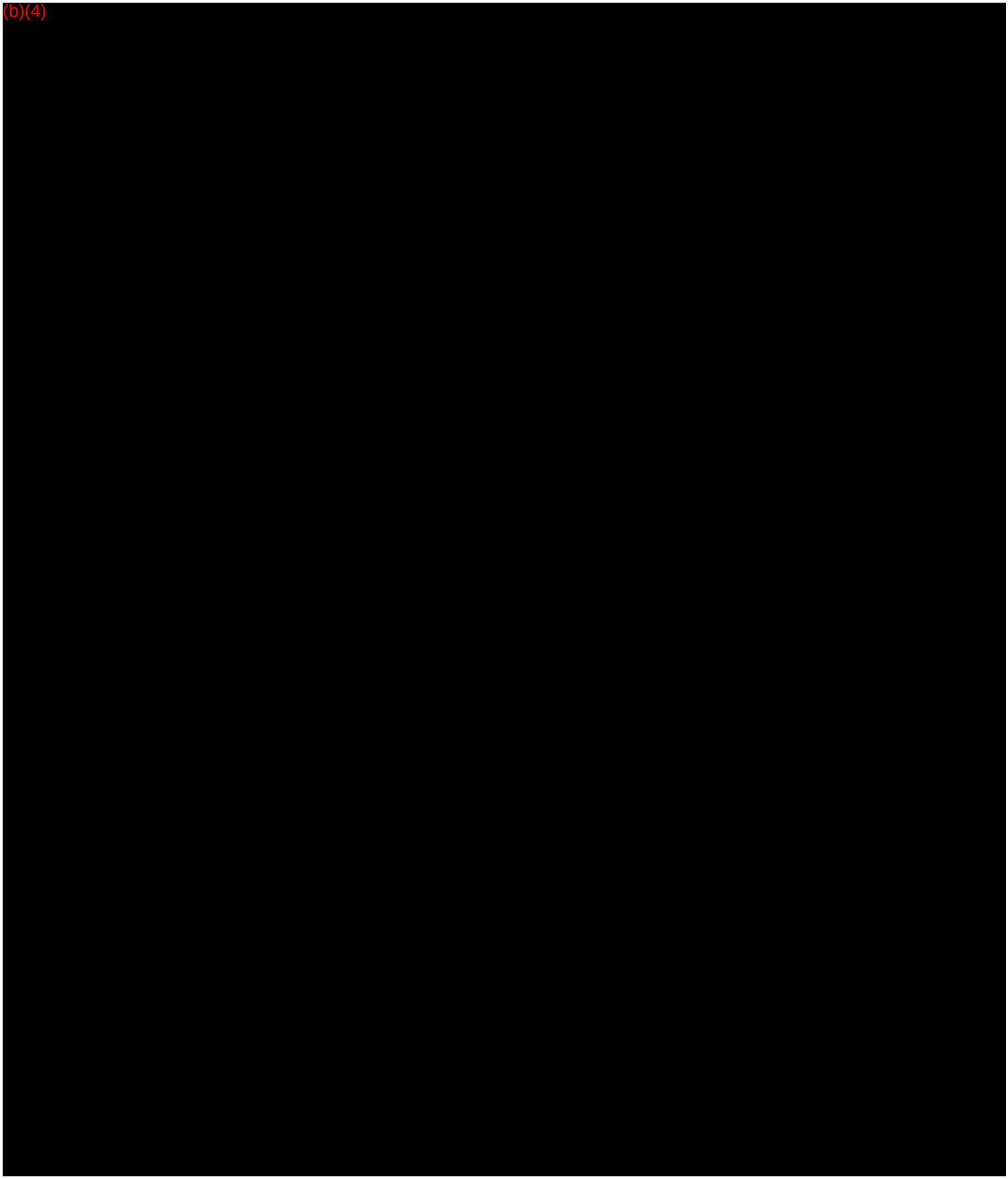

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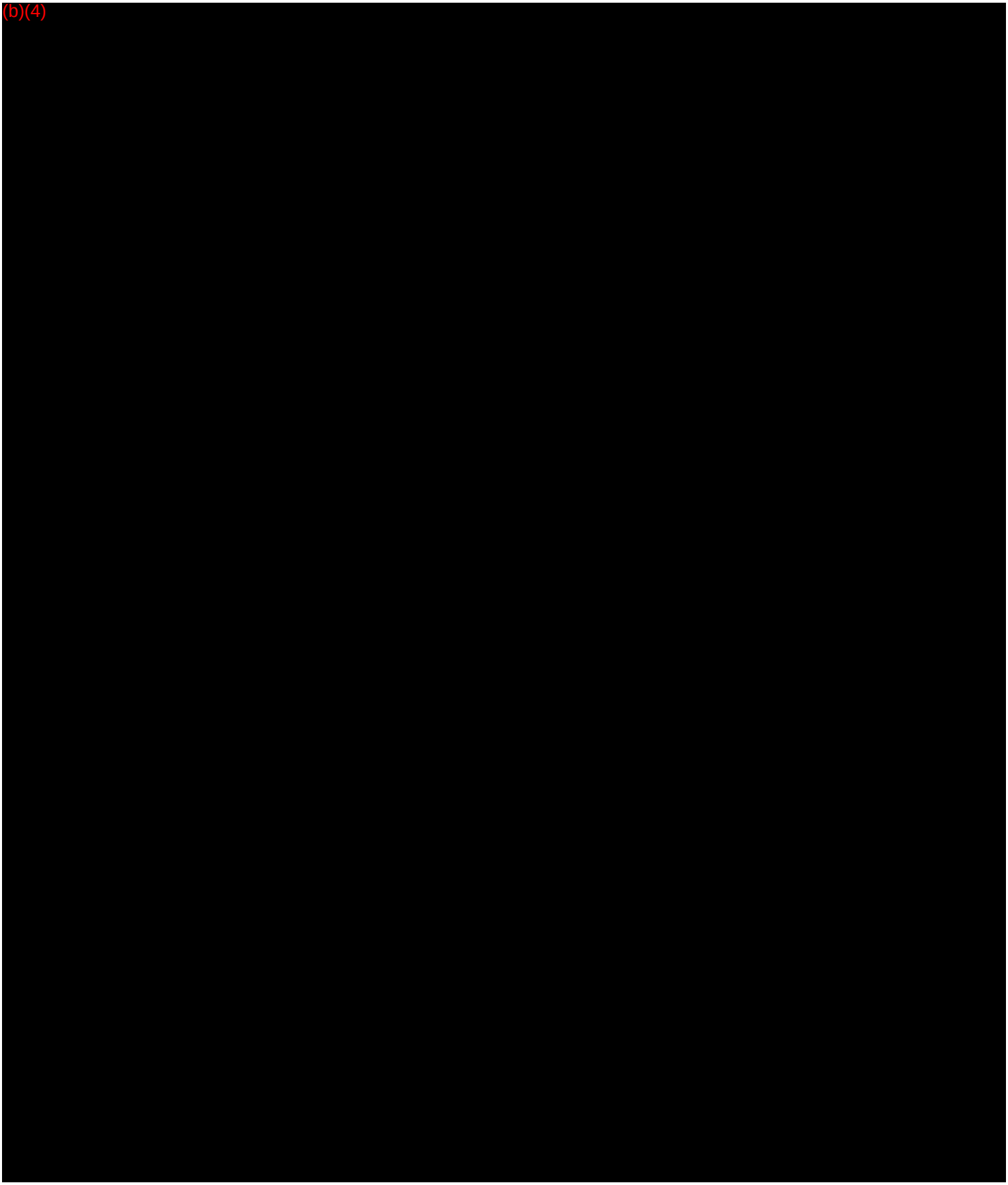

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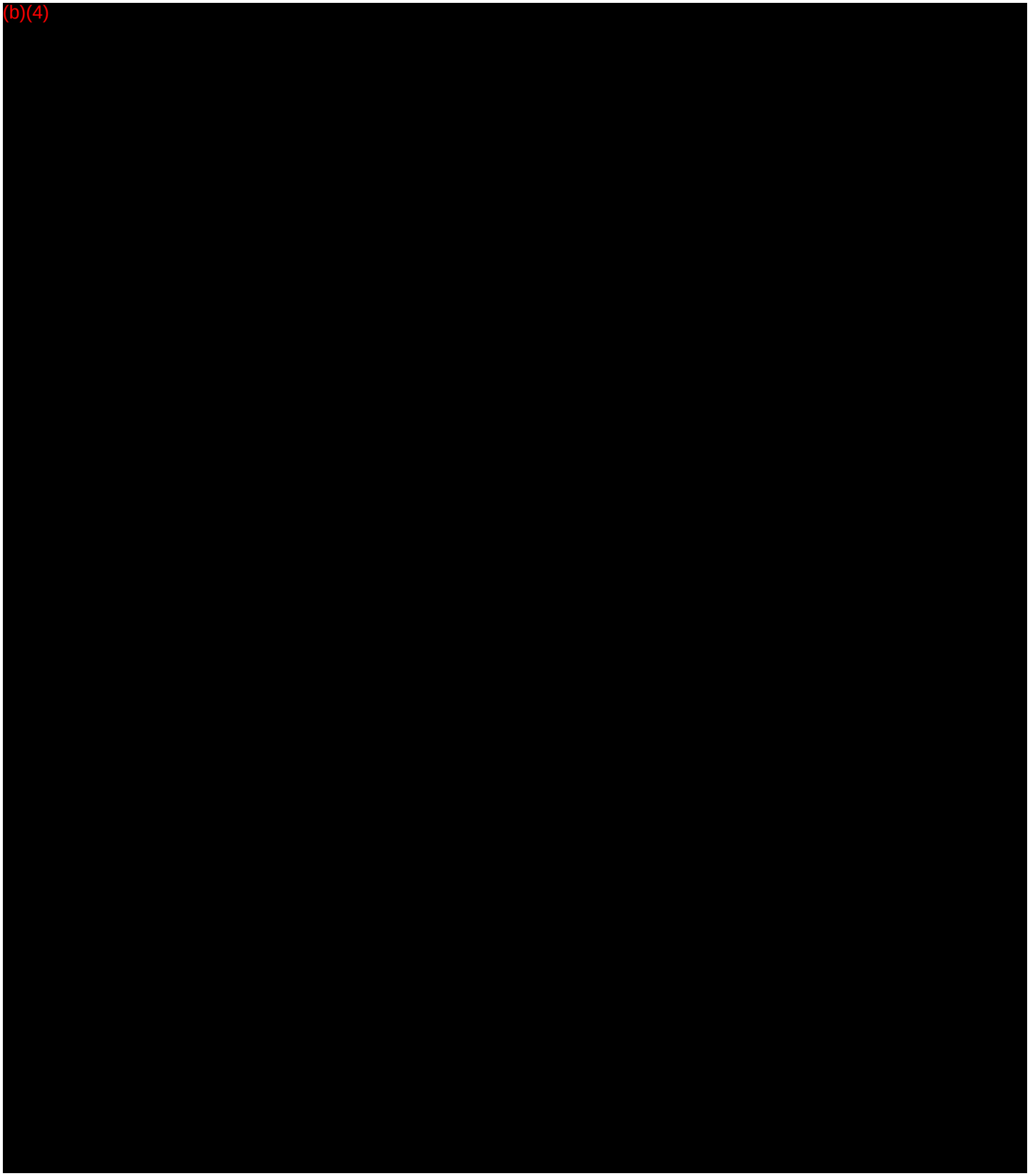

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(b)(4)

11.6 Risk Management

(b)(4)

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11.7 Manufacturing

(b)(4)

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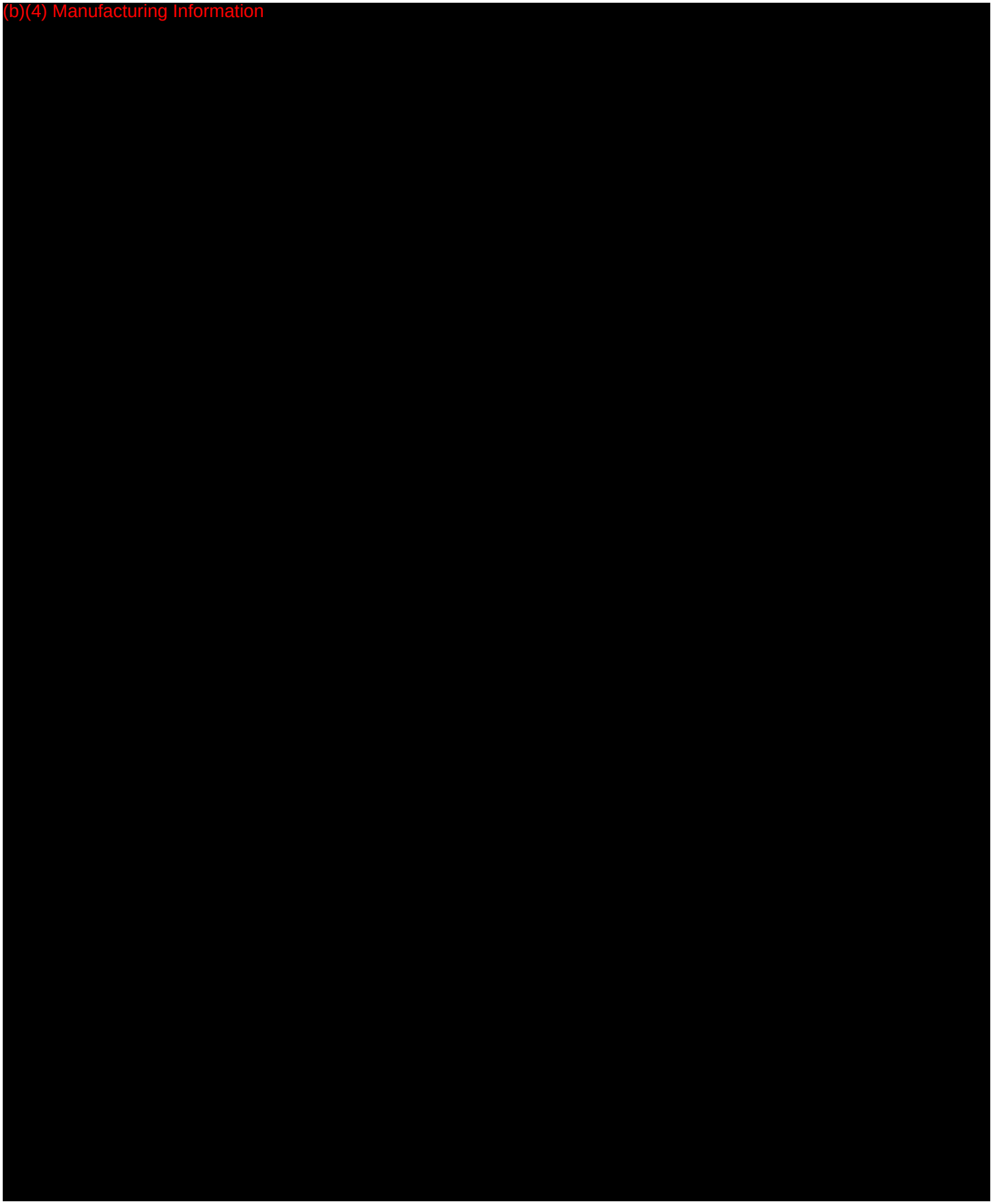

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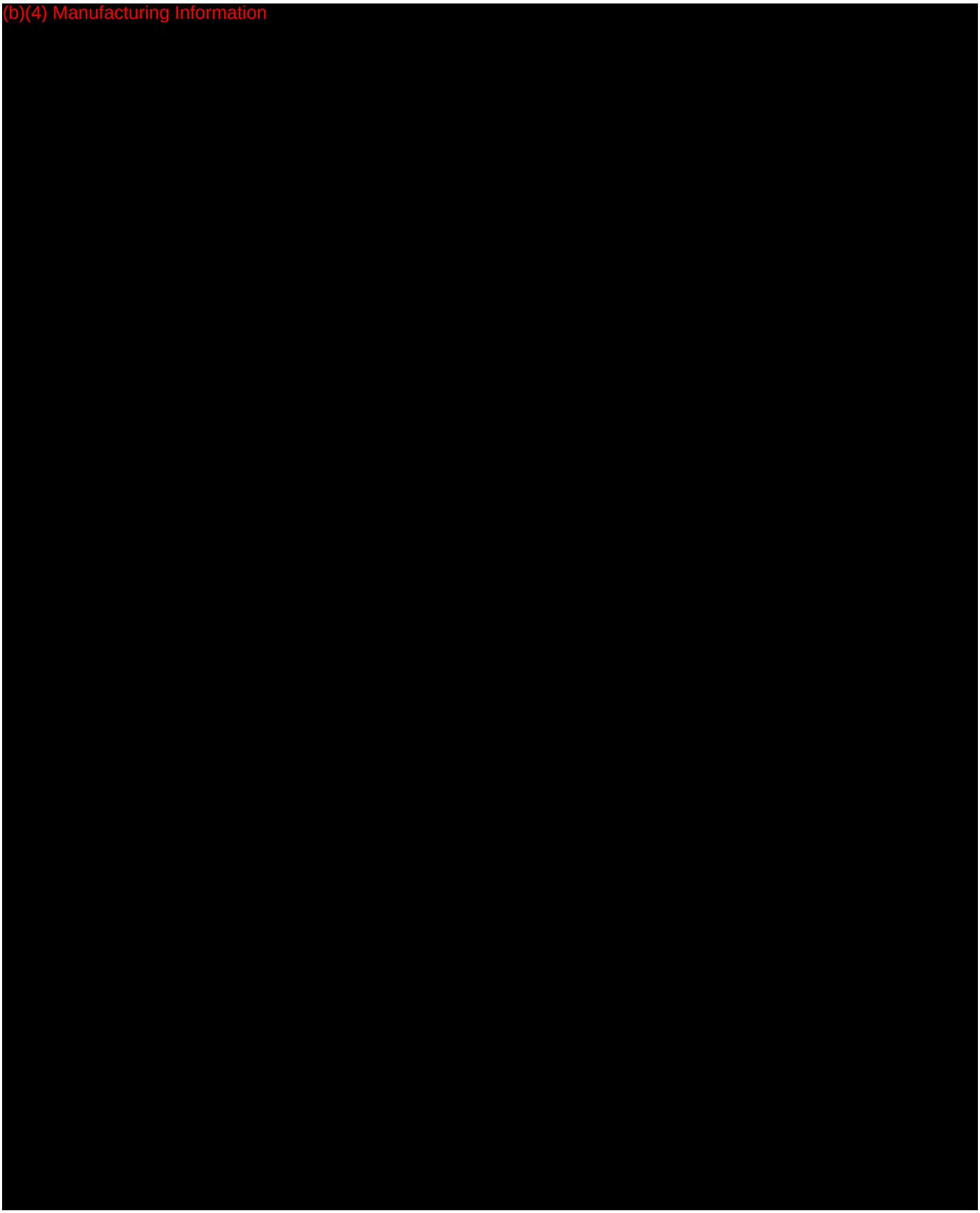

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(b)(4) Manufacturing Information

11.7.2 Manufacturing Overview

(b)(4) Manufacturing Information

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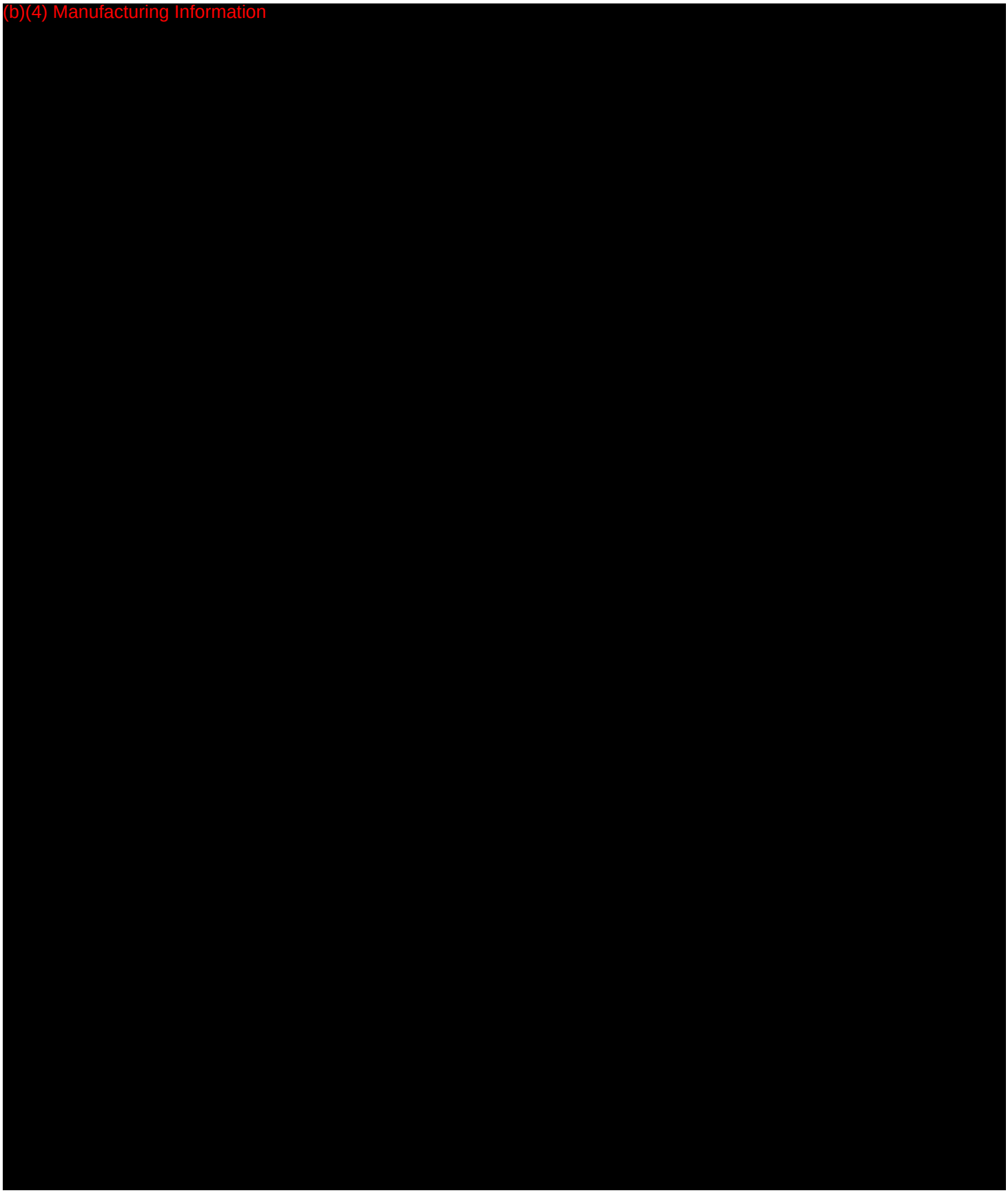

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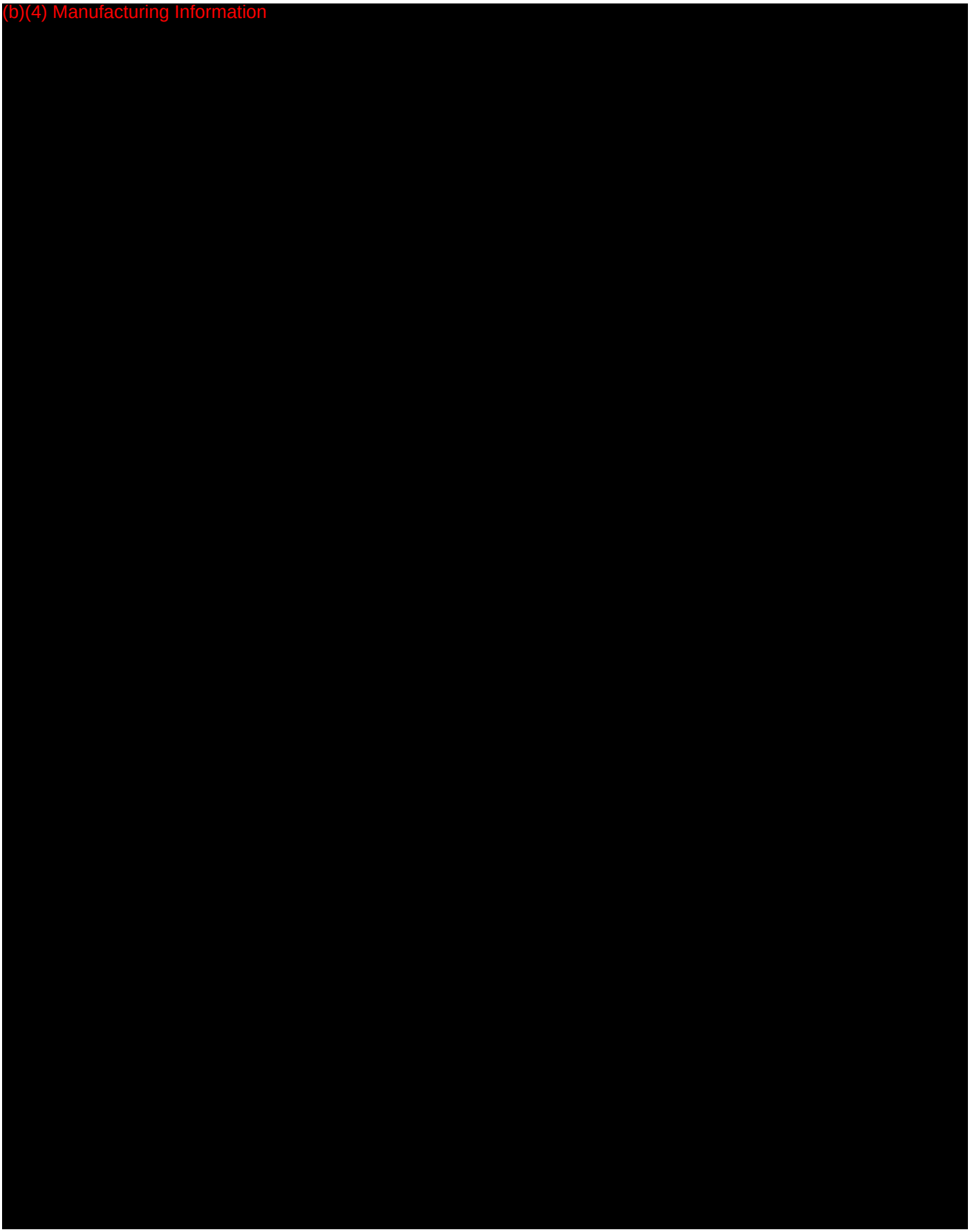

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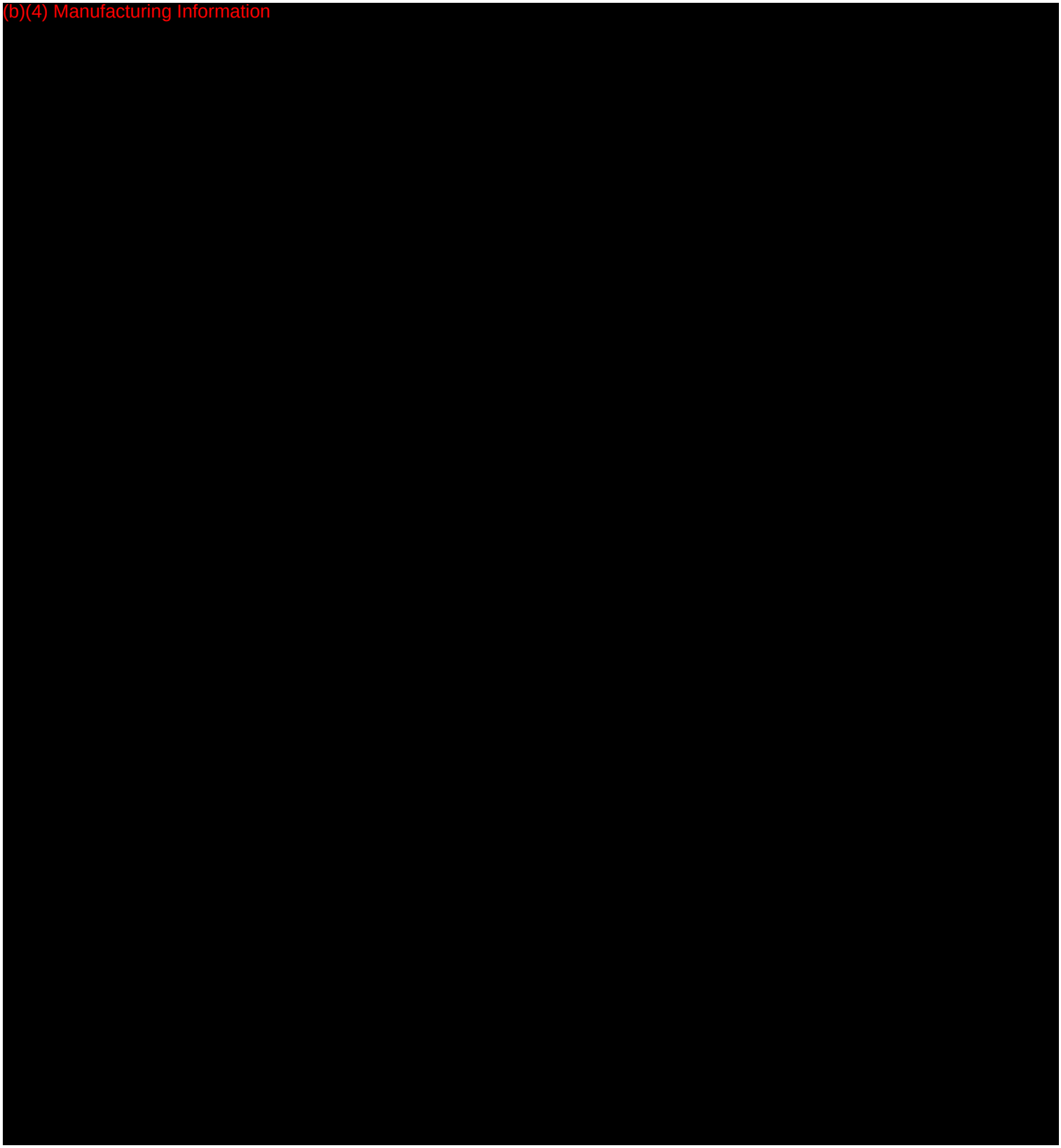

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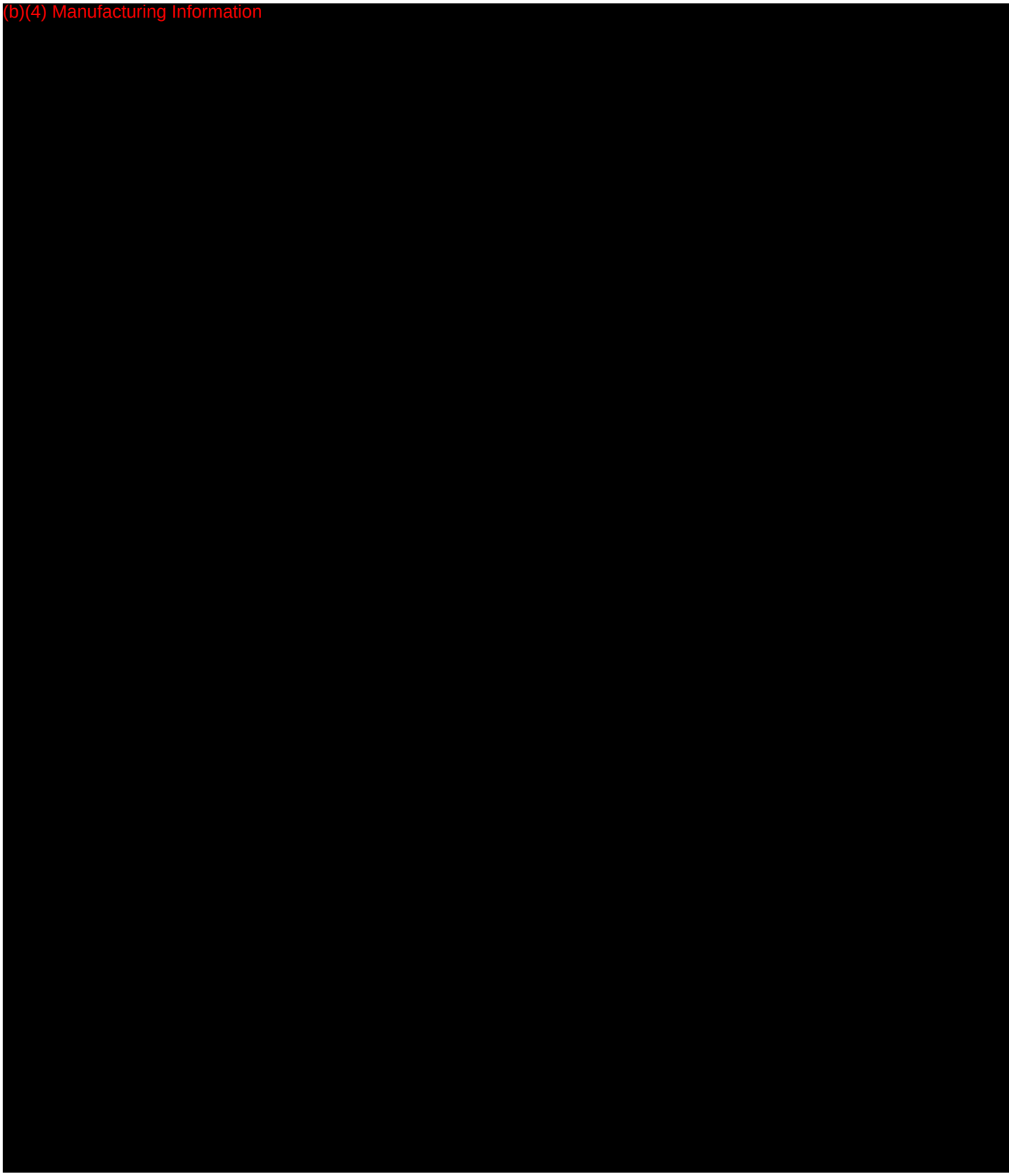

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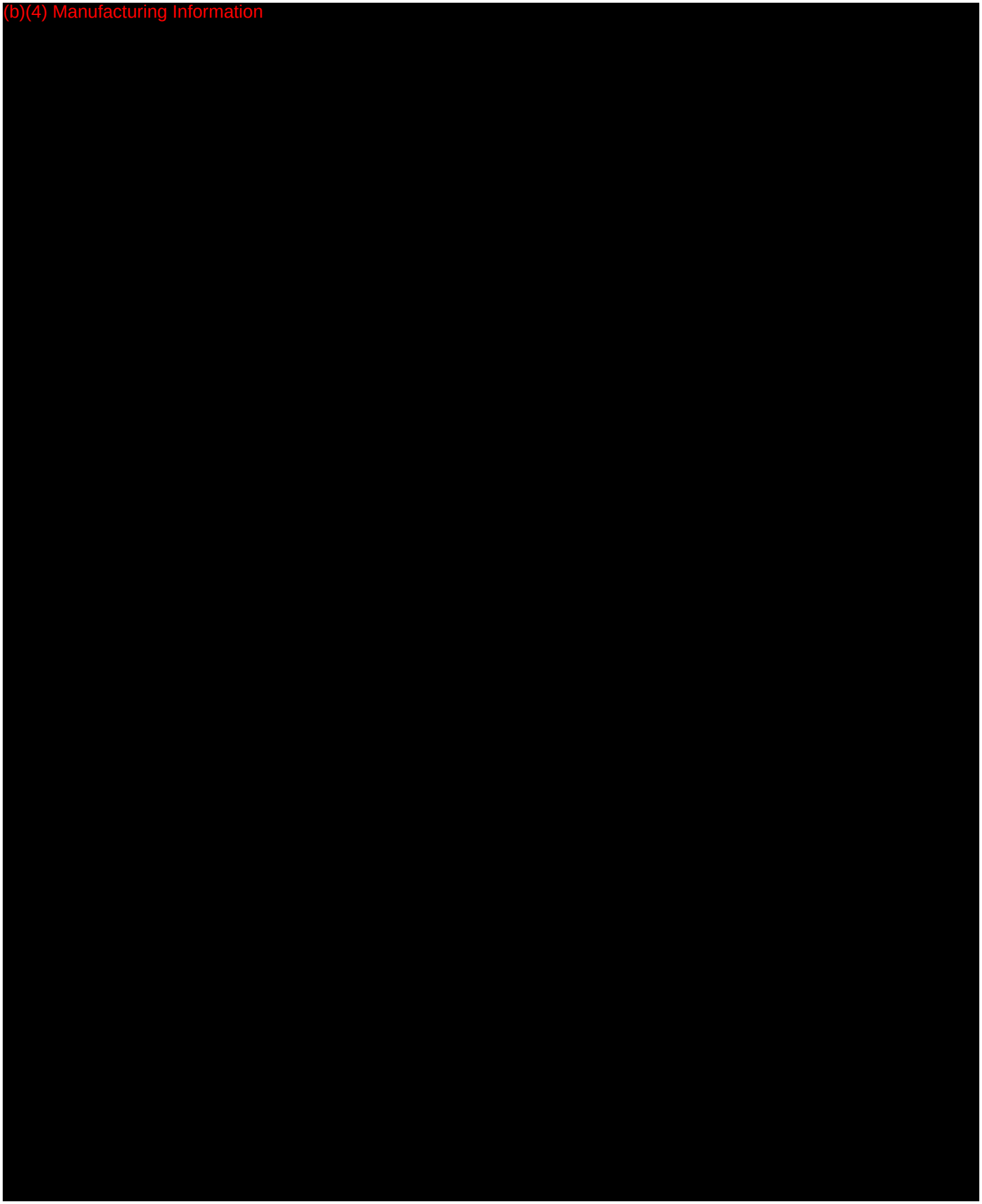

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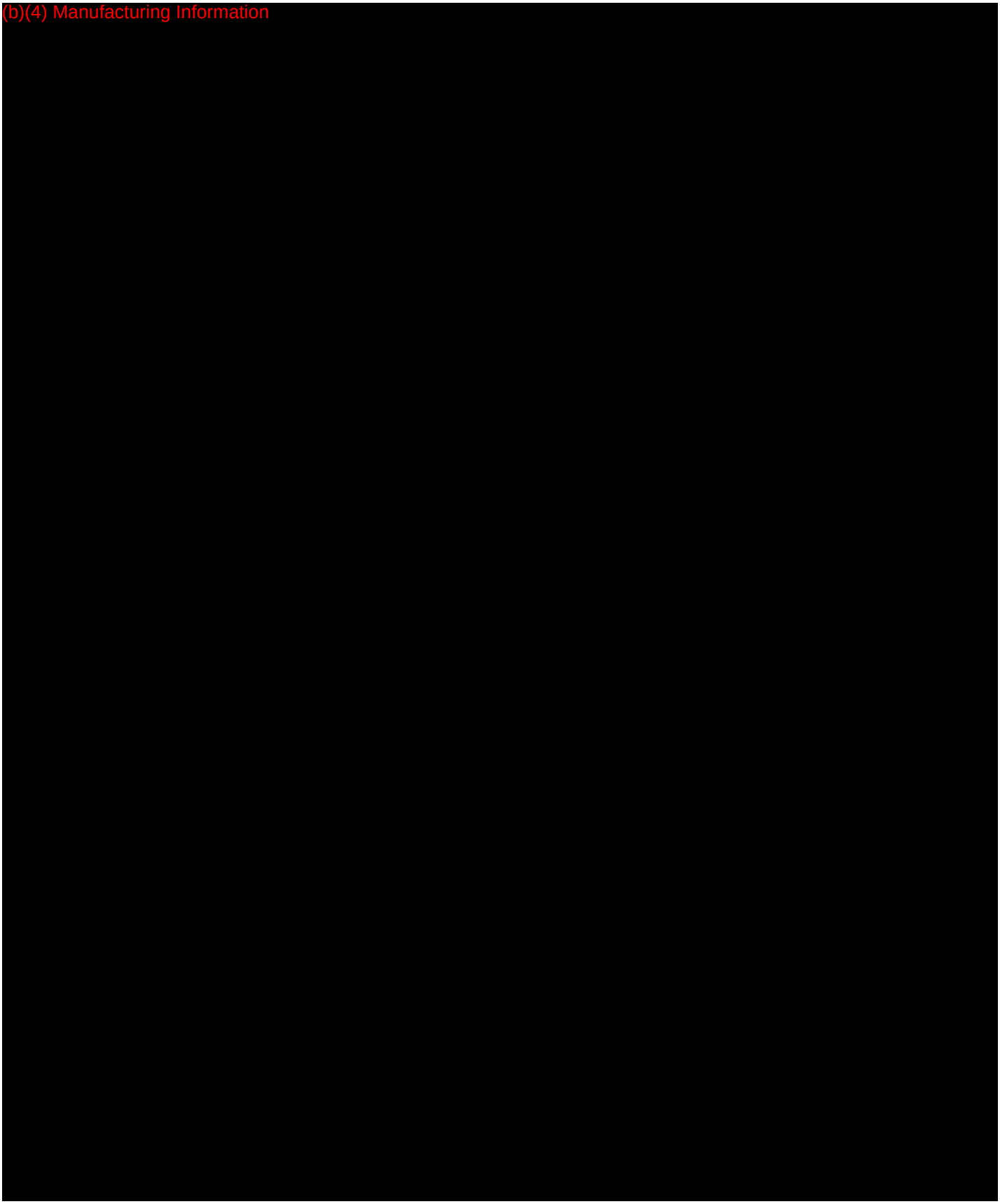

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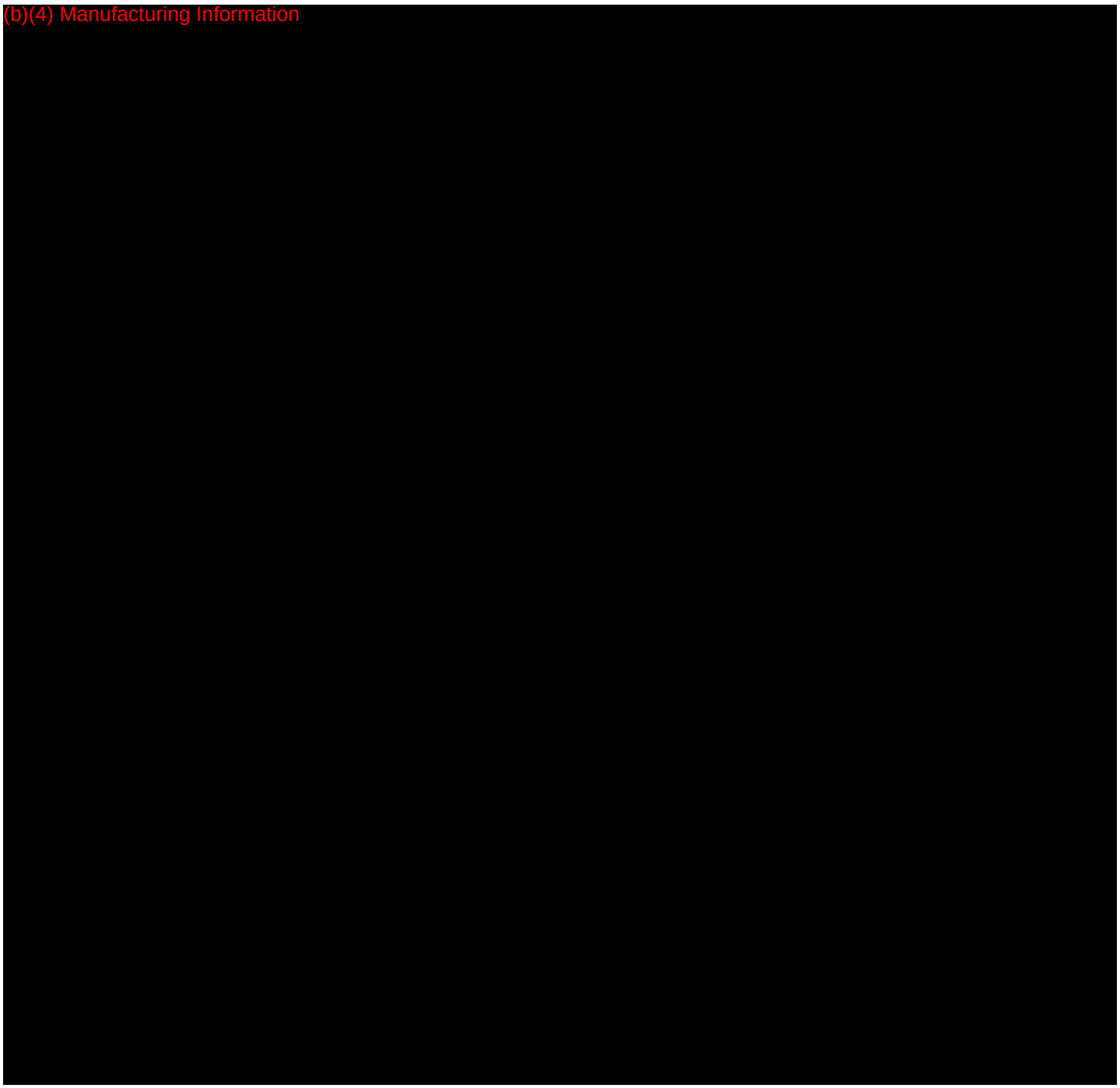

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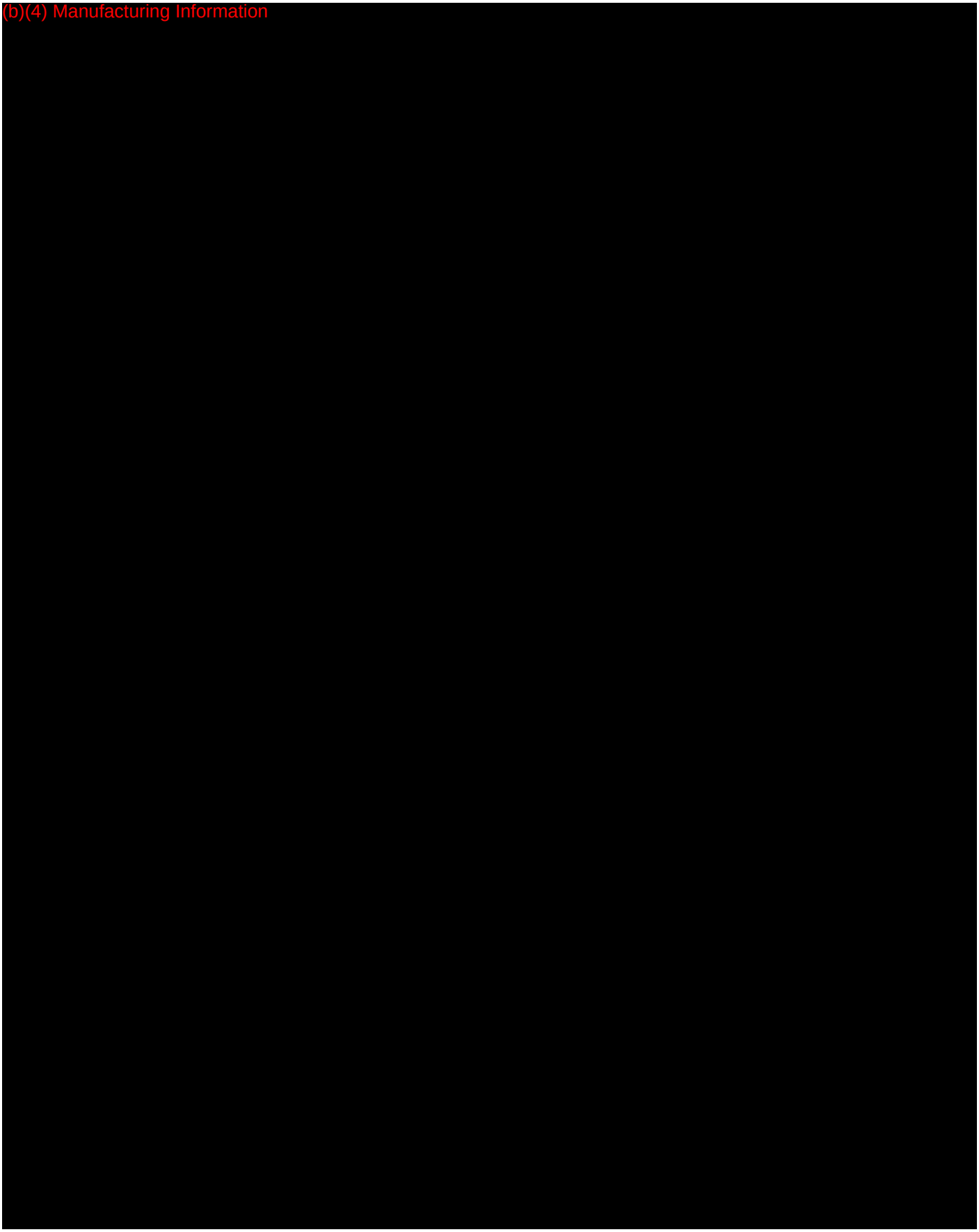

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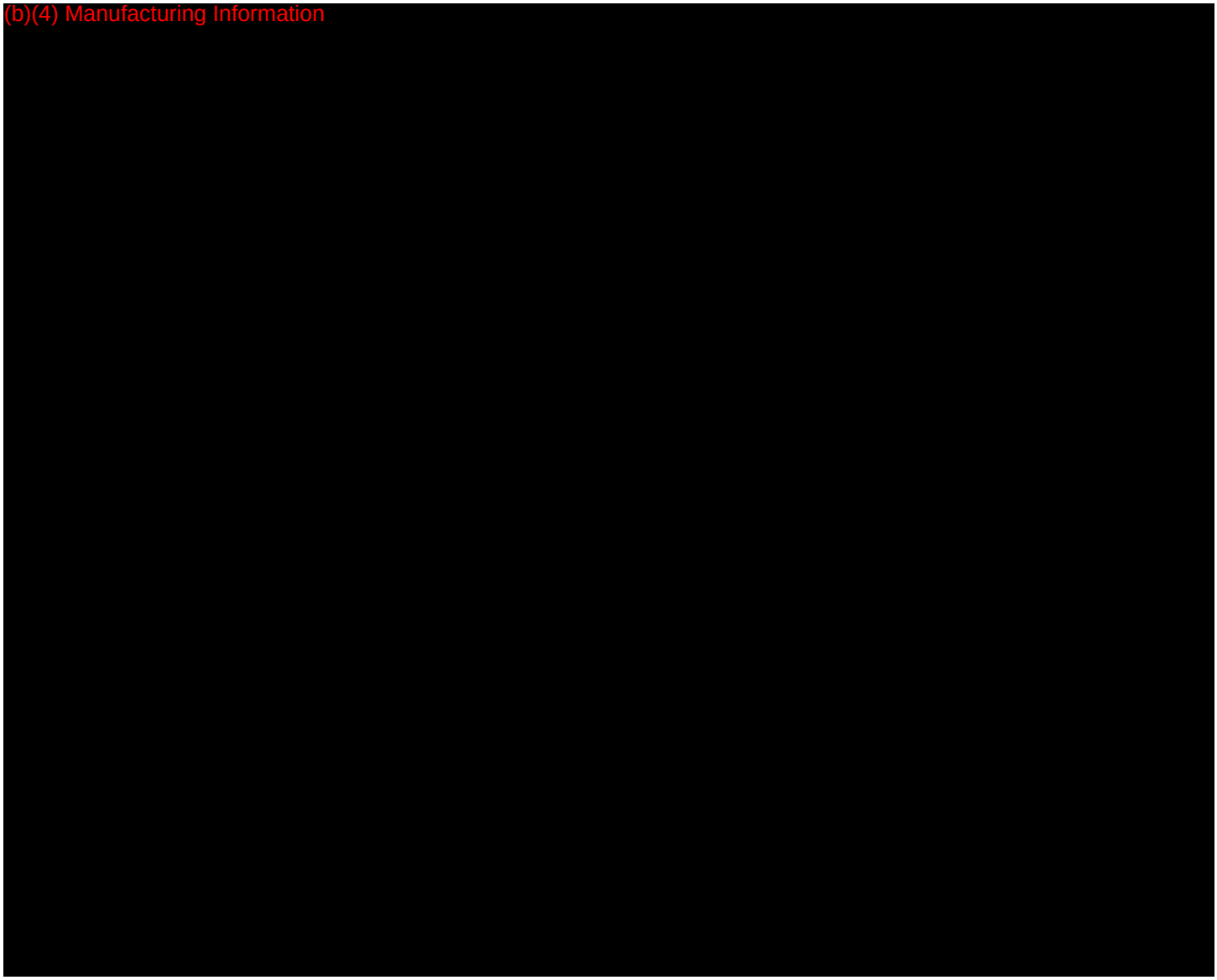

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Appendix 11-1

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

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Form Approved: OMB No. 0910-0120; Expiration Date: 8/31/10

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 13485:2003, Medical devices- Quality management systems- Requirements for regulatory purposes

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

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Form Approved: OMB No. 0910-0120; Expiration Date: 12/31/13

Department of Health and Human Services
Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

(b)(4)

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	(b)(4)	
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

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

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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]

(b)(4)

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# (b)(4)	
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: _____

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[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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Form Approved: OMB No. 0910-0120; Expiration Date: 8/31/10

Department of Health and Human Services
Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-5:1999, Biological Evaluation of Medical Devices, Part 5: Tests for In Vitro Cytotoxicity

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 2-153	
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

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Department of Health and Human Services
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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-6:2007, Biological evaluation of medical devices, Part 6: Tests for local effects after implantation

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3] # 2-120		
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

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-10:2006, Biological Evaluation of Medical Devices- Part 10: Tests for Irritation and Delayed-Type Hypersensitivity

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2] ?	☑	☐
FDA Recognition number [3] # 2-152		
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/cfStanderds/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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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-11:2006, Biological evaluation of medical devices- Part 11: Tests for systemic toxicity

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 2-118	
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: _____

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-12:2007, Biological Evaluation of Medical Devices- Part 12: Sample Preparation and Reference Materials

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 2-135	
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/sidsprog.html

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 14971:2007, Medical devices- Application of Risk Management to Medical Devices

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 5-40	
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:

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 22442-1:2007, Medical Devices Utilizing Animal Tissues and Their Derivatives- Part 1: Application of Risk Management

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: _____

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[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 22442-2:2007, Medical Devices Utilizing Animal Tissues and Their Derivatives- Part 2: Controls on Sourcing, Collection and

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).	☑	☐
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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: _____

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[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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Form Approved: OMB No. 0910-0120; Expiration Date: 8/31/10

Department of Health and Human Services
Food and Drug Administration

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(To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 22442-3:2007, Medical Devices Utilizing Animal Tissues and Their Derivatives- Part 3: Validation of the elimination and/or

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.	☑	☐
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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

(b)(4)

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.	☑	☐
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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN 1041:2008, Information supplied by the manufacturer with medical devices

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?	☑	☐
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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

(b)(4)

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Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# (b)(4)	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
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STANDARD TITLE [1]

(b)(4)

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Is this standard recognized by FDA [2] ?	☒	☐
FDA Recognition number [3]	# (b)(4)	
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Society For Biomaterials

Collagen scaffolds derived from fresh water fish origin and their biocompatibility

Falguni Pati,[1] Pallab Datta,[1] Basudam Adhikari,[2] Santanu Dhara,[1] Kuntal Ghosh,[3] Pradeep Kumar Das Mohapatra[3]

[1]School of Medical Science and Technology, Indian Institute of Technology, Kharagpur 721302, India
[2]Materials Science Centre, Indian Institute of Technology, Kharagpur 721302, India
[3]Department of Microbiology, Vidyasagar University, Midnapore 721102, India

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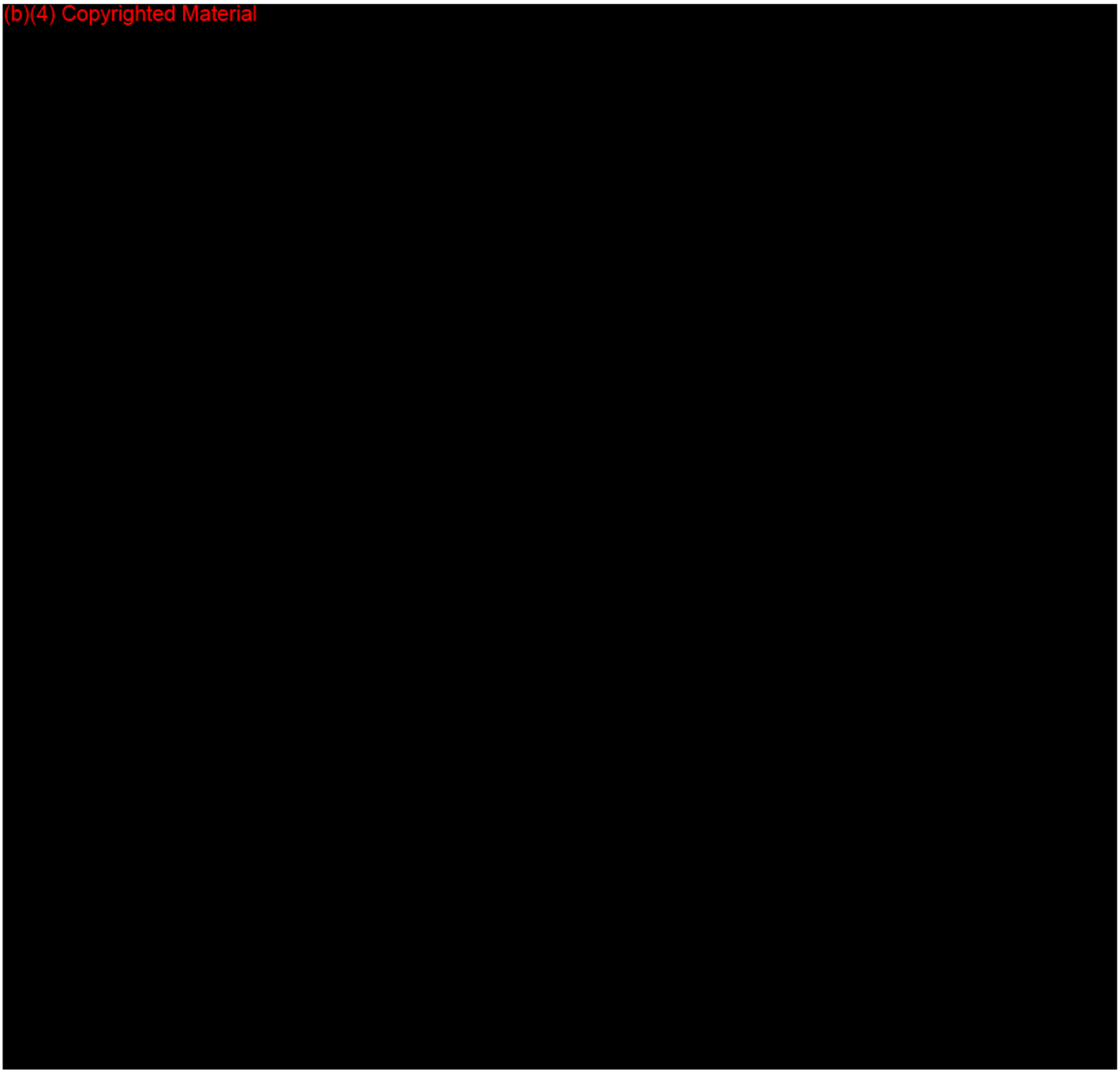

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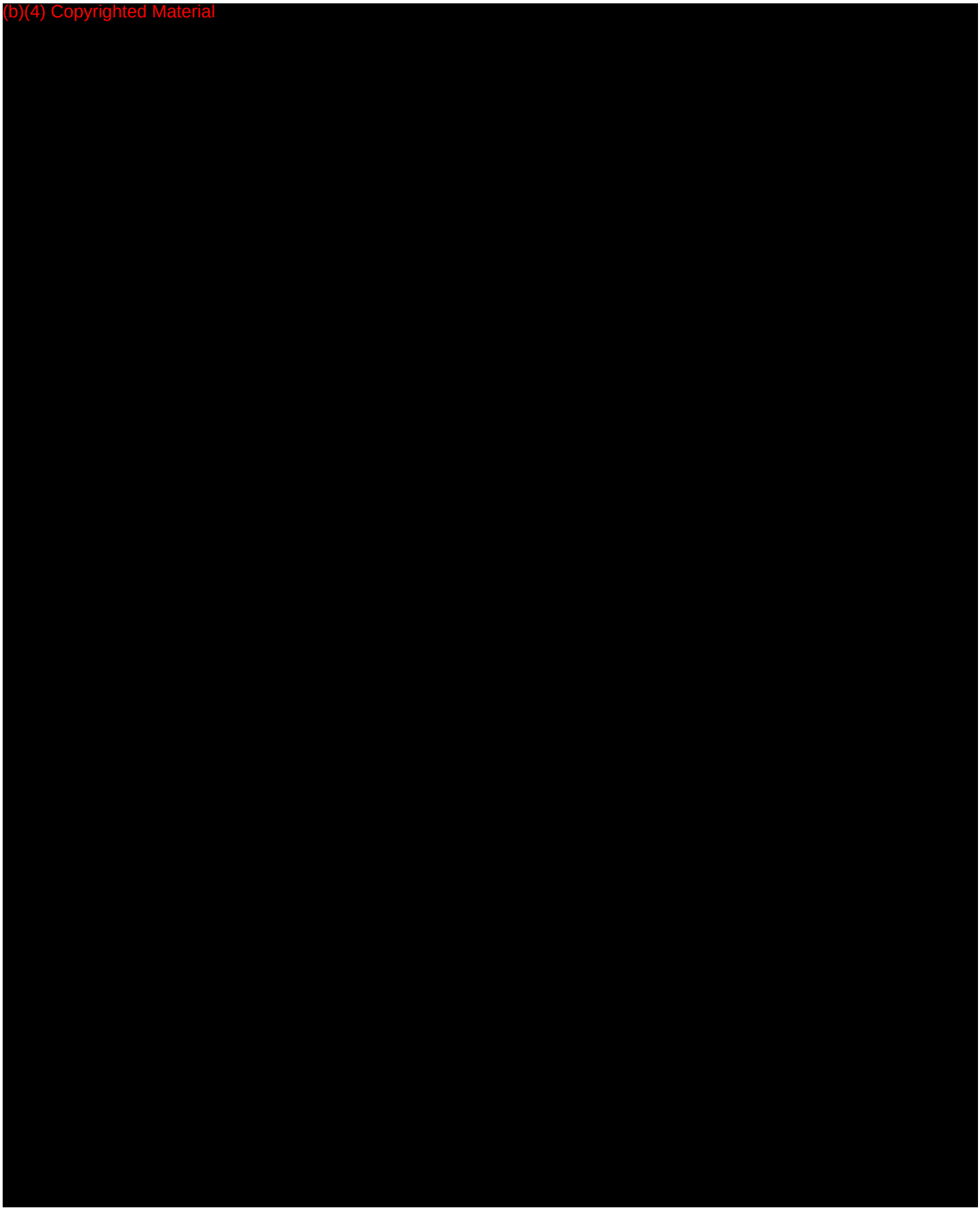

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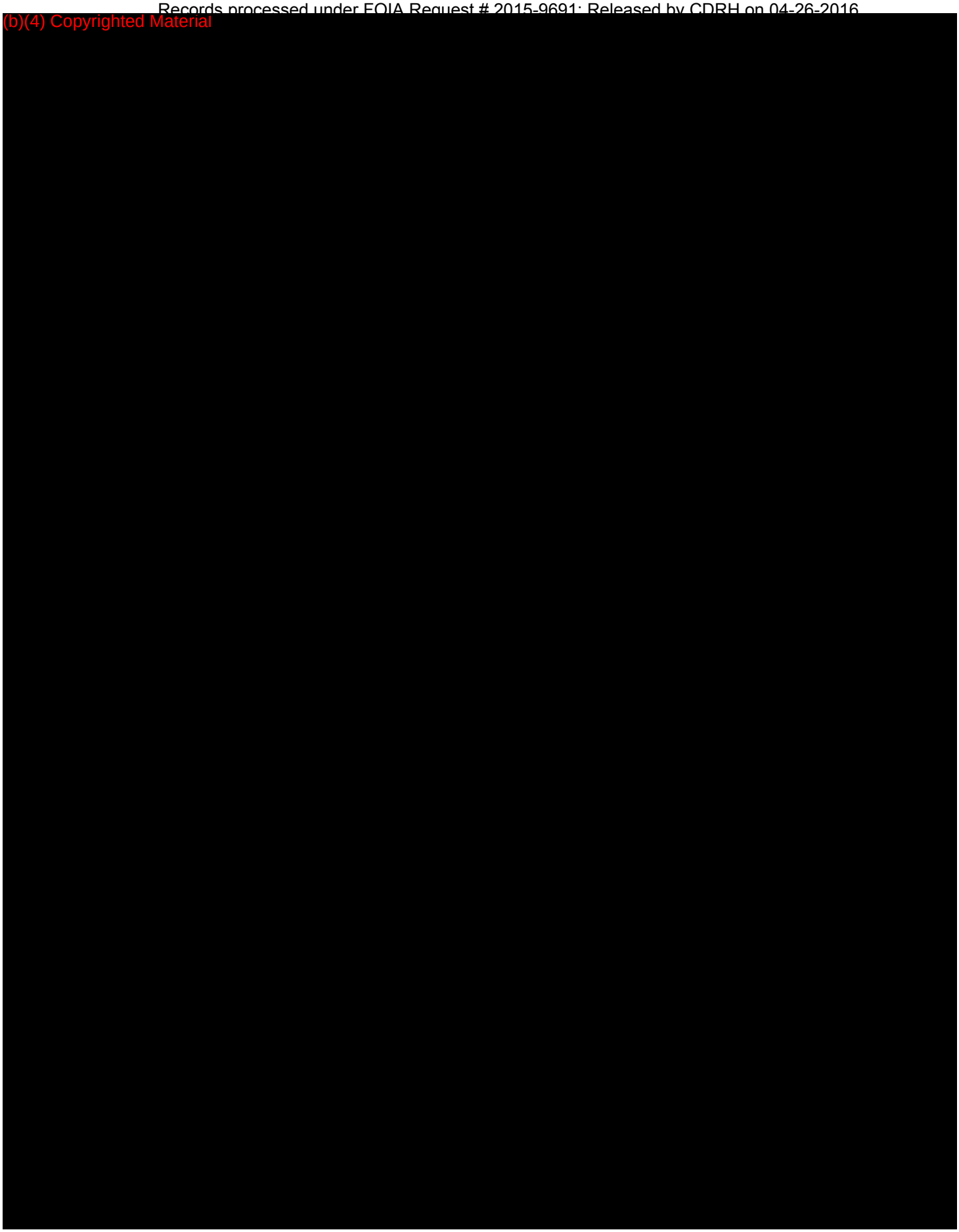

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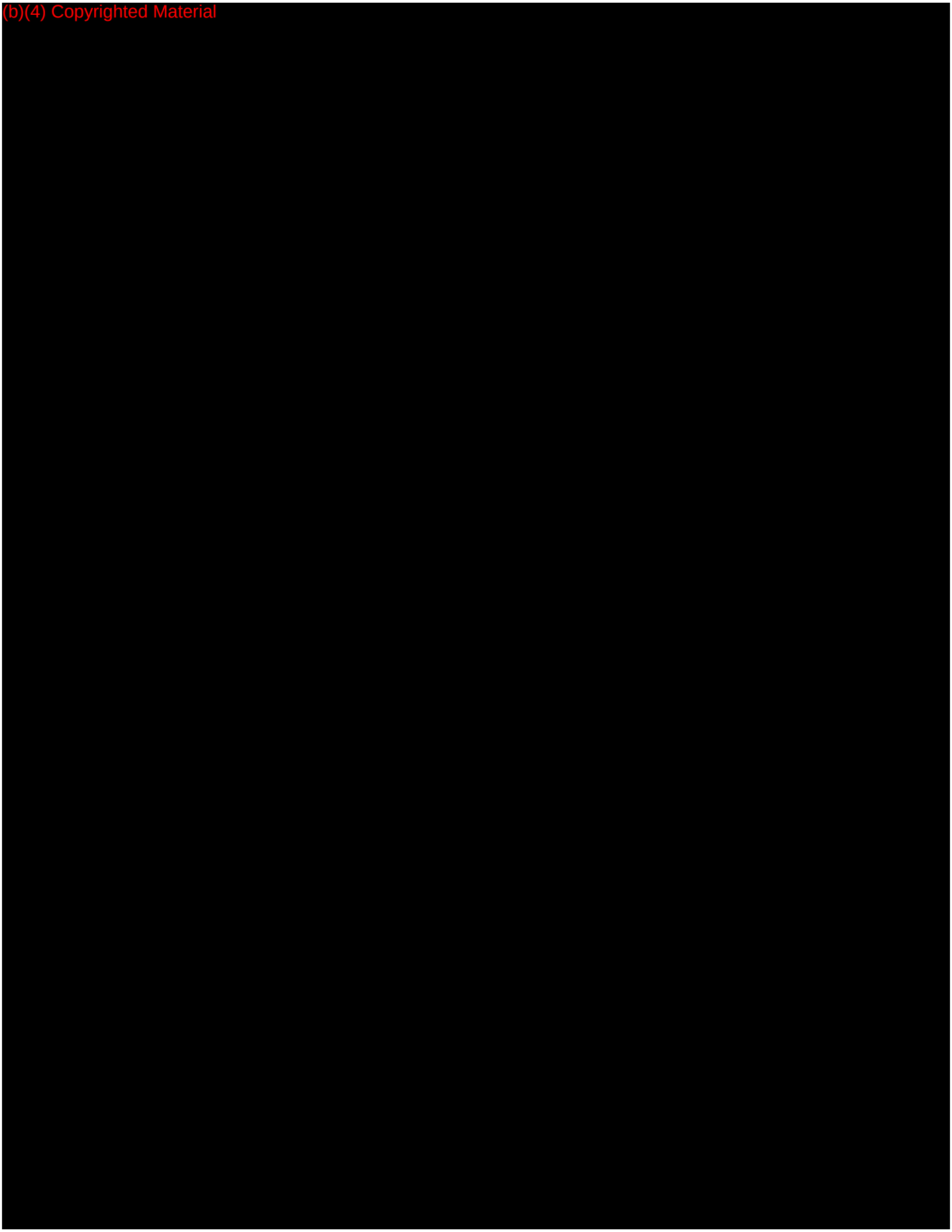

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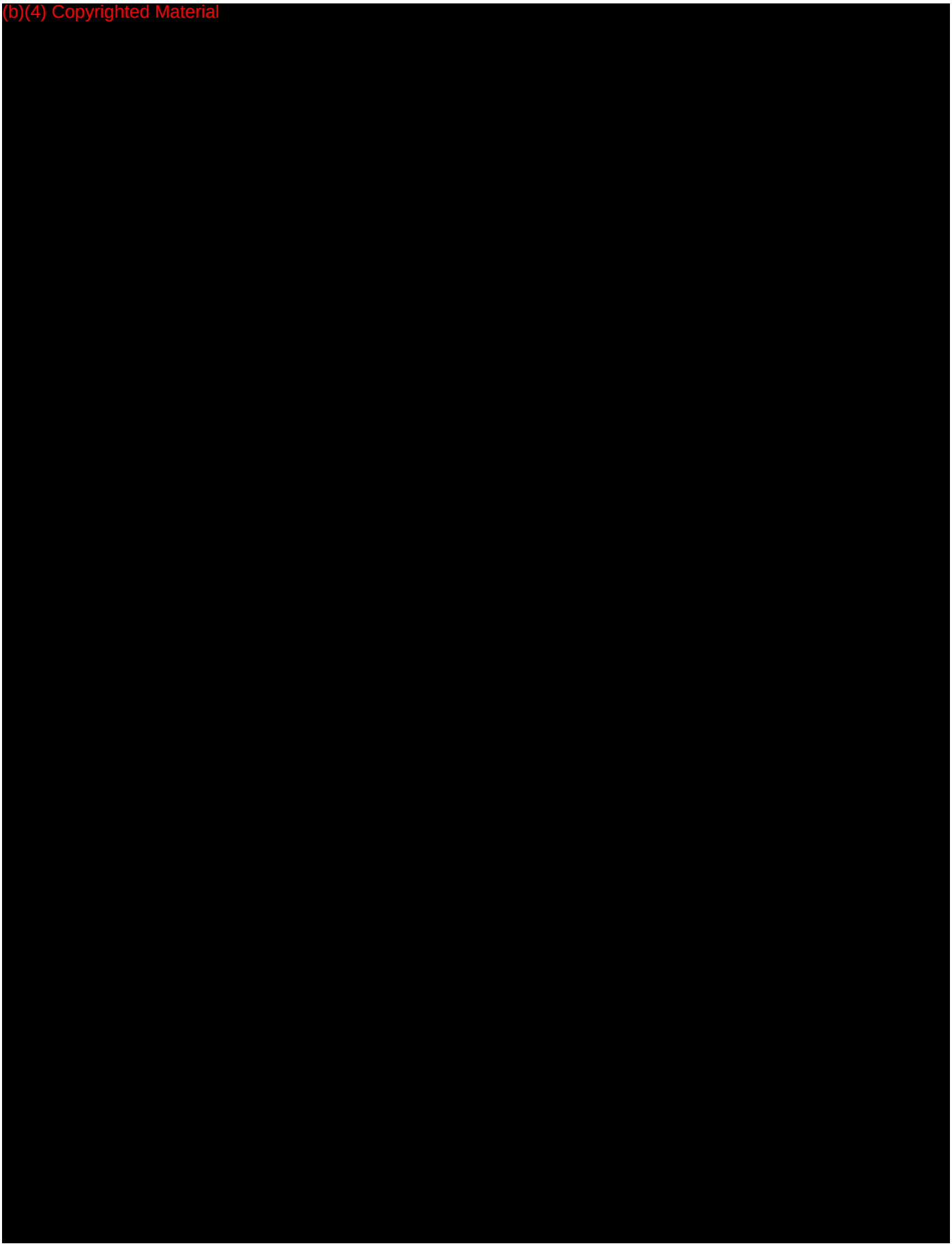

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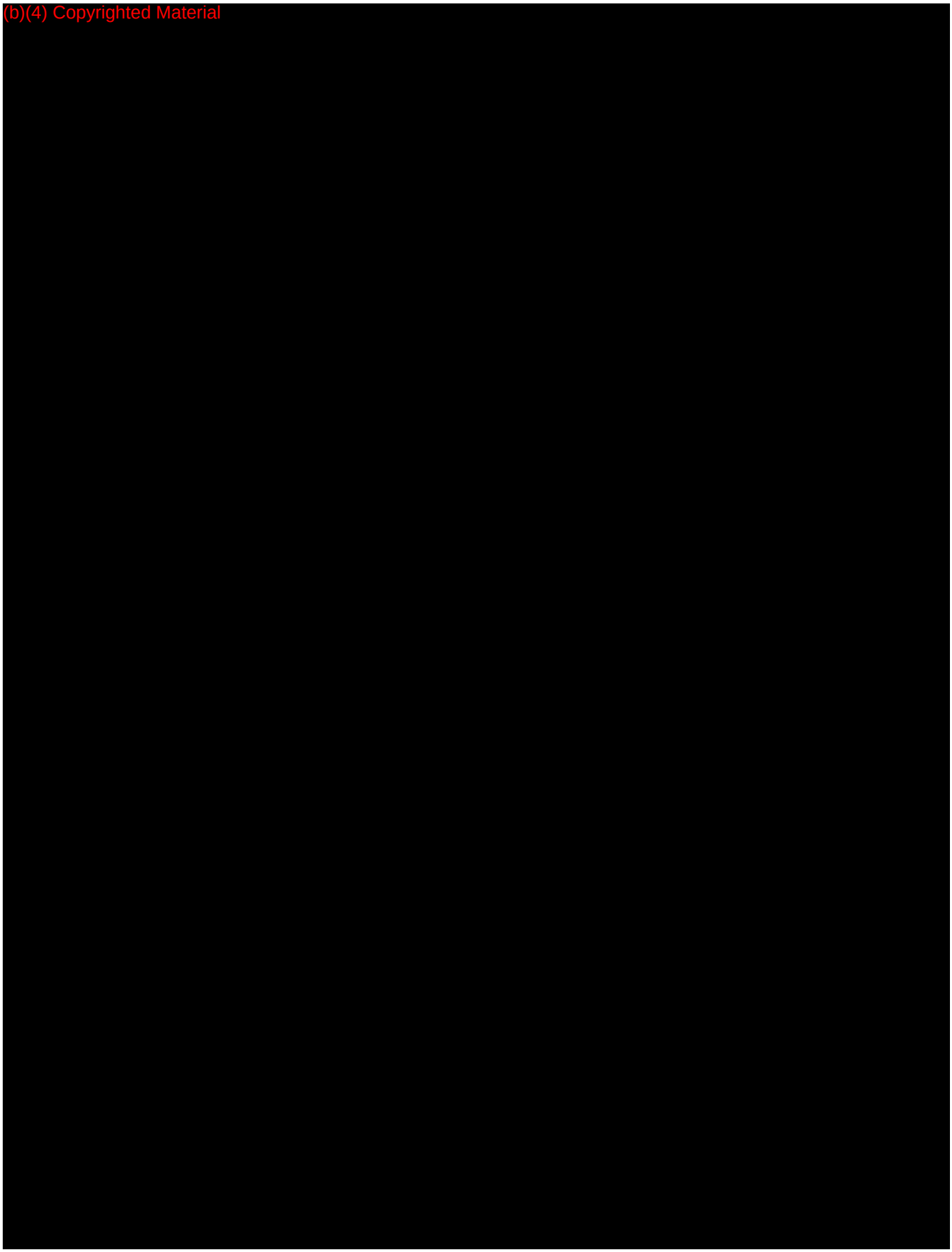

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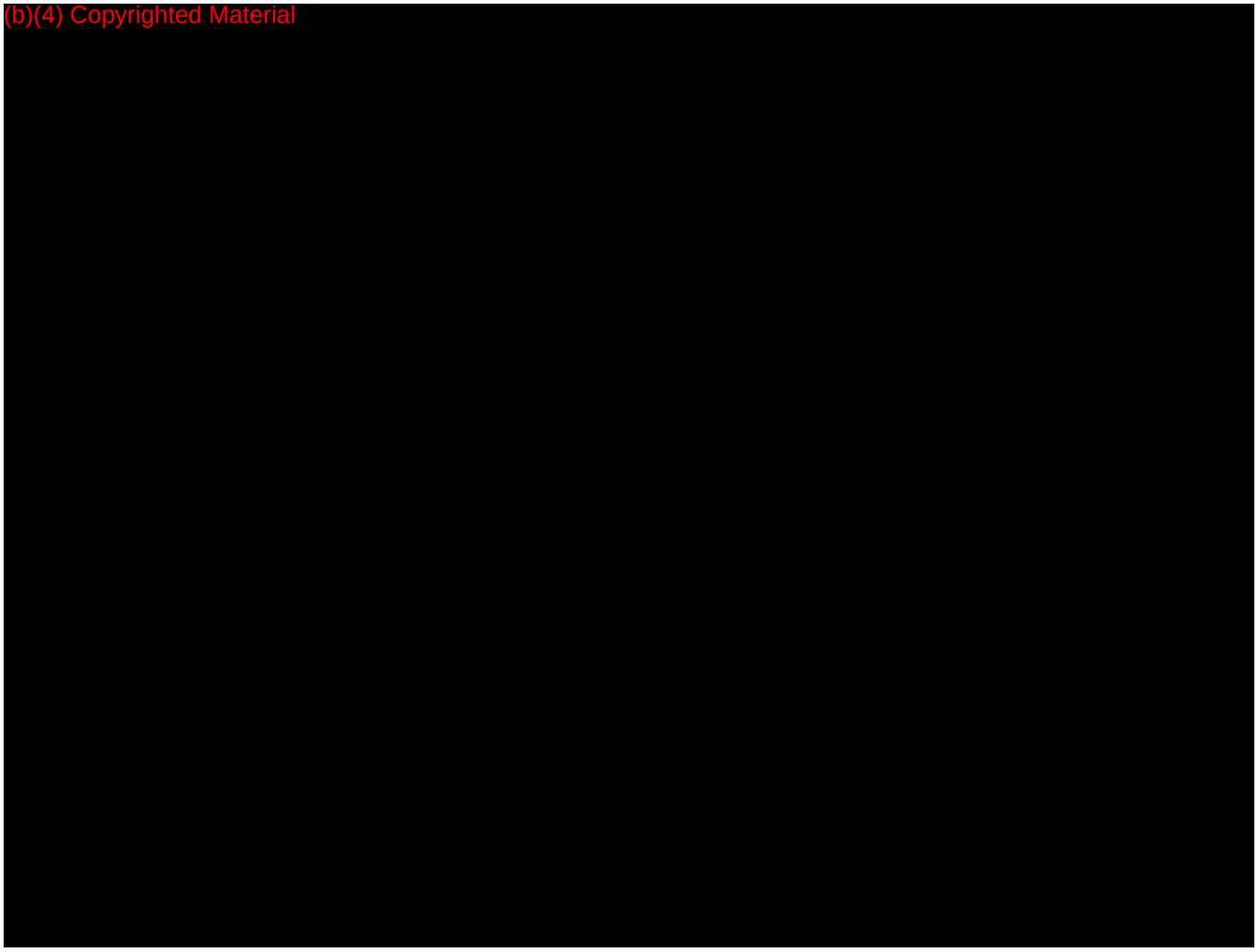

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Material Characteristics and Raw Material

(b)(4), (b)(6)

[redacted]

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Material characteristics

Index

1 List of Raw Materials for the production of MariGen Wound 2
(b)(4) 2
..... 2
..... 2
..... 3
..... 3
..... 3
..... 3
..... 4
..... 5
..... 6

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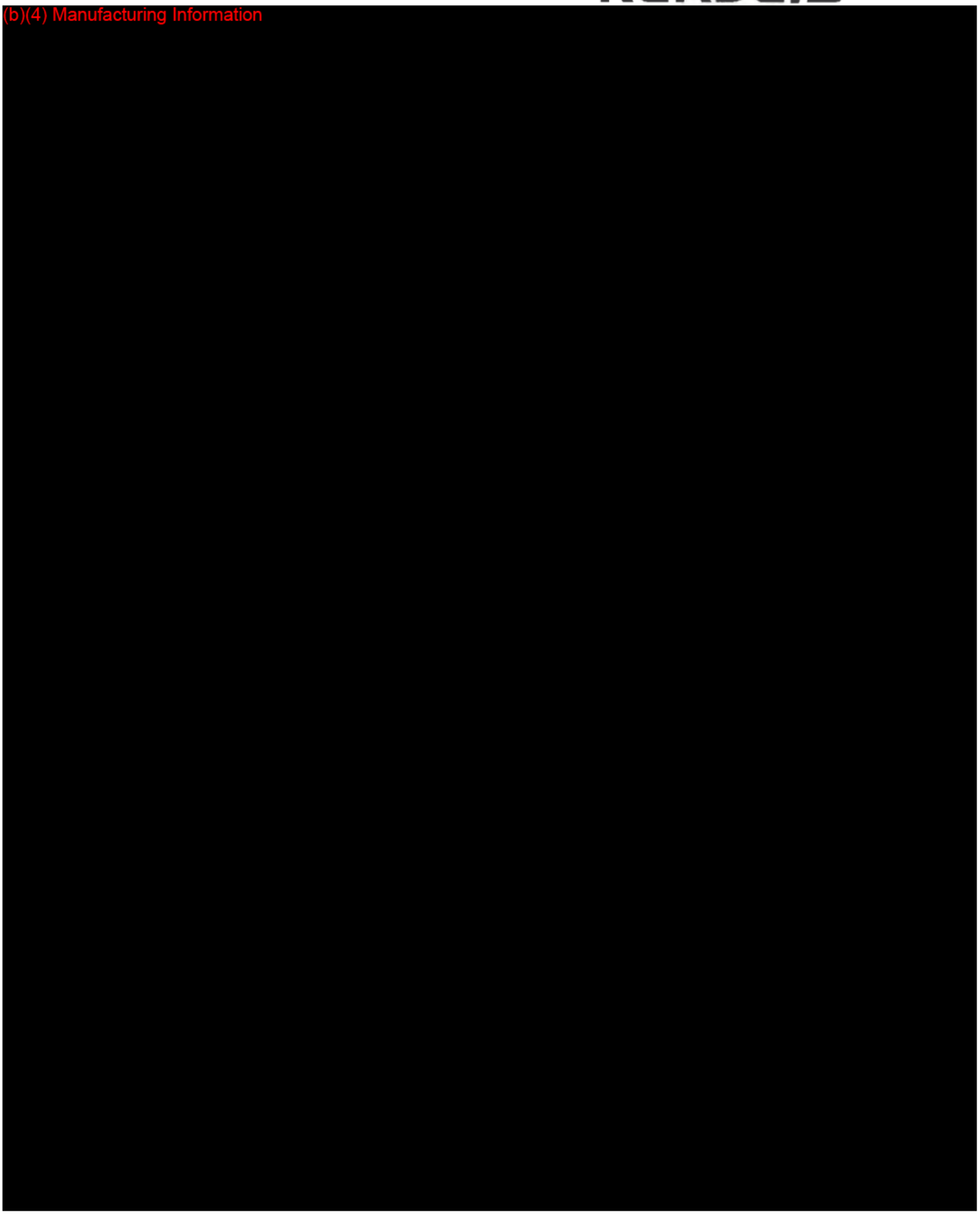
(b)(4) Manufacturing Information



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KERECIS

(b)(4) study

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KERECIS

Risk Management-(b)(4)

(b)(4)

Marigen Wound

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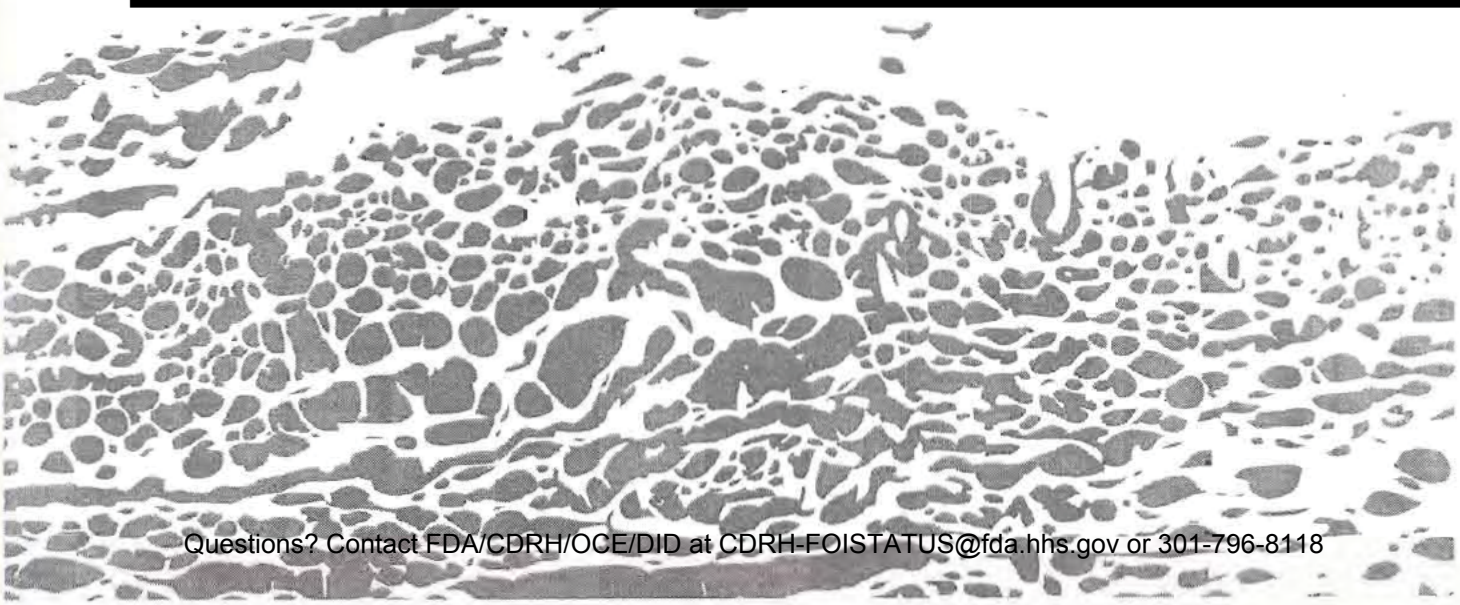

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MARIGEN™ Wound Risk Management – (b)(4)

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Appendix 11-10
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Innovation & Consumers

Biotechnology & Biomolecules

Vinnsla, virðisaukning & eldi
Value Chain, Processing & Aquaculture

Öryggi, umhverfi & erfðir
Food Safety, Environment & Genetics

Mælingar & miðlun
Analysis & Consulting

matís

Monitoring of the marine biosphere around Iceland 2010 and 2011

Hrönn Jörundsdóttir
Natasa Desnica
Þuríður Ragnarsdóttir
Helga Gunnlaugsdóttir

Öryggi, umhverfi og erfðir

Skýrsla Matís 28-12
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UMHVERFISSTOFNUN

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Skýrsluágrip Matís ohf
Icelandic Food and Biotech R&D

Report summary

ISSN: 1670-7192

Titill / Title	**Monitoring of the marine biosphere around Iceland 2010 and 2011** / Mengunarvöktun í lífríki sjávar við Ísland 2010 og 2011		
Höfundar / Authors	*Hrönn Jörundsdóttir, Natasa Desnica, Þuríður Ragnarsdóttir and Helga Gunnlaugsdóttir*		
Skýrsla / Report no.	28-12	*Útgáfudagur / Date:*	Júlí, 2012
Verknr. / project no.	2118		
Styrktaraðilar / funding:	*Umhverfisráðuneyti og sjávarútvegs- og landbúnaðarráðuneyti / Ministry for the Environment and Ministry of Fisheries and Agriculture*		
Ágrip á íslensku:	Í þessari skýrslu eru birtar niðurstöður árlegs vöktunarverkefnis sem styrkt var af umhverfisráðuneytinu og sjávarútvegs- og landbúnaðarráðuneytinu. Markmið með þessari vöktun er að uppfylla skuldbindingar Íslands varðandi Oslóar- og Parísarsamninginn (OSPAR), auk AMAP (Arctic Monitoring Assessment Program). Gögnin eru hluti af framlagi Íslands í gagnabanka Alþjóðahafrannsóknaráðsins (ICES). Hafrannsóknastofnunin sér um að afla sýna og Matís hefur umsjón með undirbúningi sýna og mælingum á snefilefnum í lífríki hafsins. Sýnin eru mæld á Matís og á Rannsóknastofu Háskóla Íslands í lyfja- og eiturefnafræði. Mæld voru ýmis ólífræn snefilefni og klórlífræn efni í þorski veiddum í árlegu vorralli Hafró í mars 2011 og í kræklingi sem safnað var á 11 stöðum í kringum landið í ágúst/sept 2010. Vöktun í lífríki sjávar við Ísland hófst 1989 og er sýnasöfnun eins frá ári til árs og unnið eftir alþjóðlegum sýnatökuleiðbeiningum. Gögnunum er safnað saman í gagnagrunn, í skýrslunni eru birtar yfirlitsmyndir fyrir sum efnanna sem fylgst er með. Kadmín er svæðisbundið hærra í íslenskum kræklingi samanborið við kræklingi frá öðrum löndum. Niðurstöður sýna breytingar í mynstri styrks klórlífrænna efna í kræklingi sem safnað var nálægt Hvalstöðinni í Hvalfirði í september 2010 sem eru sambærilegar við niðurstöður frá sama stað frá árinu 2009. Ekki voru sýnilegar breytingar í styrk þessara efna á söfnunarstað kræklings við Hvammsvík í Hvalfirði né á neinum öðrum söfnunarstað í kringum landið sem rannsakaður var 2010. Mikilvægt er að fylgjast með þessum breytingum í mynstri styrks klórlífrænna efna í kræklingi í vöktunarverkefninu á næstu árum til að sjá hvort þær eru enn til staðar. Ítarleg tölfræðigreiningu á gögnunum er í gangi þ.a. hægt sé að meta með vísindalegum aðferðum aukningu eða minnkun mengandi efna í lífríki sjávar hér við land.		
Lykilorð á íslensku:	*OSPAR, AMAP, vöktun á lífríki sjávar, ólífræn snefilefni, klórlífræn efni, þorskur, kræklingur.*		

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Skýrsluágrip Matís ohf

Icelandic Food and Biotech R&D

Report summary

ISSN: 1670-7192

Summary in English:	This report contains results of the annual monitoring of the biosphere around Iceland in 2010 and 2011. The project, overseen by the Environmental and Food Agency of Iceland, is to fulfil the OSPAR (Oslo and Paris agreement) and AMAP (Arctic Monitoring Assessment Program) agreements. The project was funded by Ministry for the Environment and Ministry of Fisheries and Agriculture. The data obtained is a part of Iceland´s contribution to the ICES databank (ices.dk). The collection of data started 1989. Matís is the coordinator for marine biota monitoring and is responsible for methods relating to sampling, preparation and analysis of samples. The samples were analyzed at Matís and the Department of Pharmacology and Toxicology at the University of Iceland. Trace metals and organochlorines were analysed in cod *(Gadus morhua)* caught in March 2011 and in blue mussel *(Mytilus edulis)* collected from 11 sites in August/Sept 2010. Marine monitoring began in Iceland 1989 and the sampling is carried out according to standardized sampling guidelines. Changes were observed in the organochlorine concentration patterns in blue mussels collected year 2010 at the sampling site Hvalstod in Hvalfjordur which are in line with results obtained year 2009. No noteworthy increase in organochlorine concentrations was however observed in blue mussels obtained at Hvammsvík in Hvalfjordur nor any of the other sample sites studied year 2010. These results need to be followed up in the annual monitoring of the biosphere around Iceland next year to see if this change in contaminant concentration pattern continues. A thorough statistical evaluation is on-going on all the available data from this monitoring program to analyse spatial and temporal trends of pollutants in the Icelandic marine biosphere.
English keywords:	*OSPAR, AMAP, monitoring, trace metals, organochlorine compounds, cod (Gadus Morhua), blue mussel (Mytilus edulis).*

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table of Contents

I. Introduction **1**

II. Sampling and preparation of samples **1**

2.1 Sampling 1
2.2 Preparation of samples prior to analysing 2

III. Analysis **2**

3.1 Metals and organic contaminants in biota 2
3.2 Methods 3
3.3 Quality assurance 3

IV. Results **4**

4.1 Biological variations 5
4.2 Heavy metals 5
4.3 Organic compounds 6

V. Conclusion **6**

VI. Acknowledgement **7**

VII. References **8**

APPENDICES

I. Biological measurements of Blue mussel (*Mytilus edulis*) 2009.
II. Biological measurements of Cod (*Gadus morhua*) 2010.
III. Quality assurance in metal analysis and in persistent organochlorines analysis.
IV. Results of trace metal analysis for Blue mussel (*Mytilus edulis*) 2009 and Cod (*Gadus Morhua*) 2010.
V. Results of persistent organochlorines analysis for Blue mussel (*Mytilus edulis*) 2009 and Cod (*Gadus morhua*) 2010.
VI. Graphs of biological variations in Cod (*Gadus morhua*) 1990-2010.
VII. Graphs of metals and organic compounds in Blue mussel (*Mytilus edulis*) 1990-2009.
VIII. Graphs of metals and organic compounds in Cod (*Gadus morhua*) 1990-2010.

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I. Introduction

This report contains the results of the annual monitoring of heavy metals and organochlorine analyses for blue mussel (*Mytilus edulis*), collected along the coast around Iceland in 2010, as well as for cod (*Gadus morhua*), which is collected in Icelandic territorial waters in 2011. Annual monitoring of trace metals in the marine biota around Iceland began in 1989 and the monitoring of organochlorine compounds a few years later, in 1991. Several reports have already been published on this matter (1-17). To meet the requirements of the OSPAR (Oslo and Paris agreement) and the AMAP (Arctic Monitoring and Assessment Program), data has been submitted to the ICES databank (www.ices.dk), the first data from 1989. The project is supervised by the Environment and Food Agency in Iceland and financed by The Ministry for the Environment as well as the Ministry of Fisheries and Agriculture and Matís. Matís is the coordinator for the marine biota monitoring and responsible for methods relating to sampling, sample preparation, analysis of samples and writing of this report. The samples were analyzed at Matís and the Department of Pharmacology and Toxicology at the University of Iceland.

II. Sampling and preparation of samples

The Marine Research Institute handles all sampling, while Matís is responsible for the storage of samples, sample preparation and chemical analysis.

2.1 Sampling

Using standard sampling guidelines (JMP, ICES and OSPAR), the sampling of cod (30-45 cm length, 2 samples (N-NW and NE)) was carried out in the annual bottom trawl survey in March 2011. Blue mussel samples, 4-6 cm length, were collected from 11 sites along the coast of the country in August/September 2010. Sampling locations for the blue mussel samples changed slightly this year i.e. the sampling location at Dvergasteinn, Álftarfjörður was moved due to limited availability of mussels at the original site. Sampling sites, i.e. coordinates, for all cod and blue mussel measured are shown in Figure 1. Icelandic waters have been divided into five main locations (N-NW, NE, SE-E, S, and SW) (6).

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	Sample	Location	Site specifications[a]	Type of industry
Blue mussel	Grímsey	66°33,134 18°01,407	B	
	Hvalstöð, Hvalfjörður	64°23,826 21°27,210	I	Landing and processing of whale catch
	Hvammsvík, Hvalfjörður	64°21,64 21°33,53	B	
	Hvítanes, Hvalfjörður	64°20,20 21°41,09	B	
	Hvassahraun	64°01,205 22°09,526	B	
	Straumur, Straumsvík	64°02,541 22°02,700	I	Aluminium factury
	Mjóifjörður I, (head)	65°11,28 14°00,48	B	
	Mjóifjörður II, (Hofsá)	65°12,156 13°47,733	B	
	Mjóifjörður III, Dalatangi	65°16,101 13°34,564	B	
	Úlfsá, Skutulsfjörður	66°03,36 23°10,02	I	Waste incineration
	Dvergasteinn, Álftafjörður	65°58,29 23°04,50	B	
Cod	Cod N NW	67°02,55 23°29,93	B	
	Cod NE	67°01,77 15°44,86	B	

a: B = Baseline, I = Impact

Figure 1. Locations for sampling of blue mussel (Mytilus edulis) 2010 and cod (Gadus morhua) 2011.

2.2 Preparation of samples prior to analysing

Each sample of mussel contained 50 ± 5 individuals. Each mussel was weighed and its length (4-6 cm), height and width measured. The flesh and the shell were then weighed separately (Appendix I). After this each sample (50 individuals) was homogenized and frozen until analysis was performed.

30-45 cm long cod was selected, each sample containing 25 ± 5 individuals. At the time of the sampling, the total weight as well as the gender of each fish was determined, livers were put in pre-weighed and pre-cleaned glass jars and, finally, the fish was gutted. All samples were kept frozen until further preparation for analysis took place. Later, the otoliths were removed for age determination, the fish was filleted, skinned, and the flesh weighed (Appendix II). Finally, each sample of flesh (25 ± 5 individuals) was homogenized and frozen until analyses were performed. The livers of each cod sample were divided into sub samples, according to the weight of the livers. All liver samples were homogenized and kept frozen until analysis took place.

III. Analysis

3.1 Metals and organic contaminants in biota

The trace metal analysis of lead, cadmium, copper, zinc, mercury, arsenic and selenium was carried out at Matís, as well as analysis of the supporting parameters, dry matter and fat. The following Persistent Organic Pollutants (POP) were analysed at the Department of Pharmacology and Toxicology at the University of Iceland: 11 PCBs, HCB, α-HCH, β-HCH and γ-HCH, p,p'-DDT o,p'-DDT, p,p'-DDE and p,p'-DDD, transnonachlor, α-chlordan, γ-chlordan, oxychlordan, Tox-26, Tox-50, Tox-62, BDE-47, BDE-99, and BDE-100. Table 1 presents the samples and all the parameters measured in each sample.

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Table 1. Parameters measured in different samples.

Species	Number of samples	Number of individuals	Type of sample	Number of group	Inorganic contaminants	Organic contaminants	Other
Mussel, 2010 (*Mytilus edulis*)	11	50			Cu, Zn, As, Se, Cd, Hg, Pb	*	Dry matter and fat
Cod, 2011 (*Gadus morhua*)	2	25	Flesh	1	Hg		Dry matter and fat
			Liver	6	Cu, Zn, As, Se, Cd, Pb	*	Dry matter and fat
Labels: Cod N NW(2) Cod NE							

* PCB # 28, 31, 52, 101, 105, 118, 138, 153, 156, 170, 180, α , β , γ HCH, HCB, p,p' DDT, o,p' DDT, p,p' DDE, p,p' DDD, *trans* nonachlor, α , γ Chlordan, Oxychlordan, Toxaphene 26, 50, 62, BDE # 47, 99 and 100.

Only three liver groups from each cod sample were analyzed to optimize the project resources compared to 5-6 liver groups in the previous years.

3.2 Methods

Inorganic contaminants (Cd, Cu, Zn, As, Se, Hg, Pb) in the samples were determined by ICP-MS after mineralization of the samples with closed vessel acid digestion. Portions (up to 200 mg weighed to 0.1 mg) of freeze dried samples (cod liver was not freeze dried and weighted wet) together with 3 ml HNO_3 and 1.5 ml H_2O_2 were transferred to 50 ml digestion bombs. Samples were digested in a Mars5 microwave oven (CEM, North Carolina, USA), according to method SV-25-02-SN in Matis Quality manual. The digested sample solutions were quantitatively transferred to 50 ml polypropylene tubes and diluted to 30 ml with Milli-Q water. The concentration of the different elements (Cd, Cu, Zn, As, Se, Hg, Pb) in these digests was determined by ICP-MS (Agilent 7500ce, Waldbronn, Germany). ^{115}In was used as internal standard. The organochlorine compounds were analysed by GC-ECD using HP5890 Series II with an automatic injector (HP7673). A detailed description of the analyses of organic compounds and supporting parameters (dry matter and fat) has been given in a previous report (7) and for the inorganic contaminants the analytical method used is presented in details in method SV-22-02-SN-1 in Matis Quality manual.

3.3 Quality assurance

The quality of the metal analysis was checked in several ways. Certified reference materials are routinely treated and analysed in the same manner as the samples. Results for analysis of reference materials and limits of detection are shown in Table 2 and 3 in appendix III. Also shown are Z scores for the reference materials. The trace analytical lab at the Matís has participated in QUASIMEME annually with satisfactory results. Also, Matís participated in SLV test with satisfactory results. The limit of detection (LOD) was calculated as follows: 20 digested blank samples were

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run and standard deviation (S.D.) calculated. LOD represents 3 x S.D. in blank samples.

For **organic contaminants,** a solvent blank and sample of certified reference material was extracted with each batch of samples. A certified standard solution was also run with the samples to check own standards. The limit of detection was estimated to be 3 x STDEV of the blanks. The Department of Pharmacology and Toxicology at the University of Iceland has participated in QUASIMEME annually with satisfactory results. Results for analysis in certificate mussel and cod liver samples are presented in appendix III, Tables 4 and 5 along with relevant detection limits in Table 6.

IV. Results

This report contains data from the years 2010 and 2011, due to budget constrains these results have not been statistically evaluated using present and previous data from the annual monitoring of the biosphere around Iceland in order to evaluate time trend or spatial difference. Similar changes as reported for the monitoring of blue mussel 2009 (17) regarding the contaminant concentration patterns were observed in blue mussels collected 2010 near the whale processing plant in Hvalfjordur, for details see Figure 5a in Appendix VII, site Hvalstod, Hvalfjordur, this sampling site is located 400m south-west of the processing plant of whale catch. The results show that the concentration of persistent organochlorine compounds in blue mussels are now highest at the site Hvalstod in Hvalfjordur, this site has until 2009 not been notably different from other sample sites in terms of POP concentrations, while year 2009 and 2010 an increase was observed for ∑3PCB, p,p´-DDE, HCB and trans-nonachlor in blue mussels from this site (Table 9a in Appendix V and Figure 5a in Appendix VII). Furthermore, the ratio PCB153/DDE has decreased from 2,8 (year 2008) to 0,4 (year 2009 and 2010). This ratio has typically been 2-4 in blue mussels at other sample sites around Iceland. This decrease in the PCB153/DDE ratio indicates that there is a new source of pollution at the site Hvalstod in Hvalfjordur. The reason for the new source pollution has not been studied, but a possible cause is that during the summer 2009 the whale processing plant in Hvalfjordur started processing fin whales (*Balaenoptera physalus*) again after a 20 year long break in its operation. No noteworthy increase in POP concentrations was observed year 2009 in blue mussels obtained from another annual sampling site in Hvalfjordur i.e. Hvítanes /Hvammsvík nor any of the other sample locations studied (Figures 5a and 5b). These results need to be followed up in the annual monitoring of the biosphere around Iceland next year to see if this change in contaminant concentration pattern continues. To be able to monitor long term trends and to indicate large scale spatial difference in the marine biota around Iceland, data from many years need to be assessed with statistical models. This work has now started as a Ph.D. project thanks to a project grant from the Icelandic Research Fund obtained January 2011.

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4.1 Biological variations

Figures 2a-d in appendix VI shows the biological variation in cod *(Gadus morhua)* 1990-2011, (average age, average weight of ungutted fish, average weight of liver, and average fat content in liver).

4.2 Heavy metals

Results for metals in blue mussel (2010) and cod (2011) are presented in Tables 7 and 8 in appendix IV. New data is presented along with data from previous years (1, 4-14) in figures 3a-f and 4a-c (Appendix VII) for blue mussel and in figures 6a-b and 7a-f (Appendix VIII) for cod, giving an overview of a period of ca. 20 years. It should be noted that results for cod are presented on wet weight basis, while the result for mussel are presented on dry weight basis.

4.2.1 Blue mussel

In the year 2010 no blue mussel sample was obtained from Eyri in Hvalfjordur as the mussels at this site were all too small < 4 cm and the sampling site was therefore moved to Hvammsvík (64°21,64-21°33,53). The annual sampling site for the blue mussel sample taken at Hvítanes in Hvalfjordur (64°21,85-21°29,8) has been moved slightly from previous location. The name of this sampling station has though not been changed in the figures in appendix VII that illustrate the results obtained for trace metals and organic compounds in blue mussels at the various sample sites around Iceland over the past 21 years.

Figures 3a-f in appendix VII, show the average concentration of heavy metals in blue mussel from the years 1990-2010, on dry weight basis. The horizontal red line shows the ICES90 75% baseline (11). Figures 4a-c in appendix VII show average concentrations (dw), of heavy metals in blue mussel from different sampling sites, 1990-2010. Metal concentrations vary considerably between years and different locations. This year the concentration of cadmium is higher in Grímsey and Dvergasteinn compared to other locations. According to the existing monitoring data (1999-2010) the concentration of arsenic is noticeably higher at Úlfsá, Skutulsfjörður than at any of the other sample locations for blue mussel. The results show low values for mercury in blue mussel when compared with ICES90 75% baseline values. The copper concentrations are generally low in blue mussel, while the zink concentrations are close to the ICES90 75% value. The cadmium levels are high in blue mussels from Icelandic coasts, compared to other areas. This cadmium is considered to be of natural origin since no anthropogenic source is known.

4.2.2 Cod

Figures 6a-b in appendix VIII show the average heavy metal concentration in livers of 30-45 cm cod (wet weight), caught in Icelandic waters in March every year between 1990-2011. Figures 7a-f in appendix VIII show average concentrations (w.w.) of heavy metals in cod livers from different sampling sites, between the years 1990-2011. Mercury is measured in the flesh instead of in the liver. Lead concentration was below the limits of detection in all samples. Variations in concentration between years

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and locations over the time interval are shown in Figures 6a-b and 7a-f in Appendix VIII. The concentration of heavy metals in cod from Icelandic waters is low compared to cod from other northern locations (6). As for the blue mussel the only exception is cadmium which is probably of natural origin reflecting the natural background values. However, the amount of cadmium in cod and other species in Icelandic coastal waters is far below the TWI (Tolerable Weekly Intake) standard of WHO, even with heavy consumption (6).

4.3 Organic compounds

Results for organic compounds in blue mussel (2010) and cod (2011) are presented in appendix V, Tables 9 and 10. The results for cod are presented on a wet-weight basis but results for blue mussel are on a dry-weight basis. New data is shown along with data from previous years (1, 4-10) in Figures 5a-b (Appendix VII) for blue mussel and in figures 8 and 9a-e (Appendix VIII) for cod, giving an overview of a 17-19 year period.

4.3.1 Blue mussel

Figures 5a-b in appendix VII, show the concentration on dry-weight basis of organic compounds in blue mussel from different locations in Iceland 1991-2010. The PCB congeners included in the Σ3PCBs are CB-118, CB-138 and CB-153 where the sum ranges from 50-80% of the sum of 11 PCB analysed. The most common organochlorines found in blue mussel are PCBs and DDE. As mentioned in results (i.e. section IV above) changes were observed in the organochlorine concentration patterns in blue mussels collected September 2010 at the sampling site Hvalstod in Hvalfjordur, for details see Figure 5a in Appendix VII and discussions in section Results IV. The concentration of PCBs in blue mussel found in Iceland are comparable with values found in mussels from remote areas of the west coast of United States and also similar to the lowest values found in mussels on the coast of the United Kingdom and Ireland (6). In general, concentrations of HCH, HCB and other DDTs except for DDE are low, close to the limit of detection.

4.3.2 Cod

Figure 8 in appendix VIII shows the average concentration on wet-weight basis of organic compounds in livers of 30-45 cm cod, caught in Icelandic waters in March every year between 1991 and 2011. Figures 9a-e in appendix VIII show the average concentrations (w.w.) of some organic compounds in cod from different sampling sites, 1991-2010. The sum of seven PCBs (CB-28, CB-52, CB-101, CB-118, CB-138, CB-153 and CB-180) is about 90% of the 11 PCBs measured. The concentrations of the organic substances that are measured in cod from Icelandic waters correspond to the lowest values observed elsewhere (6).

V. Conclusion

This report contains the results of an evaluation of trace elements in Icelandic marine biota for the years 2010 and 2011. It adds to the information gathered every year to

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

determine whether the concentration of trace elements is increasing, decreasing or not changing; if current situation is a cause for health concerns; and if the marine environment is being threatened by pollution**.**

This data has not been statistically evaluated using present and previous results in order to evaluate time trend or spatial difference. However, there are apparently no obvious changes in contaminant concentrations pattern seen in previous years. **A full statistical analysis of all data is needed to confirm changes if any.** This was done in 1998 (6) but additional data collected over the last 12 years calls for a new methodical statistical evaluation of the existing Icelandic monitoring data, this work has now started as a Ph.D. project thanks to a project grant from the Icelandic Research Fund obtained January 2011. In addition, when comparing data of livers it is necessary to keep in mind the factors (i.e. fat, age, d.w.) that may affect the quantity and concentration of trace elements.

Iceland is unique in terms of geology, oceanography and meteorology. High levels of heavy metals, particularly cadmium, occur naturally in the environment in Iceland. Therefore, natural background values need to be kept in mind when comparing contamination levels with other countries.

VI. Acknowledgement

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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Appendix I.

Biological measurements of Blue mussel (*Mytilus edulis*)

2009

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Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**12.8.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Ulfsá**	Date of preparation	28.10.2011
Coordinates:	66°03,36-23°10,02	Matis#	R11-2123-9

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	45,6	22,1	19,3	11,48	5,78	5,56
2	48,6	23,6	21,5	12,25	7,39	4,70
3	53,8	24,0	20,6	15,65	8,34	7,10
4	49,2	24,4	21,1	8,74	2,87	6,68
5	48,8	22,9	22,8	15,20	7,60	7,37
6	48,5	23,2	22,7	15,11	7,63	7,28
7	51,3	23,9	21,9	16,30	8,42	7,65
8	56,5	26,4	23,6	20,96	11,28	9,36
9	57,9	28,5	26,1	27,10	12,65	14,26
10	57,2	25,7	26,0	26,80	12,45	14,08
11	49,2	22,1	20,0	11,24	6,40	4,74
12	48,1	20,4	21,1	12,79	6,07	6,53
13	46,4	22,4	20,6	13,13	6,93	5,95
14	52,7	23,1	20,9	16,38	9,59	6,61
15	56,6	26,1	21,1	17,69	8,82	8,80
16	51,0	22,9	23,3	17,29	8,50	8,56
17	53,4	25,3	22,2	16,52	8,19	8,13
18	53,4	24,7	22,7	19,62	9,84	9,63
19	58,7	27,1	26,4	23,92	13,31	10,39
20	43,2	24,1	18,5	7,89	4,56	3,22
21	46,4	22,6	19,3	11,40	5,79	5,44
22	47,2	22,5	20,1	11,11	6,33	4,67
23	51,8	24,2	21,4	14,45	8,49	5,85
24	47,9	20,5	20,3	11,87	6,45	5,21
25	48,5	22,2	22,0	14,90	7,52	7,23
26	49,3	24,0	22,6	15,34	7,70	7,46
27	53,1	24,1	21,1	13,84	7,50	6,13
28	52,4	26,4	21,1	17,09	9,01	7,87
29	44,0	21,3	19,5	9,40	5,39	3,90
30	46,0	22,5	27,5	9,64	5,00	4,46
31	52,5	24,9	19,5	14,02	7,31	6,52
32	51,9	22,7	20,0	14,40	7,16	7,17
33	56,1	22,5	25,2	19,36	8,60	10,54
34	53,6	25,2	22,5	18,46	9,43	8,8
35	54,9	27,0	21,3	16,89	10,18	6,46
36	54,5	22,1	22,5	19,83	10,53	9,16
37	59,1	29,0	24,3	22,78	11,98	10,65
38	55,3	27,7	23,1	20,41	10,95	9,18
39	41,0	19,3	18,0	8,19	4,13	3,70
40	46,8	22,4	18,4	11,58	5,93	5,44
41	47,3	23,1	19,4	11,74	6,91	4,71
42	45,7	20,7	20,8	12,61	5,43	6,97
43	46,4	24,5	17,0	9,67	5,50	4,05
44	46,6	21,3	19,3	10,86	5,66	4,82
45	48,5	23,5	21,7	13,62	6,49	7,00
46	55,5	27,5	20,0	15,63	9,02	6,38
47	52,5	25,6	21,9	15,32	9,19	5,92
48	57,0	24,3	22,3	18,27	8,74	8,88
49	56,0	25,4	22,1	17,98	9,07	8,68
50	57,1	28,3	23,4	22,56	11,42	10,88
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	51,10	24,00	21,60	15,39	7,99	7,21
Stdev	4,48	2,23	2,20	4,56	2,32	2,41
Min	41,00	19,30	17,00	7,89	2,87	3,22
Max	59,10	29,00	27,50	27,10	13,31	14,26

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Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**14.08.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Hvassahraun**	Date of preparation	23.09.2011
Coordinates:	64°01,205-22°09,526	Matis#:	R11-2123-4

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	54,0	27,3	22,7	17,85	9,55	8,04
2	55,2	30,5	23,4	19,68	11,63	7,73
3	55,0	27,2	25,7	21,56	10,33	10,69
4	54,8	28,0	23,0	19,03	9,84	8,89
5	50,8	25,2	22,4	15,39	8,04	7,22
6	51,3	26,4	24,1	19,20	9,83	9,27
7	51,2	26,1	20,8	15,52	8,27	7,03
8	47,5	24,5	23,5	14,78	8,11	6,50
9	48,5	25,4	20,5	13,48	7,71	5,61
10	53,6	26,9	22,5	17,20	9,22	7,58
11	52,8	26,3	24,1	18,46	10,80	7,43
12	51,3	25,8	22,6	15,31	8,85	6,27
13	47,4	24,0	21,5	12,84	6,31	6,32
14	52,7	26,7	21,7	16,27	8,83	7,34
15	39,7	26,7	22,6	14,22	7,36	6,79
16	54,2	25,5	24,1	18,11	10,14	7,71
17	48,5	26,4	20,2	12,71	7,27	5,29
18	54,2	26,1	21,4	16,13	9,64	6,44
19	47,9	24,6	21,4	13,13	6,85	5,98
20	47,0	24,8	20,6	13,04	6,19	6,32
21	41,6	24,2	18,2	8,99	4,42	4,24
22	46,8	24,9	20,4	11,98	6,18	5,62
23	47,8	24,8	21,4	12,78	6,79	5,93
24	46,3	25,0	21,5	12,80	6,90	5,80
25	46,5	23,6	19,9	11,12	6,20	4,79
26	49,1	28,7	19,8	14,16	8,49	5,57
27	52,7	26,0	22,0	16,37	9,24	6,92
28	56,6	27,2	23,8	21,85	11,95	9,63
29	51,3	26,9	21,5	16,47	9,57	6,84
30	51,3	28,1	25,6	23,50	12,08	11,33
31	42,9	23,0	18,1	9,88	5,74	4,05
32	49,9	26,0	21,3	15,80	8,05	7,62
33	47,3	27,7	21,1	14,47	7,75	6,60
34	51,1	26,6	22,7	15,85	7,99	7,40
35	57,9	26,1	25,6	24,28	12,91	11,22
36	52,6	25,7	23,6	16,74	9,21	7,41
37	52,9	26,2	20,9	14,60	8,66	5,70
38	53,7	27,3	23,3	19,05	10,84	8,12
39	51,1	25,4	22,3	16,19	8,43	7,44
40	56,5	28,0	24,7	22,71	12,87	9,66
41	44,6	25,3	16,6	9,58	5,22	4,27
42	46,2	26,0	21,8	13,97	7,49	6,40
43	50,6	25,9	19,6	12,79	7,23	5,45
44	47,0	25,8	19,2	10,90	6,49	4,32
45	48,8	25,1	21,3	14,20	6,81	6,31
46	50,1	25,8	21,4	15,02	7,81	7,03
47	51,5	25,6	24,0	17,10	10,42	6,55
48	57,3	27,7	25,3	22,08	12,68	9,29
49	55,1	27,7	22,0	18,68	10,50	8,04
50	55,9	26,0	25,5	19,74	11,00	8,65
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	50,61	26,13	22,06	15,95	8,69	7,05
Stdev	4,06	1,37	2,02	3,62	2,06	1,70
Min	39,70	23,00	16,60	8,99	4,42	4,05
Max	57,90	30,50	25,70	24,28	12,91	11,33

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Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**14.08.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Straumur,Straumsvík**	Date of preparation	04.10.2011
Coordinates:	64°02,541-22°02,700	Matis#:	R11-2123-5

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	44,8	22,1	15,6	7,74	4,16	3,42
2	47,1	22,1	18,3	9,73	5,73	3,87
3	48,1	23,3	18,0	10,06	5,59	4,34
4	44,6	23,8	18,0	9,47	5,10	4,13
5	49,9	24,0	19,3	11,98	6,80	5,00
6	42,8	22,2	16,6	8,06	4,33	3,65
7	47,6	23,5	18,3	10,22	6,42	3,77
8	48,0	25,0	18,2	11,16	6,34	4,71
9	53,7	27,0	21,8	15,42	9,57	5,74
10	54,6	26,9	22,8	15,57	8,85	6,10
11	43,9	21,1	18,2	9,43	5,31	4,04
12	47,2	24,5	15,6	10,86	6,26	4,53
13	46,1	22,8	17,3	10,06	5,81	4,24
14	45,0	21,7	17,1	7,76	3,71	4,02
15	48,3	22,8	19,5	11,20	6,63	4,50
16	49,4	22,2	19,5	12,17	6,85	5,27
17	52,2	23,9	18,9	13,74	7,74	5,83
18	52,8	28,9	19,5	15,18	8,95	6,11
19	52,2	26,1	18,9	12,86	8,02	4,81
20	57,1	26,1	21,1	15,70	9,04	6,57
21	41,7	19,5	17,8	8,74	4,74	3,87
22	42,8	20,6	16,7	8,67	4,82	3,81
23	41,7	19,5	13,9	7,09	3,76	3,25
24	40,6	21,7	16,1	8,02	4,36	3,49
25	46,1	21,7	18,3	10,54	5,81	4,65
26	50,6	23,9	18,3	11,62	6,16	5,20
27	50,6	26,1	20,0	12,76	7,20	5,38
28	53,3	27,2	26,1	16,37	8,74	7,53
29	57,8	28,3	22,7	18,79	11,33	7,35
30	58,3	29,0	23,9	21,83	12,65	9,00
31	40,3	19,8	17,4	7,33	3,94	3,31
32	41,7	20,2	15,9	6,08	3,49	2,51
33	39,4	21,1	16,3	6,74	3,85	2,78
34	48,0	23,0	19,5	10,82	5,31	5,35
35	45,8	23,2	19,5	10,23	5,28	4,76
36	43,8	22,2	18,6	9,17	4,96	4,13
37	53,8	23,3	22,1	13,63	7,19	6,29
38	50,5	19,9	22,6	13,83	7,26	6,43
39	49,6	24,6	20,1	11,99	6,57	5,33
40	47,7	21,2	18,8	10,05	5,83	4,16
41	43,0	22,0	17,8	8,64	4,76	3,79
42	41,2	20,1	16,0	8,09	3,91	4,07
43	43,3	22,0	16,5	7,09	4,24	2,79
44	48,3	23,3	17,8	10,73	5,91	4,75
45	37,0	22,5	22,0	13,90	6,80	6,92
46	45,3	23,3	18,0	9,59	6,10	3,34
47	50,9	25,0	20,0	11,98	7,12	4,61
48	64,5	29,1	27,1	25,77	14,22	10,96
49	62,3	27,0	24,4	23,06	13,37	9,45
50						
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	48,07	23,48	19,12	11,66	6,55	4,98
Stdev	5,87	2,59	2,76	4,17	2,47	1,72
Min	37,00	19,50	13,90	6,08	3,49	2,51
Max	64,50	29,10	27,10	25,77	14,22	10,96

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**09.09.2010**
Length:	4 6 cm	Sampled by:	Marine Inst.
Location:	**Mjóifjörður I, head-Fjörður**	Date of preparation	22.09.2011
Coordinates:	65°11,28-14°00,48	Matis#:	R11-2123-6

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	47,1	23,1	20,0	12,06	6,27	5,57
2	51,7	22,5	21,8	13,66	7,63	5,88
3	50,5	25,1	18,3	11,75	6,69	4,92
4	51,4	24,8	20,9	15,76	9,12	6,51
5	53,1	25,2	21,3	16,58	8,75	7,49
6	53,6	25,1	21,6	13,70	7,38	5,92
7	53,8	24,7	24,2	16,60	9,33	6,82
8	53,2	27,0	21,7	18,49	11,34	7,06
9	48,2	21,4	18,5	11,23	5,79	5,39
10	56,1	27,1	22,3	18,22	10,90	6,93
11	58,4	25,0	23,3	19,80	10,51	9,27
12	56,1	28,3	24,0	21,74	12,23	9,43
13	53,3	29,4	24,9	17,27	6,96	10,23
14	52,8	24,0	20,0	15,15	8,60	6,52
15	53,4	23,9	20,0	14,67	7,53	6,93
16	51,7	25,0	22,2	15,60	8,62	6,86
17	59,4	23,3	20,0	11,73	6,03	5,53
18	51,0	24,5	20,0	13,65	6,98	6,63
19	50,5	22,8	20,6	13,96	8,43	5,52
20	50,5	24,5	19,9	13,19	6,80	6,33
21	54,5	25,0	21,1	17,23	8,51	8,62
22	52,2	23,3	20,0	14,36	7,94	6,17
23	53,3	22,6	20,1	15,71	8,34	7,22
24	50,4	23,9	17,8	11,45	6,03	5,31
25	48,3	22,2	17,8	8,11	3,92	4,13
26	48,3	22,8	16,1	9,94	4,98	4,89
27	47,8	21,7	18,3	10,28	6,32	3,87
28	50,4	22,2	18,3	11,51	5,71	5,74
29	46,7	21,6	15,1	9,49	5,02	4,35
30	46,7	21,6	19,4	11,54	6,01	5,43
31	57,8	26,2	22,3	18,90	10,64	8,13
32	58,3	24,5	22,7	18,72	9,63	9,01
33	48,4	22,2	20,6	12,11	6,30	5,78
34	49,5	24,5	19,5	12,83	6,01	6,81
35	41,2	22,2	17,7	10,60	5,25	4,95
36	48,9	23,9	19,4	12,22	6,40	5,77
37	57,2	21,1	17,8	10,64	6,10	4,40
38	42,3	20,1	17,2	8,00	3,61	4,36
39	46,1	20,6	16,1	8,75	5,42	3,27
40	44,5	21,7	16,1	9,07	4,48	4,46
41	61,2	28,9	24,5	24,22	13,17	10,64
42	58,9	27,2	22,2	20,10	9,46	10,55
43	57,2	27,2	22,8	19,71	11,02	8,62
44	53,9	24,5	20,0	14,14	6,35	7,59
45	52,3	25,0	18,4	12,93	7,25	5,59
46	51,1	22,2	21,7	15,06	7,74	7,24
47	48,9	23,4	23,4	16,14	7,69	8,42
48	42,2	20,0	17,3	9,65	4,97	4,65
49	45,0	21,7	16,7	9,60	5,52	4,01
50	41,2	22,2	17,3	10,02	5,60	4,34
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	51,21	23,86	20,06	13,96	7,43	6,40
Stdev	4,82	2,21	2,43	3,79	2,17	1,82
Min	41,20	20,00	15,10	8,00	3,61	3,27
Max	61,20	29,40	24,90	24,22	13,17	10,64

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**9.9.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Mjóifjörður II, Hofsá-brekka**	Date of preparation	19.9.2011
Coordinates:	65°12,156-13°47,733	Matis#:	R12-2123-7

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	46,5	20,2	18,8	8,69	4,39	4,11
2	45,7	22,2	17,5	10,27	4,62	5,15
3	48,9	22,6	18,6	11,88	4,96	6,58
4	47,4	22,4	18,0	10,49	4,64	5,61
5	52,0	23,4	17,8	10,73	5,94	4,53
6	52,8	25,6	17,9	11,95	6,20	5,41
7	55,5	26,6	21,3	17,77	9,52	7,86
8	64,1	26,8	23,1	20,30	12,29	7,6
9	64,8	28,8	22,0	21,49	12,82	8,36
10	64,2	29,5	23,3	22,14	13,68	8,17
11	43,2	20,4	15,8	7,46	4,13	3,22
12	44,6	21,5	15,5	8,56	4,55	3,87
13	43,1	20,0	17,2	8,49	4,32	3,88
14	48,7	21,2	17,9	9,15	4,74	4,22
15	50,7	23,3	18,9	12,35	6,87	5,28
16	50,5	24,8	20,4	14,62	6,92	7,26
17	54,5	25,3	19,5	13,44	7,38	5,71
18	54,3	27,1	21,1	16,30	8,96	7,07
19	58,3	28,0	19,9	11,44	5,57	5,59
20	58,4	28,5	21,8	18,15	10,68	7,36
21	45,3	21,5	17,1	9,22	4,96	4,04
22	46,3	24,0	19,1	12,64	6,03	6,37
23	51,2	24,4	20,4	13,76	7,45	5,99
24	51,6	24,3	21,3	15,03	8,09	6,77
25	51,6	23,9	21,4	14,00	7,26	6,49
26	51,4	24,5	18,9	12,57	6,58	5,61
27	51,4	23,7	19,4	12,18	7,22	4,68
28	52,7	26,0	24,1	18,80	9,99	8,71
29	60,0	28,7	23,7	21,57	11,63	9,69
30	60,6	19,6	21,3	16,87	9,42	6,91
31	41,2	20,7	17,8	8,83	4,20	4,24
32	43,5	20,4	17,0	8,15	4,42	3,69
33	49,2	21,0	18,9	11,11	6,28	4,63
34	48,8	23,6	19,5	12,74	7,04	5,61
35	49,8	22,9	18,0	10,84	6,20	4,5
36	55,2	25,4	21,8	13,98	7,86	5,96
37	57,0	26,0	21,4	16,38	9,19	6,49
38	56,1	28,2	21,4	13,68	7,63	5,25
39	61,1	27,9	21,1	18,17	11,83	5,85
40	66,0	30,4	26,6	23,83	14,23	9,27
41	43,9	20,9	17,2	9,53	4,84	4,59
42	44,8	22,1	17,0	8,95	5,03	3,78
43	45,5	21,6	19,0	8,38	3,40	4,9
44	44,5	20,9	17,8	8,76	3,78	4,87
45	51,0	23,5	19,7	14,24	7,85	6,22
46	45,3	21,0	18,0	8,88	4,73	3,97
47	50,2	24,5	20,5	12,45	6,69	5,63
48	54,0	25,3	21,5	14,95	8,92	5,91
49	55,2	26,8	21,3	18,01	8,64	8,81
50	63,0	29,5	23,0	20,78	12,64	7,95
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	51,9	24,2	19,8	13,50	7,34	5,88
Stdev	6,5	2,9	2,3	4,32	2,83	1,61
Min	41,2	19,6	15,5	7,46	3,40	3,22
Max	66,0	30,4	26,6	23,83	14,23	9,69

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**09.09.2010**
Length:	4 6 cm	Sampled by:	Marine Inst.
Location:	**Mjóifjörður III, Dalatangi**	Date of preparation	05.09.2011
Coordinates:	65°16,101-13°34,564	Matis#:	R11-2123-8

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	39,2	19,2	14,5	5,93	2,01	3,49
2	50,1	23,4	21,7	16,65	8,05	8,48
3	48,4	23,9	21,0	13,08	4,10	8,49
4	47,0	24,8	19,4	12,78	5,44	6,98
5	46,8	23,9	17,8	10,10	3,62	6,27
6	47,2	21,6	17,6	10,64	4,09	6,11
7	47,0	24,2	18,4	10,79	3,58	7,08
8	51,1	24,9	21,2	16,42	7,65	8,48
9	52,2	25,0	21,7	17,94	8,37	9,30
10	48,3	24,0	22,3	15,48	5,40	9,74
11	40,6	18,6	16,9	7,60	3,31	4,07
12	40,0	19,7	18,2	8,80	4,14	4,44
13	43,5	22,5	17,4	9,84	4,18	5,48
14	43,6	21,2	17,7	9,90	4,74	4,99
15	46,0	21,5	17,8	9,50	5,13	3,95
16	44,1	20,3	19,0	9,11	4,76	4,22
17	52,4	24,4	18,8	12,55	6,92	5,45
18	51,3	25,7	19,9	18,28	7,62	10,55
19	52,1	23,7	22,8	16,50	7,14	9,18
20	47,0	23,9	22,2	15,79	7,39	8,29
21	42,5	20,3	17,1	7,72	4,19	3,37
22	43,0	21,5	20,4	11,62	5,78	5,65
23	48,6	22,3	17,9	11,48	5,56	5,76
24	49,9	25,3	22,3	18,19	8,04	9,90
25	50,7	26,9	22,6	20,10	10,03	10,68
26	42,0	20,7	16,7	8,25	3,84	4,22
27	44,5	21,8	15,9	9,29	4,40	4,69
28	45,3	20,2	18,3	8,63	3,73	4,69
29	44,3	22,1	19,5	10,33	5,33	4,84
30	48,5	24,7	17,9	10,99	6,00	4,58
31	46,7	22,9	15,7	8,15	3,99	3,75
32	42,5	20,1	17,5	8,66	4,33	4,16
33	42,5	22,4	17,8	9,56	3,99	5,35
34	44,2	21,5	18,2	10,07	4,26	5,52
35	47,0	22,7	16,9	9,20	4,62	4,47
36	43,3	20,4	18,9	8,58	3,88	4,46
37	51,4	23,8	20,8	15,15	6,43	8,45
38	52,6	24,9	18,6	11,98	3,98	7,71
39	54,1	24,3	21,4	14,26	6,73	7,52
40	52,3	22,5	19,3	13,52	6,02	7,40
41	41,8	21,5	17,6	8,93	4,42	4,33
42	41,4	21,8	17,2	8,04	4,07	3,86
43	41,9	20,8	18,6	9,47	4,24	5,16
44	46,4	20,9	17,4	8,63	5,11	3,36
45	47,3	23,6	18,7	12,51	5,65	6,65
46	47,0	22,4	24,8	15,92	6,64	9,07
47	49,8	23,0	21,4	16,88	8,16	8,30
48	54,5	23,0	22,9	15,44	6,98	8,33
49	53,5	24,2	22,1	17,71	7,79	9,72
50	53,1	24,5	21,7	16,39	8,13	8,24
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	47,01	22,67	19,25	12,07	5,48	6,38
Stdev	4,14	1,86	2,25	3,61	1,72	2,17
Min	39,20	18,60	14,50	5,93	2,01	3,36
Max	54,50	26,90	24,80	20,10	10,03	10,68

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**12.8.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Hvalstöð, Hvalfjörður**	Date of preparation	27.9.2011
Coordinates:	64°23,826-21°27,210	Matis#:	R11-2123-2

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	52,1	24,1	19,1	13,19	6,65	6,36
2	51,0	24,1	21,7	14,12	7,21	6,69
3	55,5	27,0	23,2	18,24	9,76	8,67
4	57,3	24,2	23,8	17,97	9,10	8,55
5	56,7	27,0	22,9	19,66	9,20	10,29
6	58,8	25,9	24,5	19,65	10,17	9,38
7	59,2	27,5	24,6	21,73	12,47	9,12
8	56,9	27,4	22,7	19,77	10,09	9,47
9	58,7	26,2	25,1	22,41	11,09	10,90
10	58,4	26,4	27,1	23,54	11,49	11,85
11	53,8	23,8	22,5	16,55	8,09	8,21
12	58,3	27,8	23,0	20,13	10,32	9,44
13	51,2	23,6	23,2	16,30	8,18	7,67
14	54,6	25,8	23,7	18,64	9,86	8,55
15	54,9	24,2	21,2	16,83	8,87	7,56
16	56,5	27,1	23,5	20,85	10,97	9,57
17	57,0	25,2	25,0	21,21	10,87	10,12
18	53,3	26,5	22,8	18,63	9,50	8,90
19	55,0	25,3	23,3	18,59	9,42	8,97
20	55,1	27,3	23,9	20,30	9,95	10,02
21	44,0	23,0	19,2	9,09	4,83	4,17
22	55,0	25,9	19,8	15,45	7,85	7,35
23	59,2	25,0	24,1	21,74	11,05	10,38
24	48,0	24,9	22,4	13,14	7,35	5,66
25	57,0	25,7	24,8	21,06	10,02	10,75
26	56,5	25,7	22,5	17,33	9,02	8,07
27	55,2	27,7	23,3	21,15	10,06	10,72
28	57,7	28,3	22,8	19,60	11,08	8,37
29	56,9	26,0	26,3	20,80	11,03	9,53
30	55,0	25,8	22,2	17,65	9,37	7,97
31	62,0	28,4	26,0	26,29	14,07	12,04
32	60,0	28,2	28,6	29,24	15,16	13,87
33	60,0	26,2	26,1	23,70	12,60	10,84
34	58,7	26,0	24,2	20,54	11,34	9,05
35	57,1	25,9	26,7	22,97	12,77	10,02
36	58,9	25,5	25,4	21,60	10,97	10,27
37	53,6	24,3	25,0	19,89	9,57	10,04
38	47,5	25,4	18,0	10,53	4,95	5,00
39	56,0	25,2	23,6	19,32	10,22	8,84
40	50,6	23,2	22,9	16,28	8,74	7,20
41	48,2	22,2	21,8	12,63	6,33	5,96
42	58,5	27,5	23,8	20,92	11,32	9,26
43	55,2	24,4	24,5	19,65	9,39	9,77
44	50,5	24,8	21,4	14,75	7,99	6,52
45	52,1	22,5	21,5	14,97	7,74	7,04
46	59,6	26,0	24,8	24,99	11,59	12,83
47	57,2	24,0	25,3	22,24	10,76	11,24
48	58,3	28,0	23,5	21,96	11,20	10,45
49	60,2	25,6	25,8	24,23	12,68	11,09
50	62,0	27,1	25,0	27,09	12,66	13,56
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	55,70	25,70	23,56	19,38	9,94	9,16
Stdev	3,84	1,55	2,06	4,05	2,09	2,05
Min	44,00	22,20	18,00	9,09	4,83	4,17
Max	62,00	28,40	28,60	29,24	15,16	13,87

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**18.8.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Seljaland, Álftafjörður**	Date of preparation	3.11.2011
Coordinates:	65°58,29-23°04,50	Matis#:	R11-2123-10

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	49,1	23,7	18,6	10,82	6,20	4,53
2	49,5	23,0	23,1	14,22	8,07	5,93
3	49,5	22,2	20,9	10,83	6,55	4,03
4	42,5	22,0	16,8	8,32	4,40	3,75
5	51,7	24,6	20,0	12,93	7,13	5,74
6	46,6	21,8	20,3	10,67	6,17	4,42
7	50,7	23,7	21,0	13,66	7,46	6,16
8	47,3	23,1	17,4	10,10	5,98	3,93
9	51,0	24,2	19,8	12,76	7,14	5,56
10	52,1	27,0	22,5	15,07	8,79	6,24
11	47,8	21,7	18,5	9,20	5,68	3,43
12	47,2	24,2	20,2	10,55	5,93	4,57
13	47,4	23,6	18,9	10,70	6,34	4,28
14	46,1	23,7	19,2	11,12	6,33	4,75
15	49,7	23,7	20,7	12,33	7,97	4,27
16	46,9	23,6	18,5	10,39	6,52	3,75
17	47,7	24,2	19,2	10,82	6,52	4,14
18	54,4	24,0	22,7	15,46	8,80	6,62
19	55,8	26,1	21,3	15,80	9,03	6,64
20	58,3	27,6	24,2	19,59	11,68	7,76
21	45,3	22,3	17,9	8,37	4,78	3,50
22	46,0	22,1	18,2	8,36	4,54	3,75
23	46,4	22,4	19,2	9,91	5,86	3,94
24	45,5	20,7	16,9	8,25	5,11	3,08
25	49,3	24,2	18,3	10,96	6,98	3,93
26	47,4	22,5	20,5	10,73	6,55	4,12
27	50,3	23,8	22,0	13,18	8,50	4,62
28	52,5	24,6	20,3	13,74	8,06	5,51
29	50,7	26,9	22,3	15,02	8,47	6,43
30	49,0	24,1	19,1	11,97	6,87	5,00
31	44,9	21,3	22,0	11,35	6,39	4,81
32	46,5	22,3	19,7	9,83	5,59	4,12
33	48,2	21,2	20,9	11,75	6,60	5,10
34	49,0	24,2	18,6	10,59	6,09	4,42
35	50,8	23,5	19,8	11,17	7,17	3,90
36	49,3	21,8	22,9	12,33	7,43	4,85
37	50,0	24,9	20,9	10,54	5,63	4,83
38	48,8	22,8	21,1	12,11	7,02	5,05
39	50,3	25,2	18,7	11,70	7,15	4,50
40	54,8	24,3	22,6	16,46	9,27	7,02
41	44,1	22,7	19,3	10,32	5,05	5,12
42	46,2	20,4	21,6	11,08	6,28	4,66
43	47,0	22,7	19,5	10,40	5,92	4,27
44	46,4	22,2	20,2	11,44	5,52	5,68
45	47,8	22,8	18,5	10,54	5,62	4,76
46	54,1	25,1	21,4	14,04	8,08	5,74
47	50,2	23,7	21,3	13,10	6,98	5,85
48	48,7	24,4	21,5	12,85	7,46	5,23
49	51,4	25,4	21,5	13,93	8,66	5,16
50	53,1	25,8	21,9	15,82	8,03	7,49
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	49,1	23,6	20,2	11,94	6,89	4,94
Stdev	3,1	1,6	1,7	2,33	1,39	1,07
Min	42,5	20,4	16,8	8,25	4,40	3,08
Max	58,3	27,6	24,2	19,59	11,68	7,76

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**26.8.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Grímsey**	Date of preparation	24.10.2011
Coordinates:	66°33,134-18°01,407	Matís#	R11-2123-1

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	52,4	22,7	23,3	15,92	5,03	10,80
2	49,8	25,0	19,2	13,19	6,56	6,31
3	45,9	23,3	20,5	9,27	1,46	7,71
4	42,3	20,8	15,8	6,25	2,33	3,58
5	40,2	20,5	16,8	9,14	3,18	5,31
6	42,5	21,1	16,7	8,00	3,86	3,81
7	41,5	19,3	18,9	8,06	2,07	5,53
8	40,5	20,7	17,9	7,00	2,65	3,87
9	46,8	22,1	20,8	14,61	6,05	7,94
10	46,0	22,7	20,1	13,20	6,09	7,00
11	35,8	17,9	16,1	4,43	0,56	3,43
12	44,1	22,2	18,2	10,71	5,15	5,40
13	43,7	20,4	19,4	8,61	3,56	4,74
14	46,4	24,1	19,2	10,46	4,08	5,91
15	47,0	22,1	18,6	11,63	5,47	5,89
16	47,5	22,5	17,7	10,70	5,37	4,99
17	48,8	23,9	19,6	13,71	6,21	7,08
18	53,7	24,0	25,1	14,40	6,10	8,13
19	55,0	24,2	23,6	20,59	9,80	10,57
20	38,2	19,1	17,2	6,54	2,47	3,98
21	40,4	21,1	17,5	9,09	4,06	4,59
22	42,8	20,5	18,8	7,55	2,79	4,55
23	41,0	21,3	21,2	11,85	5,05	6,59
24	**	**	**	**	**	**
25	43,7	22,7	18,5	8,31	3,46	4,61
26	40,6	20,6	14,9	6,58	3,26	2,97
27	41,8	22,1	20,0	12,00	4,87	6,77
28	47,6	21,4	21,0	10,37	3,18	6,80
29	54,0	25,8	21,8	14,33	6,86	7,18
30	50,9	24,5	23,2	17,25	8,45	8,47
31	42,8	19,9	18,2	9,06	4,59	4,31
32	40,9	20,4	16,6	8,77	4,01	4,60
33	**	**	**	**	**	**
34	45,5	20,9	18,0	10,64	5,46	5,08
35	42,1	20,3	18,6	7,30	2,67	4,41
36	46,5	22,1	18,3	12,05	5,84	6,01
37	37,6	18,9	19,4	8,76	3,61	4,99
38	42,2	20,4	19,7	9,86	2,71	6,95
39	42,7	22,0	19,2	9,02	3,03	5,81
40	42,3	20,2	18,0	9,36	5,24	3,88
41	48,2	24,7	19,6	14,03	7,24	6,57
42	45,8	23,1	19,0	11,20	5,55	5,51
43	50,0	21,5	20,2	12,66	7,06	5,44
44	52,2	24,6	18,4	13,39	7,18	6,10
45	51,6	22,4	21,3	14,94	7,93	6,86
46	51,0	23,2	21,0	14,92	7,51	7,23
47	51,5	23,3	20,1	15,18	7,42	7,61
48	49,3	24,4	22,5	13,08	5,92	7,19
49	51,9	24,8	21,8	15,20	8,28	6,79
50	52,8	23,9	19,0	13,97	7,74	6,14
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	45,79	22,08	19,39	11,19	4,98	5,96
Stdev	4,83	1,84	2,11	3,31	2,07	1,69
Min	35,80	17,90	14,90	4,43	0,56	2,97
Max	55,00	25,80	25,10	20,59	9,80	10,80

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**12.8.2010**
Length:	4-6 cm	Sampled by:	Marine Inst.
Location:	**Hvammsvík**	Date of preparation	25.10.2011
Coordinates:	64°21,64-21°33,53	Matís#	R11-2123-3

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	42,2	19,2	19,9	8,81	4,70	3,89
2	44,1	24,3	21,4	12,32	6,84	5,27
3	46,3	21,2	16,9	8,55	4,37	4,04
4	49,0	24,1	19,6	12,98	7,24	5,44
5	47,4	21,5	20,0	11,19	6,47	4,56
6	47,3	21,2	21,1	11,35	6,26	4,89
7	49,3	21,8	22,3	14,79	7,40	7,22
8	45,7	21,5	19,6	10,91	4,92	5,68
9	47,6	24,9	20,8	12,60	6,97	5,44
10	53,0	26,6	22,3	15,36	9,32	5,86
11	49,0	25,7	20,9	13,25	7,59	5,54
12	57,1	21,2	19,3	10,01	5,44	4,51
13	45,6	24,9	20,7	14,13	7,50	6,51
14	51,3	22,8	20,1	12,44	7,11	5,27
15	52,0	26,8	20,2	16,82	9,03	7,53
16	50,3	23,7	22,3	16,16	8,37	7,63
17	52,9	26,1	22,4	16,22	9,31	6,73
18	55,7	25,7	23,1	16,86	10,34	6,40
19	57,7	26,5	25,5	21,98	12,87	8,95
20	57,9	27,6	23,5	20,14	11,42	8,61
21	44,6	21,1	19,8	10,28	5,51	4,68
22	46,1	21,6	21,1	12,15	7,20	4,84
23	47,4	23,9	21,5	13,02	6,65	6,30
24	47,5	23,5	21,0	12,87	7,64	5,15
25	47,2	23,7	19,2	11,40	6,35	4,96
26	52,3	23,2	21,0	14,75	8,19	6,45
27	51,7	23,7	23,1	15,65	8,50	7,00
28	52,8	26,7	21,6	16,21	9,76	6,33
29	57,5	25,6	21,2	17,39	8,99	8,24
30	58,3	27,2	24,0	21,81	11,84	9,86
31	44,2	21,0	17,7	8,07	4,89	3,05
32	40,7	20,8	17,6	8,73	4,80	3,81
33	45,6	21,3	21,3	11,51	6,24	5,15
34	49,5	23,8	19,6	12,14	6,69	5,37
35	45,3	23,2	21,7	11,72	7,40	4,25
36	53,0	24,1	20,4	14,11	8,37	5,60
37	51,1	25,4	19,4	14,20	7,26	6,83
38	48,5	24,0	20,7	13,85	7,44	6,32
39	50,3	25,1	19,9	13,42	7,62	5,68
40	55,9	24,6	23,5	17,04	9,37	7,58
41	43,1	22,0	18,7	9,16	5,51	3,56
42	44,9	21,9	16,7	9,23	4,63	4,49
43	45,4	20,2	18,9	10,88	5,97	4,75
44	51,2	24,5	22,0	14,48	8,20	6,03
45	50,4	25,5	20,8	14,18	7,70	6,34
46	46,3	22,2	20,8	12,51	6,56	5,84
47	47,7	24,5	23,2	13,06	7,10	5,84
48	47,7	24,3	21,9	14,03	7,82	6,12
49	49,9	24,6	21,4	12,94	7,45	5,40
50	42,6	22,3	18,3	9,35	5,33	3,85
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	49,20	23,66	20,80	13,34	7,41	5,79
Stdev	4,42	2,04	1,81	3,16	1,86	1,42
Min	40,70	19,20	16,70	8,07	4,37	3,05
Max	58,30	27,60	25,50	21,98	12,87	9,86

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Blue mussel (*Mytilus edulis*)**	Date of sampling:	**12.8.2010**
Length:	4-6 cm	Sampled by:	Marine. Inst.
Location:	**Naust Laxárvogi, Hvalfjörður**	Date of preparation	27.10.2011
Coordinates:	64°20,20-21°41,09	Matis#:	R11-2123-11

	Length (mm)	Width (mm)	Height (mm)	Total weight (g)	Weight soft body (g)	Weight shell (g)
1	45,5	24,1	18,0	10,07	5,50	4,49
2	52,7	26,3	22,9	18,36	9,12	9,13
3	55,7	27,3	21,0	16,24	9,82	6,24
4	56,8	27,6	24,8	20,70	11,41	9,11
5	59,8	29,9	25,9	25,58	14,50	10,97
6	58,5	30,3	26,1	24,18	13,26	10,53
7	60,6	30,9	22,5	23,81	12,97	10,66
8	59,8	29,7	24,8	26,67	13,44	13,03
9	62,6	31,2	27,2	17,83	7,79	9,79
10	45,1	22,3	17,2	8,20	4,87	3,17
11	45,6	23,3	17,8	8,73	5,36	3,26
12	43,0	22,7	19,1	10,70	5,80	4,79
13	48,6	23,5	20,4	11,35	6,93	4,32
14	50,5	24,6	20,8	13,35	7,61	5,67
15	49,8	23,2	20,8	13,50	7,65	5,76
16	51,2	26,7	20,6	13,83	8,62	5,10
17	62,2	29,0	26,8	26,32	15,09	11,12
18	60,1	30,3	24,5	24,00	13,05	10,76
19	44,9	23,4	18,7	9,43	5,77	3,45
20	46,8	22,9	19,7	11,11	7,02	4,01
21	50,9	23,1	20,8	15,58	8,00	7,29
22	52,7	26,9	22,0	16,59	9,09	7,30
23	52,8	26,2	22,6	16,45	8,99	7,32
24	53,5	27,4	24,0	18,72	10,13	8,49
25	61,0	28,0	26,9	25,92	14,04	11,64
26	58,5	26,5	27,6	23,34	13,14	9,94
27	62,3	28,1	28,2	26,56	15,44	10,93
28	59,4	31,1	25,9	26,77	14,17	12,44
29	46,9	21,7	19,1	10,37	5,53	4,68
30	46,1	24,3	17,0	10,00	5,76	4,15
31	43,8	21,8	18,1	9,98	5,54	4,29
32	48,3	26,3	19,7	13,35	6,89	6,27
33	56,1	29,6	22,9	22,68	11,26	10,77
34	55,8	28,1	23,1	19,35	11,22	7,99
35	54,3	27,0	25,6	19,85	11,52	8,17
36	56,8	29,1	24,5	21,10	12,56	8,36
37	60,3	27,8	26,2	25,69	13,81	11,76
38	58,1	29,0	23,9	21,94	12,91	8,91
39	40,1	21,9	16,1	6,62	3,48	2,90
40	41,2	24,1	17,5	8,13	4,81	3,15
41	48,5	24,1	24,2	13,67	7,78	5,62
42	43,3	24,2	18,4	11,62	5,33	5,81
43	48,5	24,3	18,7	10,97	5,94	4,88
44	50,7	29,5	20,5	13,66	8,56	4,94
45	52,0	24,3	23,3	16,48	9,42	6,83
46	53,4	27,0	23,1	17,60	9,85	7,60
47	57,0	27,2	25,1	21,05	12,01	8,72
48	57,2	32,6	27,0	27,14	14,04	12,78
49	60,6	28,8	29,3	29,08	16,37	12,39
50	**	**	**	**	**	**
	Length	**Width**	**Height**	**Total weight**	**Weight soft body**	**Weight shell**
Average	52,9	26,5	22,5	17,43	9,66	7,59
Stdev	6,3	2,9	3,5	6,41	3,48	3,02
Min	40,1	21,7	16,1	6,62	3,48	2,90
Max	62,6	32,6	29,3	29,08	16,37	13,03

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix II.

Biological measurements of Cod (*Gadus morhua*) 2010

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

			exped./station			date	n
Species:	**Cod (*Gadus Morhua*)**		TJ1-2011			11,03,2011	25
Location:	**North- Northwest of Iceland (2)**	n	station	°N	°W		
Lenght:	30-45cm	3	79	661995	254349		
Ship:	Jón Vídalín	22	80	662150	254390		
Expd.leader:	Hjalti Karlsson						
						R12-383-1	

Group	exped.-station	Weight jar IFL g	Weight jar and liver g	Weight liver g	Weight ungutted fish, g	Sex 2=female 1=male	Lenght cm	Weight gutted fish, g	Weight fillets g	Age
H 1	80	98,67	109,11	10,44	330	2	35	298	95	3
	80	102,36	114,87	12,51	203	2	30	182	58	3
	80	98,76	112,74	13,98	435	2	37	369	138	3
	80	99,07	114,55	15,48	404	2	36	352	102	3
			Sum	52,41	1372,0		138,0	1201,0	393,0	12,0
			Average	13,10	343,0		34,5	300,3	98,3	3,0
			STDEV	2,15	103,2		3,1	84,4	32,8	0,0
			Min	10,44	203,0		30,0	182,0	58,0	3,0
			Max	15,48	435,0		37,0	369,0	138,0	3,0
H 2	80	105,95	123,83	17,88	385	2	35	313	110	3
	80	99,14	117,29	18,15	336	1	34	283	66	3
	80	98,25	119,44	21,19	398	2	35	340	120	3
	79	98,82	120,93	22,11	455	2	36	392	134	3
	80	98,46	120,83	22,37	480	1	36	411	140	3
			Sum	101,70	2054,0		176,0	1739,0	570,0	15,0
			Average	20,34	410,8		35,2	347,8	114,0	3,0
			STDEV	2,17	57,4		0,8	53,4	29,3	0,0
			Min	17,88	336,0		34,0	283,0	66,0	3,0
			Max	22,37	480,0		36,0	411,0	140,0	3,0
H 3	80	98,30	125,00	26,70	388	2	35	322	109	3
	80	98,71	128,28	29,57	658	1	40	572	173	3
	80	98,46	129,29	30,83	521	1	38	430	134	3
	80	98,46	130,92	32,46	419	2	35	345	96	4
	80	99,05	133,91	34,86	433	2	37	354	125	3
			Sum	154,42	2419,0		185,0	2023,0	637,0	16,0
			Average	30,88	483,8		37,0	404,6	127,4	3,2
			STDEV	3,06	109,2		2,1	102,0	29,4	0,4
			Min	26,70	388,0		35,0	322,0	96,0	3,0
			Max	34,86	658,0		40,0	572,0	173,0	4,0
H 4	80	98,64	135,16	36,52	681	2	41	575	190	3
	80	98,59	139,96	41,37	623	1	39	537	186	3
	80	98,64	140,44	41,80	610	1	38	502	181	3
	80	99,06	141,02	41,96	521	1	37	430	114	3
			Sum	161,65	2435,0		155,0	2044,0	671,0	12,0
			Average	40,41	608,8		38,8	511,0	167,8	3,0
			STDEV	2,61	66,1		1,7	61,7	36,0	0,0
			Min	36,52	521,0		37,0	430,0	114,0	3,0
			Max	41,96	681,0		41,0	575,0	190,0	3,0
H5	80	98,68	144,80	46,12	635	2	39	527	177	3
	79	98,86	145,76	46,90	685	2	43	591	189	3
	80	102,88	150,49	47,61	668	2	41	541	188	3
	80	97,73	147,31	49,58	693	2	40	564	202	3
	80	98,55	149,88	51,33	706	1	42	601	212	3
			Sum	241,54	3387,0		205,0	2824,0	968,0	15,0
			Average	48,31	677,4		41,0	564,8	193,6	3,0
			STDEV	2,12	27,4		1,6	31,6	13,6	0,0
			Min	46,12	635,0		39,0	527,0	177,0	3,0
			Max	51,33	706,0		43,0	601,0	212,0	3,0
H6	79	98,81	156,79	57,98	697	2	42	584	206	3
	80	98,65	162,50	63,85	707	2	41	587	240	3
			Sum	121,83	1404,0		83,0	1171,0	446,0	12,0
			Average	60,92	702,0		41,5	585,5	223,0	3,0
			STDEV	4,15	7,1		0,7	2,1	24,0	0,0
			Min	57,98	697,0		41,0	584,0	206,0	3,0
			Max	63,85	707,0		42,0	587,0	240,0	3,0
H1, H2, H3, H4, H5, H6			**Sum**	833,55	13071,0		942,0	11002,0	3685,0	76,0
			Average	33,34	522,8		37,7	440,1	147,4	3,0
			STDEV	15,11	147,5		3,1	122,0	48,4	0,2
			Min	10,44	203,0		30,0	182,0	58,0	3,0
			Max	63,85	707,0		43,0	601,0	240,0	4,0

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Species:	**Cod (*Gadus Morhua*)**	**exped./station**			**date**	**n**
Location:	**Northeast of Iceland**	TB1-2011	651540	113940	12,03,2011	25
Lenght:	30-45cm					
Ship:	Bjartur NK					
Expd.leader:	Valur Bogason			**R12-383-2**		

Group	exped.-station	Weight jar IFL g	Weight jar and liver g	Weight liver g	Weight ungutted fish, g	Sex 2=female 1=male	Lenght cm	Weight gutted fish, g	Weight fillets g	Age
H 1	72	98,74	110,38	11,64	331	2	35,0	290	76	4
	72	102,40	115,27	12,87	378	1	35,0	315	88	3
	72	98,70	112,90	14,20	503	2	39,0	425	126	4
	72	98,68	113,49	14,81	414	2	35,0	360	99	3
	72	99,05	114,77	15,72	430	2	36,0	365	126	3
	72	99,02	114,99	15,97	322	2	34,0	275	85	4
			Sum	85,21	2378,0	11,0	214,0	2030,0	600,0	21,0
			Average	14,20	396,3	1,8	35,7	338,3	100,0	3,5
			STDEV	1,68	67,8	0,4	1,8	55,8	21,4	0,5
			Min	11,64	322,0	1,0	34,0	275,0	76,0	3,0
			Max	15,97	503,0	2,0	39,0	425,0	126,0	4,0
H 2	72	98,55	117,97	19,42	705	1	43,0	595	197	5
	72	98,19	119,23	21,04	338	2	35,0	280	85	3
	72	98,62	120,88	22,26	450	1	37,0	380	98	4
	72	99,21	123,72	24,51	438	1	37,0	370	133	4
			Sum	87,23	1931,0		152,0	1625,0	513,0	16,0
			Average	21,81	482,8		38,0	406,3	128,3	4,0
			STDEV	2,14	156,4		3,5	133,6	50,1	0,8
			Min	19,42	338,0		35,0	280,0	85,0	3,0
			Max	24,51	705,0		43,0	595,0	197,0	5,0
H 3	72	98,41	123,85	25,44	539	2	40,0	440	116	4
	72	99,25	125,03	25,78	493	2	38,0	410	126	4
	72	98,93	125,99	27,06	454	2	38,0	380	119	4
	72	98,82	126,08	27,26	577	1	40,0	480	145	4
	72	98,88	126,19	27,31	474	1	37,0	385	110	4
	72	99,00	127,89	28,89	534	1	39,0	445	134	4
			Sum	161,74	3071,0		232,0	2540,0	750,0	24,0
			Average	26,96	511,8		38,7	423,3	125,0	4,0
			STDEV	1,24	46,1		1,2	38,7	12,8	0,0
			Min	25,44	454,0		37,0	380,0	110,0	4,0
			Max	28,89	577,0		40,0	480,0	145,0	4,0
H 4	72	97,91	130,18	32,27	498	1	39,0	420	132	4
	72	99,61	132,17	32,56	520	2	39,0	440	130	4
	72	98,88	131,77	32,89	600	2	42,0	500	141	4
	72	98,94	131,93	32,99	581	2	41,0	475	157	4
	72	99,32	135,05	35,73	673	1	43,0	545	172	4
	72	98,45	138,09	39,64	571	1	40,0	475	138	4
			Sum	206,08	3443,0		244,0	2855,0	870,0	24,0
			Average	34,35	573,8		40,7	475,8	145,0	4,0
			STDEV	2,88	62,0		1,6	44,2	16,3	0,0
			Min	32,27	498,0		39,0	420,0	130,0	4,0
			Max	39,64	673,0		43,0	545,0	172,0	4,0
H5	72	98,48	144,53	46,05	754	1	45,0	610	195	4
	72	104,88	151,79	46,91	736	1	43,0	605	171	4
			Sum	92,96	1490,0		88,0	1215,0	366,0	8,0
			Average	46,48	745,0		44,0	607,5	183,0	4,0
			STDEV	0,61	12,7		1,4	3,5	17,0	0,0
			Min	46,05	736,0		43,0	605,0	171,0	4,0
			Max	46,91	754,0		45,0	610,0	195,0	4,0
H6	72	98,65	158,48	59,83	765	1	44,0	620	181	4
			Sum	59,83	765,0		44,0	620,0	181,0	4,0
			Average	59,83	765,0		44,0	620,0	181,0	4,0
			STDEV							
			Min	59,83	765,0		44,0	620,0	181,0	4,0
			Max	59,83	765,0		44,0	620,0	181,0	4,0
H1, H2, H3, H4, H5, H6			**Sum**	693,05	13078,0		974,0	10885,0	3280,0	97,0
			Average	27,72	523,1		39,0	435,4	131,2	3,9
			STDEV	11,75	129,5		3,1	102,1	33,8	0,4
			Min	11,64	322,0		34,0	275,0	76,0	3,0
			Max	59,83	765,0		45,0	620,0	197,0	5,0

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix III.

Quality assurance in metal analysis and persistent organochlorines analysis

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 2. Results for trace metals in certified reference materials (DOLT-3, Quasimeme R93 and Mussel tissue) for the year 2011.

Analyte		QTM093BT Quasimeme R68 µg/g	I Z-scoreI	DOLT-3 NRC-CNRC mg/kg	I Z-score*I	Mussel tissue ERM-CE278 mg/kg	I Z-score*I	MLOD** mg/kg
As								
	Measured	2000,0		9,78		6,71		
	Certified	2,1	-0,2	10,2	-0,36	6,07	0,86	0,002
Cd								
	Measured	30,2		22,087		0,287		
	Certified			19,4	1,35	0,348	-0,93	0,03
Cu								
	Measured	151,0		35,242		7,675		
	Certified	168,3	-0,2	31,2	1,36	9,45	-1,65	0,002
Hg								
	Measured	106,00				0,183		
	Certified	116,5	-0,4			0,196	-0,33	0,06
Pb								
	Measured	3,0		0,329		1,67		
	Certified	7,1	-1,2	0,32	0,16	2,00	-1,15	0,04
Se								
	Measured	311,0				9,136		
	Certified	320	-0,2			7,06	2,47	
Zn								
	Measured	3,0		86,89				
	Certified	2,8	0,2	86,6	0,04			

* Z-score (calculated accoding to method SV-22-02 SN-1 in Matís quality manual)

** MLOD is on dry weight basis

NA: not analyzed

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 3. Results for trace metals in certified reference materials (DORM-3 and Quasimeme R68) for the year 2011.

Analyte	QTM094BT Quasimeme R68 µg/g	I Z-scoreI	DORM-3 NRC-CNRC mg/kg	I Z-score*I	MLOD** mg/kg
As					
Measured	10,00		8,126		
Certified	9,42	0,5	6,88	1,51	0,002
Cd					
Measured	26,00		0,300		
Certified	26,02	0,0	0,29	0,18	0,03
Cu					
Measured	2377,0		15,451		
Certified	2422,0	-0,1	15,5	-0,03	0,002
Hg					
Measured	81,00		0,352		
Certified	75,21	0,3	0,382	-0,42	0,06
Pb					
Measured	12,0		0,41		
Certified	17,24	-1,1	0,395	0,2	0,04

* Z-score (calculated accoding to method SV-22-02 SN-1 in Matís quality manual)

** MLOD is on dry weight basis

NA: not analyzed

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 4. Qualitative assurance. Persistent organochlorines (ng/g ww) in a certified mussel sample from QUASIMEME, that were analysed with the mussel samples from 2010

Blue mussel control								assign			
chemical	CRM	weight basis	anal. 1	anal. 2	anal.3	mean	SD	value	time	I Z I**	det. Lim.
CB28	QOR096BT	wet weight	0,16			0,16		0,15		0,32	0,02
CB31	QOR096BT	wet weight	0,1			0,10		0,10		0,00	0,02
CB52	QOR096BT	wet weight	0,26			0,26		0,26		0,00	0,02
CB101	QOR096BT	wet weight	1,12			1,12		1,10		0,13	0,01
CB105	QOR096BT	wet weight	0,22			0,22		0,21		0,26	0,01
CB118	QOR096BT	wet weight	0,94			0,94		0,92		0,16	0,01
CB138	QOR096BT	wet weight	2,1			2,10		2,28		-0,60	0,01
CB153	QOR096BT	wet weight	3,68			3,68		3,52		0,35	0,01
CB156	QOR096BT	wet weight	0,08			0,08		0,08		0,00	0,01
CB180	QOR096BT	wet weight	0,17			0,17		0,16		0,30	0,02
HCB	QOR096BT	wet weight	0,05			0,05		0,06		-0,50	0,01
a-HCH	QOR096BT	wet weight	<0.05			<0.02		0,03		c	0,05
b-HCH	QOR096BT	wet weight	0,02			0,02		0,02		0,00	0,02
g-HCH	QOR096BT	wet weight	<0.05			<0.02		0,03		c	0,05
pp'-DDE	QOR096BT	wet weight	0,7			0,70		0,66		0,42	0,01
pp'-DDD	QOR096BT	wet weight	0,24			0,24		0,22		0,49	0,01
pp'-DDT	QOR096BT	wet weight	<0.2			<0.2		*			0,05
op'-DDT	QOR096BT	wet weight	<0.1			<0.1		*			0,05
transn-chlor	QOR096BT	wet weight	0,05			0,05		0,06		-0,5	0,01

* no assigned value in this sample

**Z=(assigned value-mean)/assigned value*%error by the quasimeme laboratories

a- and g-chlordane, oxychlordane, toxaphenes and PBDEs are not certified in this sample by quasimeme

c: consistent

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 5. Qualitative assurance. Persistent organochlorines (ng/g ww) in a certified cod liver sample from QUASIMEME, that were analysed with the cod liver samples from 2011

Cod liver control				assign		
chemical	CRM	weight basis	mean	value	I Z I	det. Lim.
CB28	QOR0108BT	wet weight	10,7	10,55	0,11	0,20
CB31	QOR0108BT	wet weight	4,18	3,78	0,82	0,20
CB52	QOR0108BT	wet weight	25,32	23,7	0,54	0,1
CB101	QOR0108BT	wet weight	65,28	63,7	0,20	0,2
CB105	QOR0108BT	wet weight	17,21	16,3	0,44	0,10
CB118	QOR0108BT	wet weight	71,01	69,9	0,13	0,10
CB138	QOR0108BT	wet weight	138,01	148	-0,54	0,1
CB153	QOR0108BT	wet weight	236,72	219	0,65	0,1
CB156	QOR0108BT	wet weight	8,69	8,41	0,26	0,10
CB180	QOR0108BT	wet weight	45,79	45,5	0,05	0,12
HCB	QOR0108BT	wet weight	14,72	14,0	0,41	0,1
a-HCH	QOR0108BT	wet weight	1,41	1,37	0,22	0,10
b-HCH	QOR0108BT	wet weight	1,37	1,40	-0,16	0,1
g-HCH	QOR0108BT	wet weight	0,55	0.60*		0,2
pp'-DDE	QOR0108BT	wet weight	88,92	83,1	0,56	0,10
pp'-DDD	QOR0108BT	wet weight	26,85	26,7	0,04	0,1
pp'-DDT	QOR0108BT	wet weight	<0.4	*0.48**		0,4
op'-DDT	QOR0108BT	wet weight	<0.8	*0.83**		0,80
transn-chlor	QOR0108BT	wet weight	8,06	7,43	0,67	0,1

*** "assigned value" only "indicative". Quasimeme does not assign %error and thus Z-score can not be calculated.**

a- and g-chlordane, oxychlordane, toxaphenes and PBDEs are not certified in this sample by quasimeme

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 6. Detection limits* (ng/g)

	Detection limits	
chemical	**mussel ng/g sample dw**	**Cod liver ng/g sample ww**
a-HCH	0,05	0,05
HCB	0,02	0,05
b-HCH	0,10	0,05
g-HCH	0,10	0,16
PCB-31	0,20	0,20
PCB-28	0,25	0,20
PCB-52	0,10	0,10
oxychlordane	0,10	0,20
gamma-Chl.	0,20	0,05
PCB-101	0,10	0,20
alfa-Chl.	0,05	0,05
transnonachlor	0,05	0,05
4,4'-DDE	0,10	0,10
tox 26	0,05	0,10
PCB-118	0,10	0,05
4,4'-DDD	0,05	0,12
2,4'-DDT	0,10	0,20
PCB-153	0,05	0,05
PCB-105	0,05	0,05
4,4'-DDT	0,20	0,20
PCB-138	0,05	0,05
tox 50	0,10	0,10
PCB-156	0,05	0,05
PCB-180	0,05	0,12
tox 62	0,10	0,20
PCB-170	0,05	0,05
PBDE-47	0,05	0,20
PBDE-100	0,10	0,20
PBDE-99	0,10	0,20

***detection limits are 3 x std of blanks, or 3 x noise level or higher when other peaks interfer.**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix IV.

Results of trace metal analysis for Blue mussel (*Mytilus edulis*) 2009 and Cod (*Gadus morhua*) 2010

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Table 7. Results of trace metals in Blue mussel *(Mytilus edulis)* 2010 (dw)

Samples	Fat		Dry matter		Pb, mg/kg		Cd, mg/kg		Cu, mg/kg		Zn, mg/kg		As, mg/kg		Se, mg/kg		Hg, mg/kg	
	%	±	%	±	dw	±	dw	±	dw	±	dw	±	dw	±	dw	±	dw	±
Grímsey	0,18	0,01	7,20	0,3	0,07	0,015	3,64	0,7	7,19	1	314,58	63	14,40	3	2,44	0,5	0,08	0,02
Hvalstöð, Hvalfjörður	0,44	0,04	9,40	0,4	0,01	0,001	1,29	0,3	4,35	1	143,78	29	9,83	2	2,31	0,5	0,09	0,02
Hvammsvík, Hvalfjörður	0,22	0,02	8,30	0,3	0,00	0,001	1,31	0,3	3,56	1	133,36	27	9,11	2	2,91	0,6	0,04	0,01
Hvassahraun	0,25	0,02	5,80	0,23	0,02	0,003	1,44	0,3	5,76	1	183,03	37	19,41	4	2,30	0,5	0,06	0,01
Straumur,Straumsvík	0,69	0,06	8,90	0,36	0,01	0,001	1,73	0,3	4,85	1	125,10	25	11,64	2	2,89	0,6	0,06	0,01
Mjóifjörður , head-Fjörður	0,20	0,02	7,60	0,30	0,01	0,001	2,60	0,5	4,18	1	112,59	23	8,92	2	2,28	0,5	0,07	0,01
Mjóifjörður , Hofsá-brekka	0,26	0,02	7,90	0,32	0,01	0,002	2,75	0,5	3,80	1	128,73	26	9,94	2	1,83	0,4	0,08	0,02
Mjóifjörður , Dalatangi	0,15	0,01	6,80	0,27	0,01	0,001	1,84	0,4	3,51	1	138,57	28	16,14	3	1,50	0,3	0,08	0,02
Úlfsá, Skutulsfj.	0,20	0,02	7,50	0,30	0,06	0,012	0,84	0,2	3,68	1	97,50	20	59,74	12	2,10	0,4	0,07	0,01
Seljaland, Álftafjörður	0,32	0,03	6,50	0,26	0,02	0,003	3,98	0,8	5,74	1	104,69	21	13,39	3	5,00	1,0	0,07	0,01
Naust Laxárvogi	0,51	0,04	11,30	0,45	0,06	0,011	1,46	0,3	10,48	2	120,56	24	10,05	2	3,35	0,7	0,04	0,01
Limit of detection for samples (MLOD)					0,04		0,03		0,002		0,002		0,002		0,07		0,06	

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 8. Results of trace metals in liver and flesh of Cod (*Gadus morhua*) 2010 (ww)

Sample	Fat %		Dry matter %		Pb, mg/kg		Cd, mg/kg		Cu,mg/kg		Zn, mg/kg		As, mg/kg		Se, mg/kg		Dry matter %		Fat %		Hg, mg/kg	
	Liver	±	Liver	±	Liver		Liver	±	Liver	±	Liver	±	Liver	±	Liver	±	Flesh*	±	Flesh*	±	Flesh*	±
Cod N-NW (2) 07																						
Group 1	46,6	4	59,8	2	<0,04		0,33	0,07	3,9	0,8	15,2	3	6,0	1	1,1	0,2						
Group 3	57,8	5	68,7	3	<0,04		0,24	0,05	1,9	0,4	9,9	2	5,8	1	0,7	0,1						
Group 5	66,0	5	73,7	3	<0,04		0,13	0,03	2,9	0,6	9,6	2	5,2	1	0,5	0,1						
Average	***56,8***		***67,4***				***0,23***		***2,9***		***11,6***		***5,7***		***0,8***		***19,2***	***0,8***	***0,09***	***0,007***	***0,028***	***0,006***
Cod NA07																						
Group 1	44,3	4	56,9	2	<0,04		0,25	0,05	4,3	0,9	14,3	3	9,1	2	1,3	0,3						
Group 3	51,1	4	62,0	2	<0,04		0,19	0,04	2,7	0,5	11,8	2	6,2	1	1,0	0,2						
Group 5	55,1	4	63,8	3	<0,04		0,12	0,02	2,1	0,4	10,1	2	5,5	1	0,9	0,2						
Average	***50,2***		***60,9***				***0,19***		***3,0***		***12,1***		***7,0***		***1,1***		***18,7***	***0,7***	***0,04***	***0,003***	***0,032***	***0,006***
Average of all measurements					<0,04		0,21		3,0		11,8		6,3		0,9						0,02	
Limit of detection for samples (MLOD)					0,04		0,03		0,002		0,002		0,002		0,07						0,06	

*Flesh was pooled into one sample

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix V.

Results of organochlorine analysis for Blue mussel (*Mytilus edulis*) 2009 and Cod (*Gadus morhua*) 2010

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 9 a. Persistent organochlorines in Blue mussel (Mytulis edulis, ng/g dw) 2010

	Grímsey 10	Hvammsvík 10	Hvalstöð 10	Úlfsá 10	Seljaland 10	Hvassahraun 10
PCB28	<0.25	<0.25	<0.25	<0.25	<0.25	0,33
PCB31	<0.20	<0.20	<0.20	<0.20	<0.20	0,31
PCB52	<0.1	0,166	0,919	0,161	<0.1	0,32
PCB101	0,06	0,34	1,60	0,66	0,12	0,19
PCB105	0,05	0,13	0,36	0,17	0,08	0,08
PCB118	0,06	0,39	1,61	0,55	0,16	0,17
PCB138	0,18	0,90	2,61	1,08	0,29	0,38
PCB153	0,27	1,10	4,50	1,56	0,35	0,48
PCB156	<0.05	<0.05	0,124	<0.05	<0.05	<0.05
PCB170	<0.05	<0.05	0,073	<0.05	<0.05	<0.05
PCB180	<0.05	<0.05	0,48	0,09	<0.05	<0.05
S3PCB**	0,51	2,39	8,72	3,19	0,80	1,03
HCB	0,08	0,07	0,20	0,32	0,09	0,06
a-HCH	0,12	0,06	0,08	<0.05	<0.05	<0.05
b-HCH	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
g-HCH	<0.1	0,14	0,15	<0.1	<0.1	0,23
p,p'-DDE	0,26	0,55	11,33	0,49	0,21	0,26
p,p'-DDD	<0.05	0,12	1,65	0,12	<0.05	<0.05
p,p'-DDT	<0.2	<0.2	0,24	<0.2	<0.2	<0.2
o,p'-DDT***	<0.1	<0.1	0,33	<0.1	<0.1	<0.1
PCB153/DDE	1,0	2,0	0,4	3,2	1,7	1,85
transnonachlor	0,11	0,16	2,58	0,35	0,14	0,06
a-chlordan	0,06	0,09	0,24	0,08	0,08	0,07
g-chlordan	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2
oxychlordan	<0.1	<0.1	0,31	<0.1	<0.1	<0.1
Tox-26	0,12	0,17	0,59	0,22	0,16	0,08
Tox-50	0,12	0,19	0,75	0,24	0,21	0,10
Tox-62	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
PBDE-47	1,17	0,23	0,62	0,74	<0.05	<0.05
PBDE-99	0,26	<0.1	0,17	0,30	<0.1	<0.1
PBDE-100	<0.1	<0.1	0,10	0,19	<0.1	<0.1
% extracted fat	26,0%	31,0%	43,0%	32,0%	31,0%	20,0%
% dw (Matis)	7,16	7,6	9,5	7,55	6,16	5,96

**** PCB # 118, 138 and 153**

*****Values are highly suspect and these are not certified in QUASIMEME blue mussel**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 9 b. Persistent organochlorines in Blue mussel (Mytulis edulis, ng/g dw) 2010

	Straumur 10	Dalatangi 10	Brekka 10	Fjörður 10	Naust 10
PCB28	0,93	0,24	<0.25	<0.25	<0.25
PCB31	0,69	0,23	<0.20	0,22	<0.20
PCB52	0,70	0,30	0,26	0,22	0,20
PCB101	0,63	0,32	0,40	0,09	0,44
PCB105	0,18	0,15	0,13	<0.05	0,16
PCB118	0,54	0,34	0,35	0,07	0,45
PCB138	1,16	0,42	1,51	0,19	0,86
PCB153	1,61	0,38	1,75	0,21	1,29
PCB156	0,08	<0.05	0,11	<0.05	<0.05
PCB170	<0.05	<0.05	<0.05	<0.05	<0.05
PCB180	0,08	<0.05	0,17	<0.05	0,11
S3PCB**	3,31	1,14	3,60	0,47	2,60
HCB	0,14	0,10	0,13	0,10	0,24
a-HCH	0,09	0,07	0,11	0,07	0,13
b-HCH	<0.1	<0.1	<0.1	<0.1	<0.1
g-HCH	0,31	0,44	0,67	0,58	0,15
p,p'-DDE	0,74	0,14	0,63	0,18	0,52
p,p'-DDD	0,32	<0.05	0,09	<0.05	0,09
p,p'-DDT	0,48	<0.2	<0.2	<0.2	<0.2
o,p'-DDT***	0,31	<0.1	<0.1	<0.1	<0.1
PCB153/DDE	2,17	2,70	2,78	1,15	2,46
transnonachlor	0,18	0,09	0,27	0,12	0,23
a-chlordan	0,13	0,09	0,13	0,09	0,13
g-chlordan	<0.2	<0.2	<0.2	<0.2	<0.2
oxychlordan	<0.1	<0.1	<0.1	<0.1	<0.1
Tox-26	0,22	0,11	0,24	0,17	0,21
Tox-50	0,26	0,15	0,36	0,23	0,24
Tox-62	<0.1	<0.1	<0.1	<0.1	<0.1
PBDE-47	0,507	<0.05	0,097	<0.05	0,31
PBDE-99	0,243	<0.1	<0.1	<0.1	0,116
PBDE-100	0,159	<0.1	<0.1	<0.1	<0.1
% extracted fat	71,0%	23,5%	36,0%	36,0%	62,0%
% dw (Matis)	9,04	7	7,94	7,79	11,12

**** PCB # 118, 138 and 153**

*****Values are highly suspect and these are not certified in QUASIMEME blue mussel**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 10 a. Persistent organochlorines in cod liver 2011 (ng/g ww)

	COD NE	COD NE	COD NE
	H1	H3	H5
PCB28	2,0	2,1	2,1
PCB31	1,0	1,2	1,2
PCB52	3,5	3,8	3,8
PCB101	5,9	5,3	5,3
PCB105	2,1	1,8	1,8
PCB118	9,1	7,8	7,8
PCB138	15,5	10,0	10,0
PCB153	27,3	16,9	16,9
PCB156	0,84	0,62	0,62
PCB170	2,5	1,2	1,2
PCB180	7,6	3,5	3,5
S7PCB**	70,8	49,4	49,4
HCB	13,9	17,2	17,2
a-HCH	1,9	2,2	2,2
b-HCH	0,48	0,55	0,55
g-HCH	0,64	0,76	0,76
p,p'-DDE	50,9	34,4	34,4
p,p'-DDD	10,5	11,4	11,4
p,p'-DDT****	4,2	4,3	4,3
o,p'-DDT****	2,5	3,3	3,3
SDDT	68,2	53,4	53,4
PCB153/DDE	0,54	0,49	0,49
transnonachlor	21,1	17,8	17,8
a-chlordan	12,9	14,1	14,1
g-chlordan	4,1	4,8	4,8
oxychlordan	3,7	3,0	3,0
SCHL	41,8	39,7	39,7
Tox-26	17,3	16,6	16,6
Tox-50	23,2	22,3	22,3
Tox-62	10,5	13,2	13,2
PBDE-47	2,3	2,2	2,2
PBDE-99	<0.2	<0.2	<0.2
PBDE-100	0,44	0,41	0,41
% extracted fat	43,9%	50,2%	54,3%

**** PCB # 28, 52, 101, 118, 138, 153, 180**

***** Contamination prevents accurate quantification**

****** Not certified values (indicative) in QUASIMEME cod liver**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 10 b. Persistent organochlorines in cod liver 2011 (ng/g ww)

	COD NNW2	COD NNW2	COD NNW2
	H1	H3	H5
PCB28	2,5	2,2	2,5
PCB31	1,4	1,1	1,4
PCB52	4,7	3,4	3,9
PCB101	6,9	4,7	4,8
PCB105	2,2	1,7	1,5
PCB118	9,4	6,9	6,4
PCB138	12,2	9,9	8,4
PCB153	19,4	15,0	12,9
PCB156	0,8	0,5	0,5
PCB170	1,4	1,2	0,8
PCB180	3,9	3,1	2,2
S7PCB**	59,0	45,1	41,1
HCB	15,7	14,7	16,7
a-HCH	2,0	2,6	2,6
b-HCH	0,52	0,64	0,68
g-HCH	0,62	0,79	0,78
p,p'-DDE	42,0	30,2	26,1
p,p'-DDD	12,6	10,4	10,9
p,p'-DDT****	3,6	2,9	3,0
o,p'-DDT****	3,0	2,4	2,7
SDDT	61,2	45,8	42,7
PCB153/DDE	0,46	0,50	0,50
transnonachlor	20,1	15,1	14,9
a-chlordan	13,9	11,1	12,8
g-chlordan	4,6	3,9	4,4
oxychlordan	4,2	3,8	3,5
SCHL	42,8	33,9	35,6
Tox-26	18,6	15,8	17,6
Tox-50	23,3	19,2	23,8
Tox-62	10,8	8,7	13,2
PBDE-47	2,6	2,0	1,8
PBDE-99	<0.2	<0.2	<0.2
PBDE-100	0,48	0,35	0,41
% extracted fat	48,5%	57,1%	63,9%

**** PCB # 28, 52, 101, 118, 138, 153, 180**

***** Contamination prevents accurate quantification**

****** Not certified values (indicative) in QUASIMEME cod liver**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix VI.

Graphs of biological variation in Cod (Gadus morhua) 1990-2010

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Biological variation in 30-45 cm Cod (Gadus morhua) from Icelandic waters in March 1990-2011

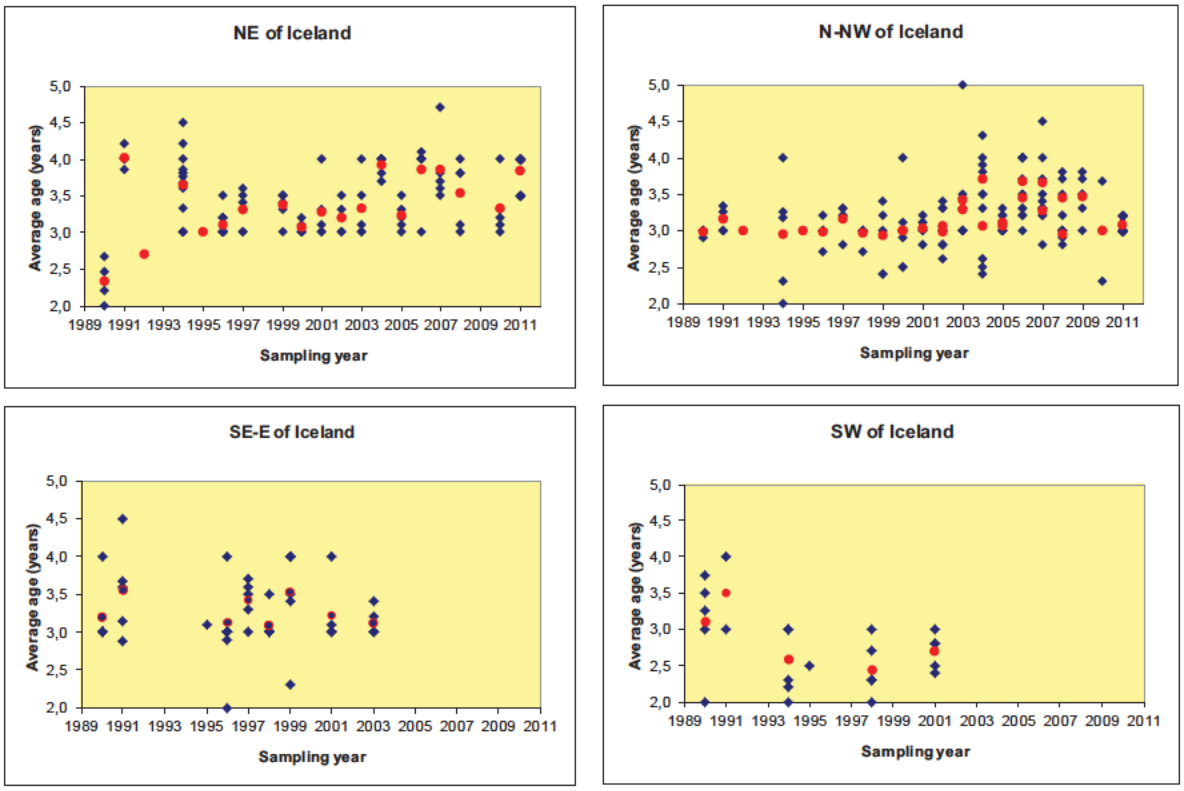

Figure 2a. Average age in 30-45 cm Cod (Gadus morhua) from Icelandic waters in March 1990-2011.The red dots represent the average values.

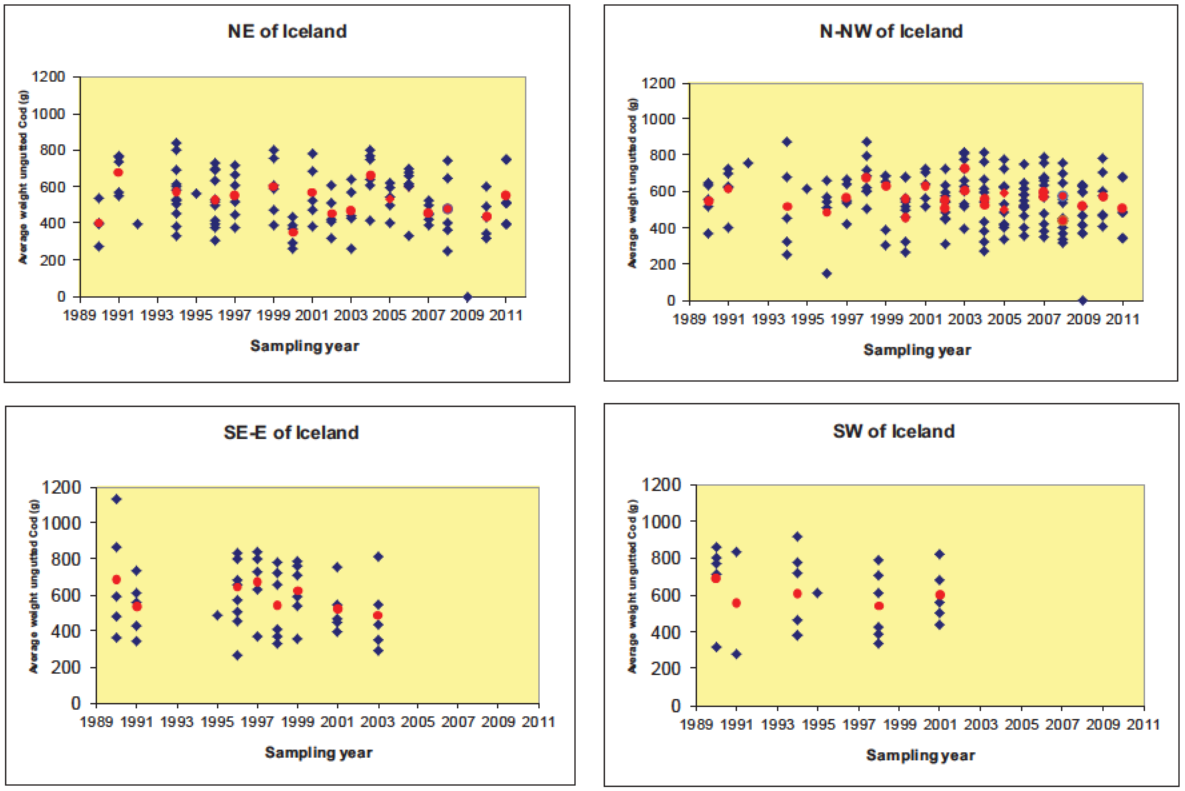

Figure 2b. Average weight ungutted Cod (Gadus morhua), 30-45 cm, from Icelandic waters in March 1990-2011.The red dots represent the average values.

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Biological variation in 30-45 cm Cod (Gadus morhua) from Icelandic waters in March 1990-2011

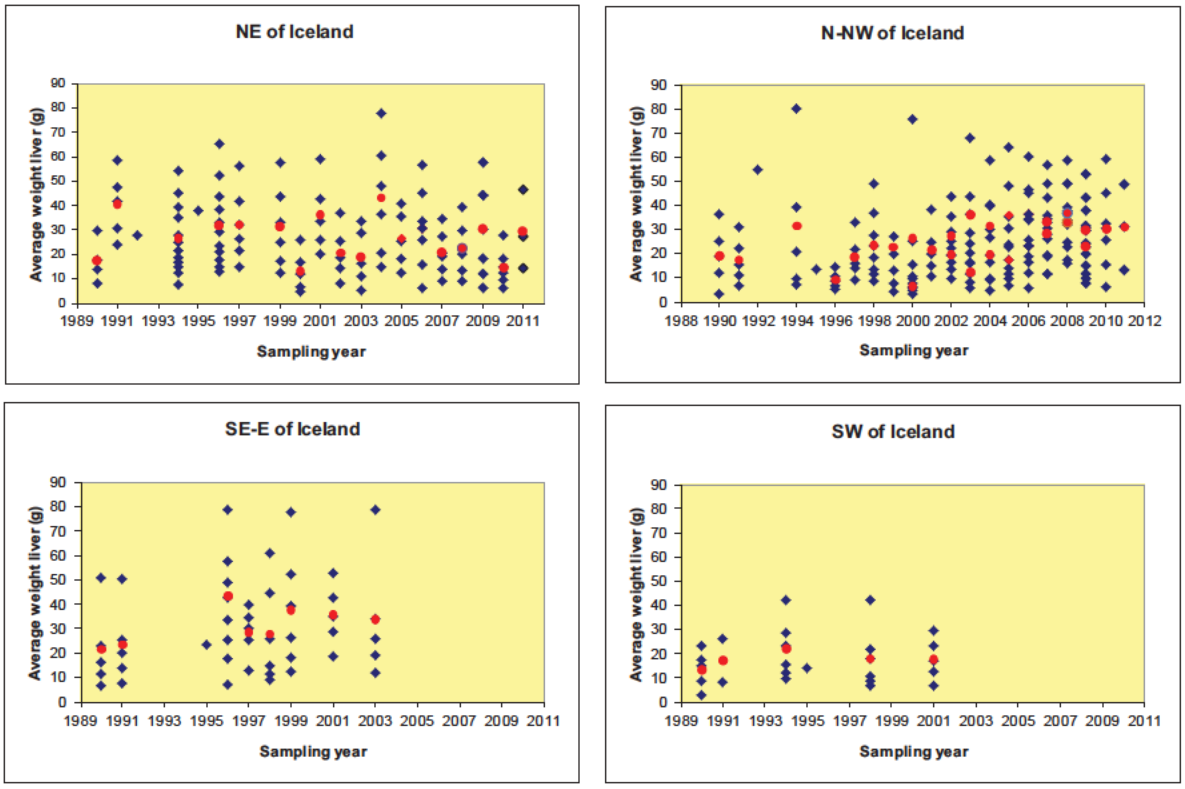

Figure 2c. Average weight liver of Cod (Gadus morhua), 30-45 cm, from Icelandic waters in March 1990-2011.The red dots represent the average values.

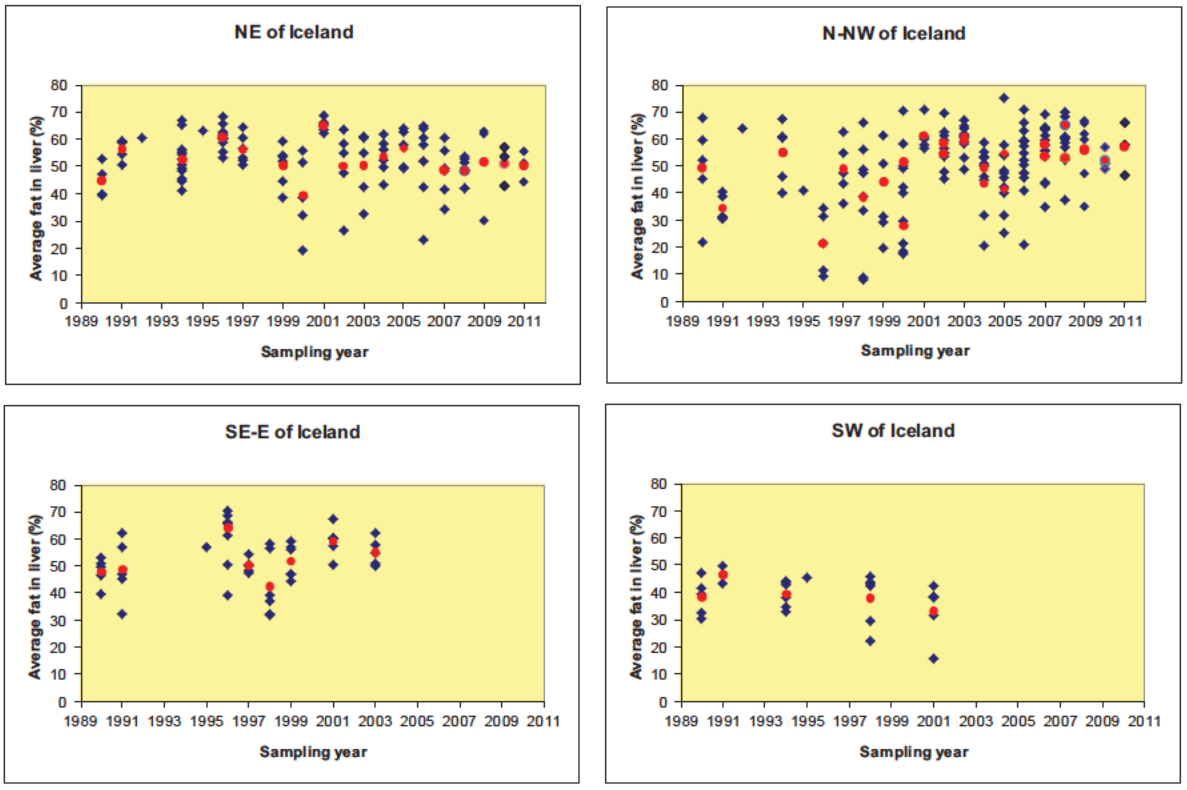

Figure 2d. Average fat (%) in liver of Cod (Gadus morhua), 30-45 cm, from Icelandic waters in March 1990-2011.The red dots represent the average values.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix VII.

Graphs of metals and organic compounds in Blue mussel (*Mytilus edulis*) 1990-2009

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

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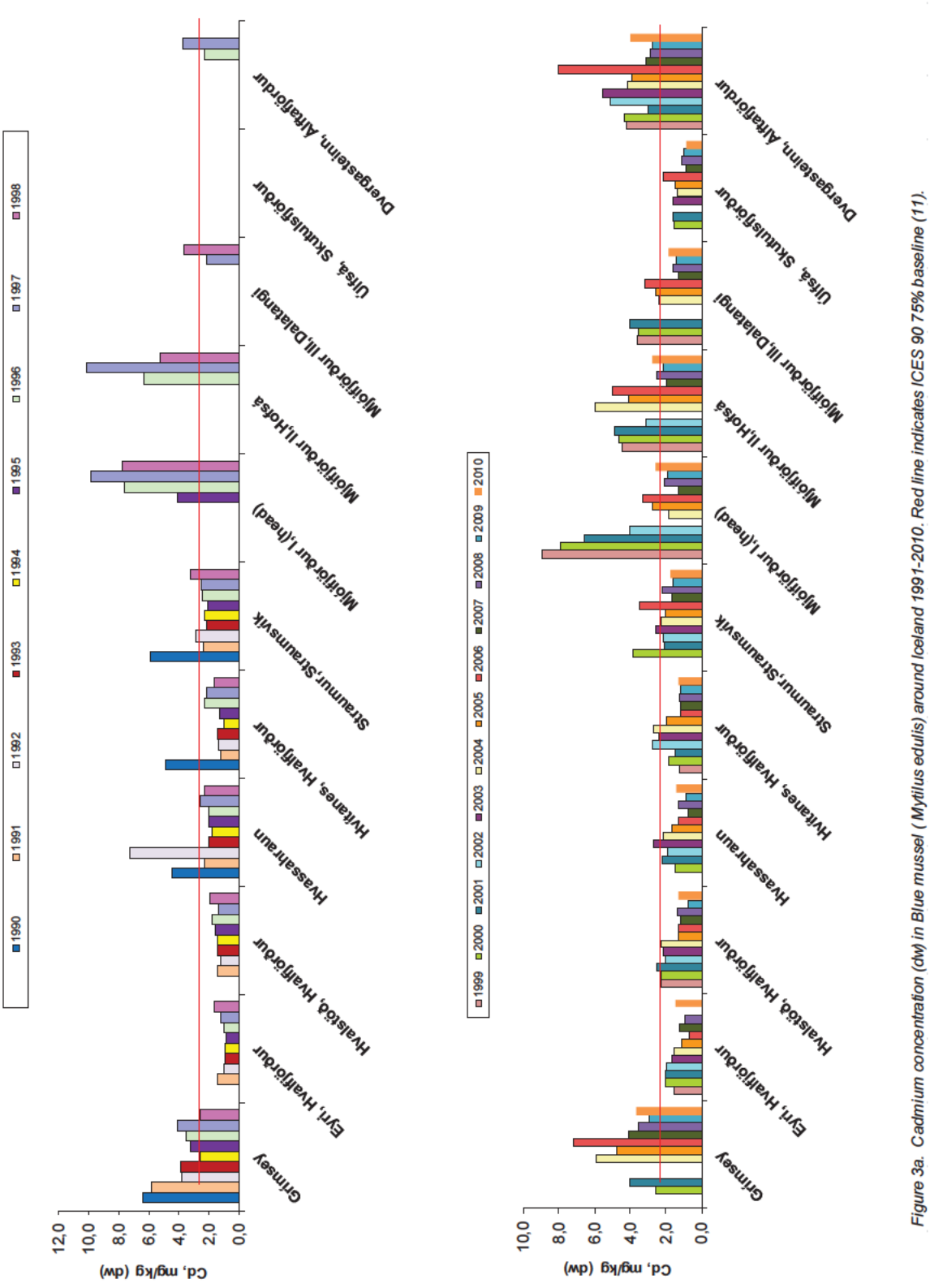

Figure 3a. Cadmium concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1991-2010. Red line indicates ICES 90 75% baseline (11).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

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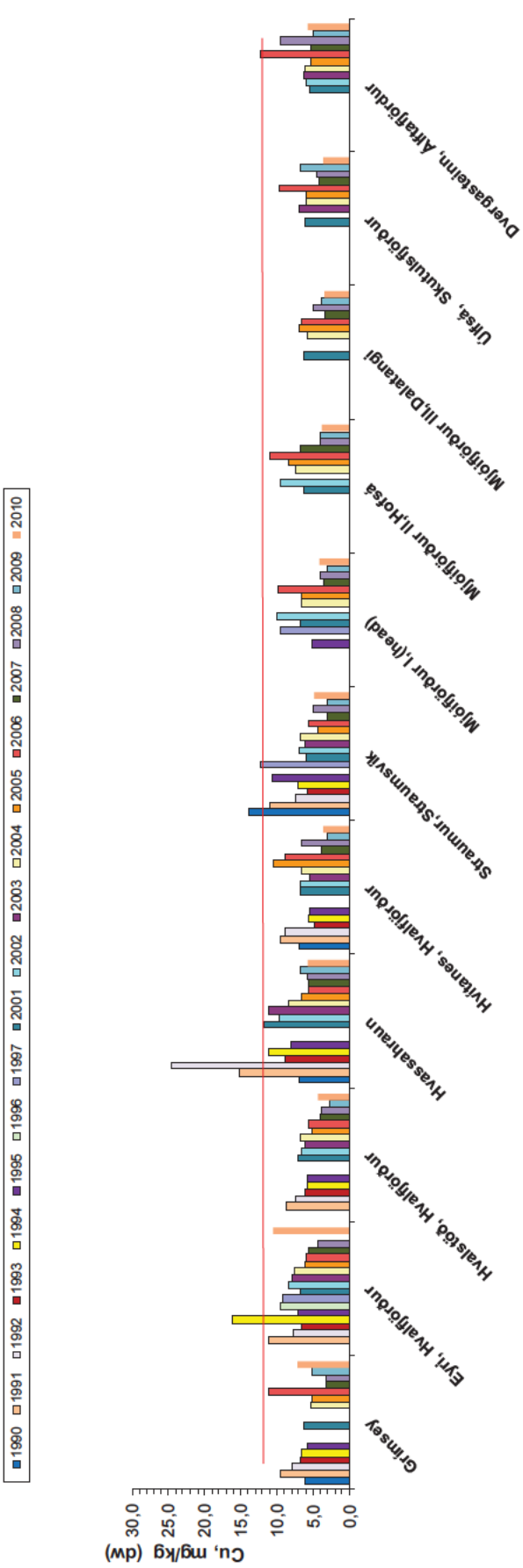

Figure 3b. Copper concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1990-2010. Red line indicates ICES 90 75% baseline (11).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

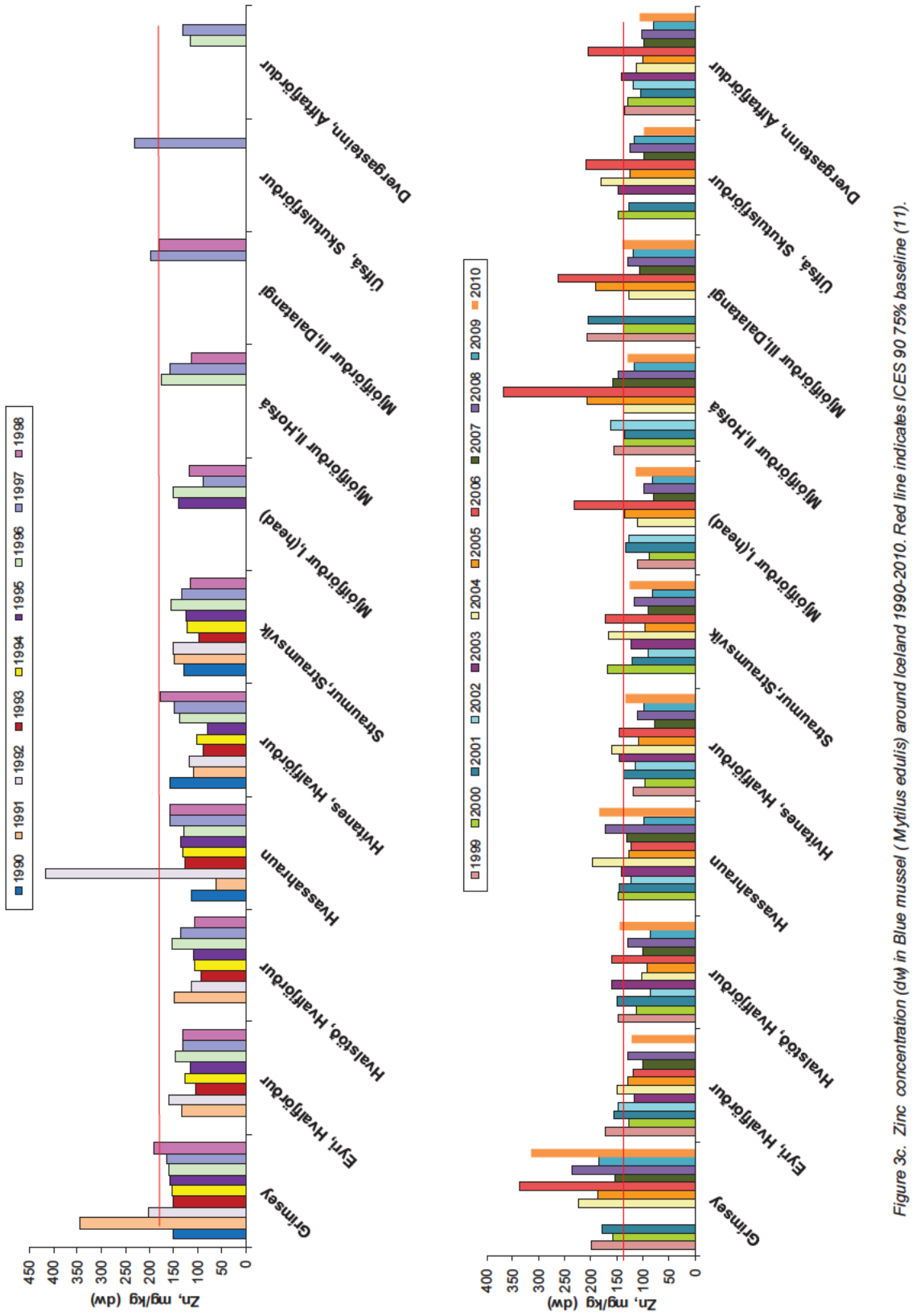

Figure 3c. Zinc concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1990-2010. Red line indicates ICES 90 75% baseline (11).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

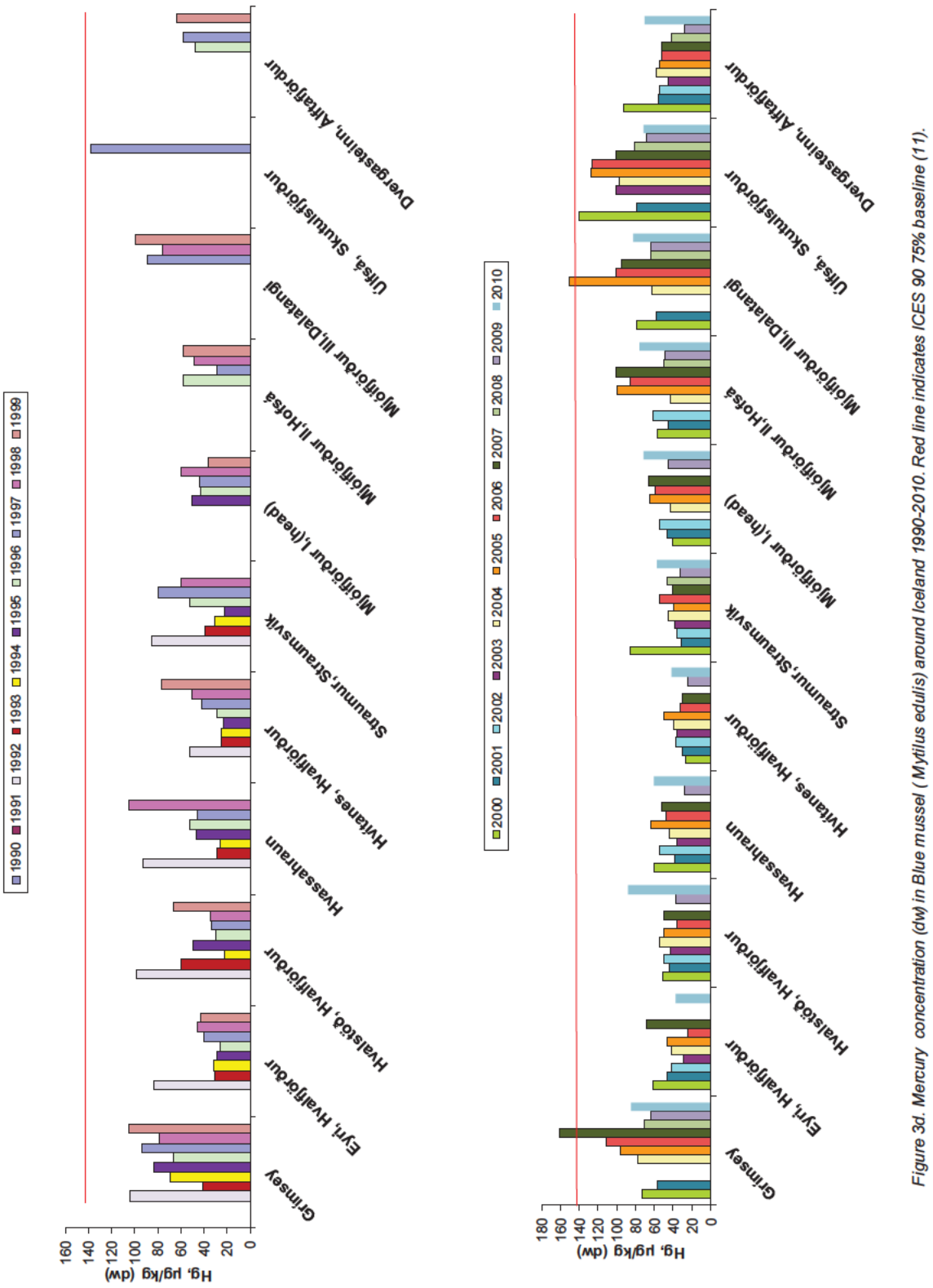

Figure 3d. Mercury concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1990-2010. Red line indicates ICES 90 75% baseline (11).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

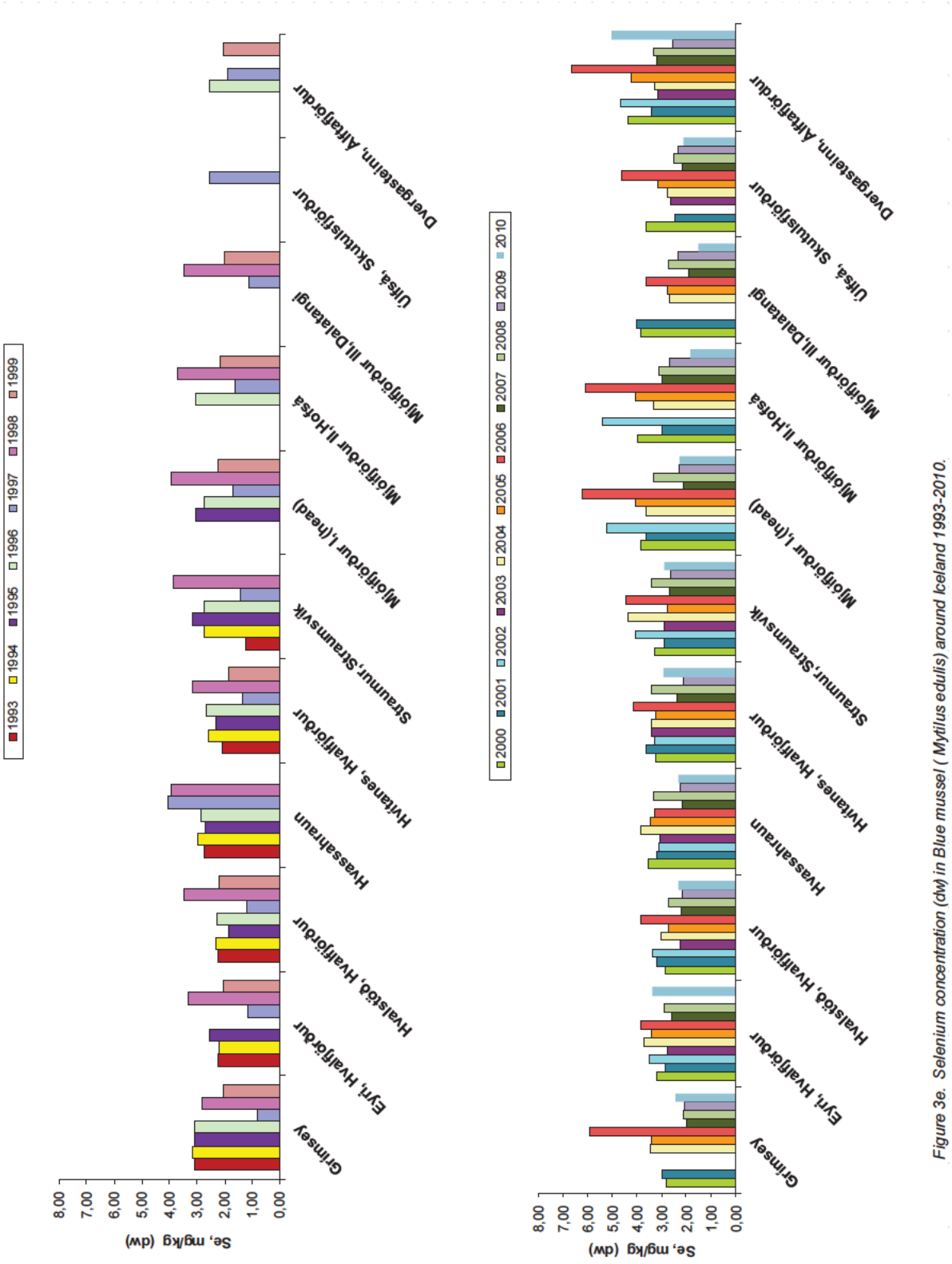

Figure 3e. Selenium concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1993-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

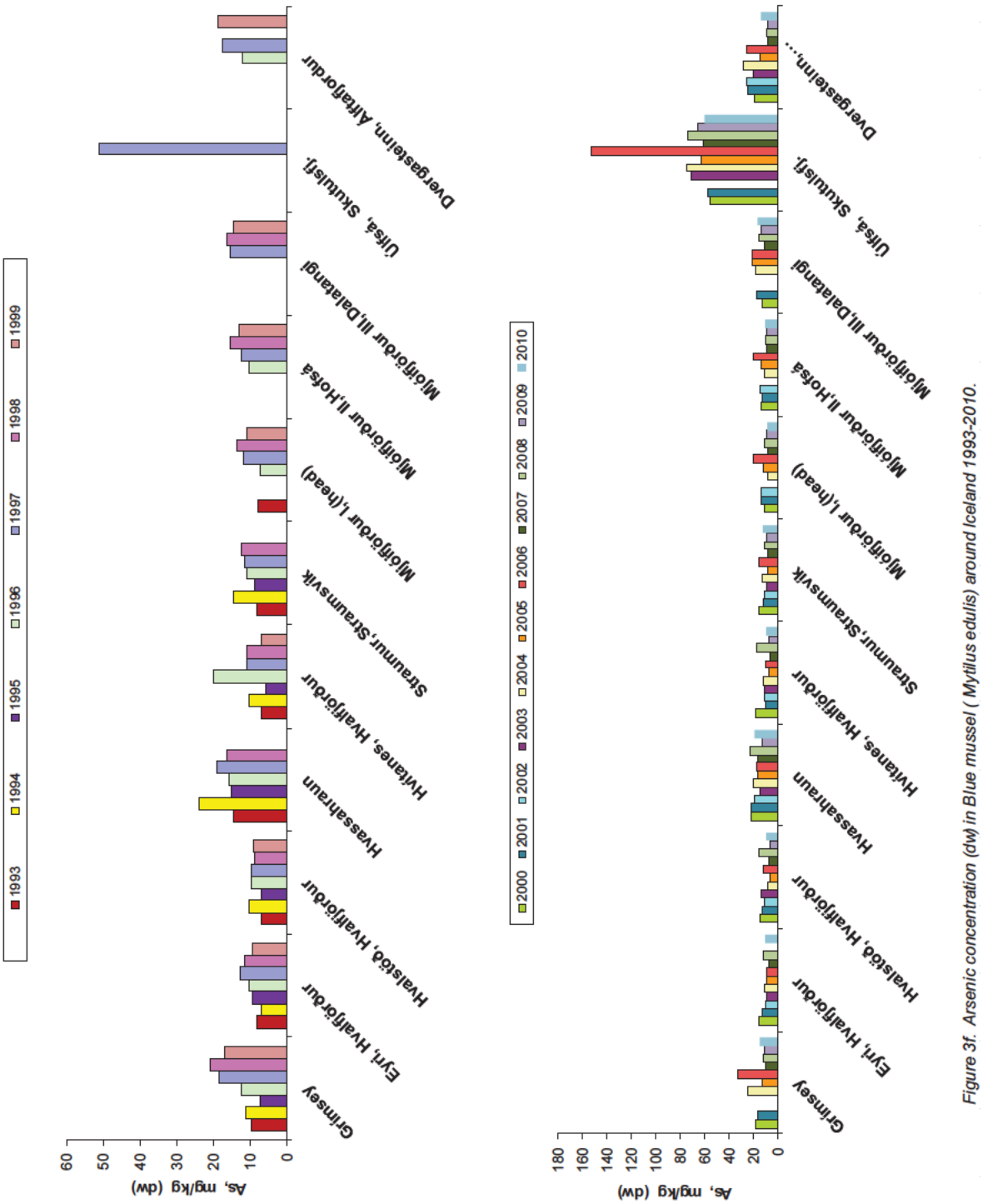

Figure 3f. Arsenic concentration (dw) in Blue mussel (Mytilus edulis) around Iceland 1993-2010.

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

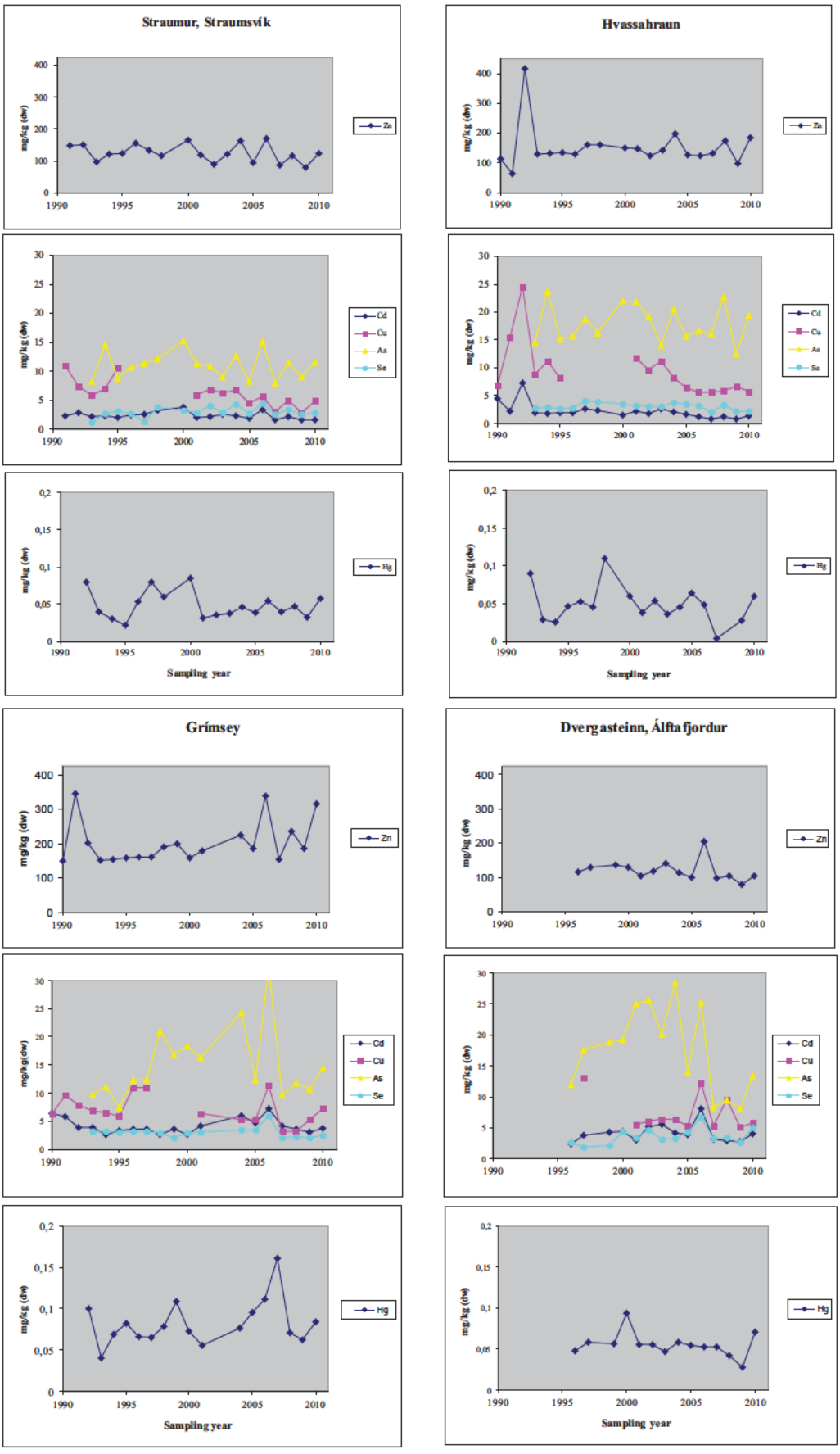

Figure 4a. Concentration of heavy metals (dry weight) in Blue mussel from different sampling sites around Iceland, 1990-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

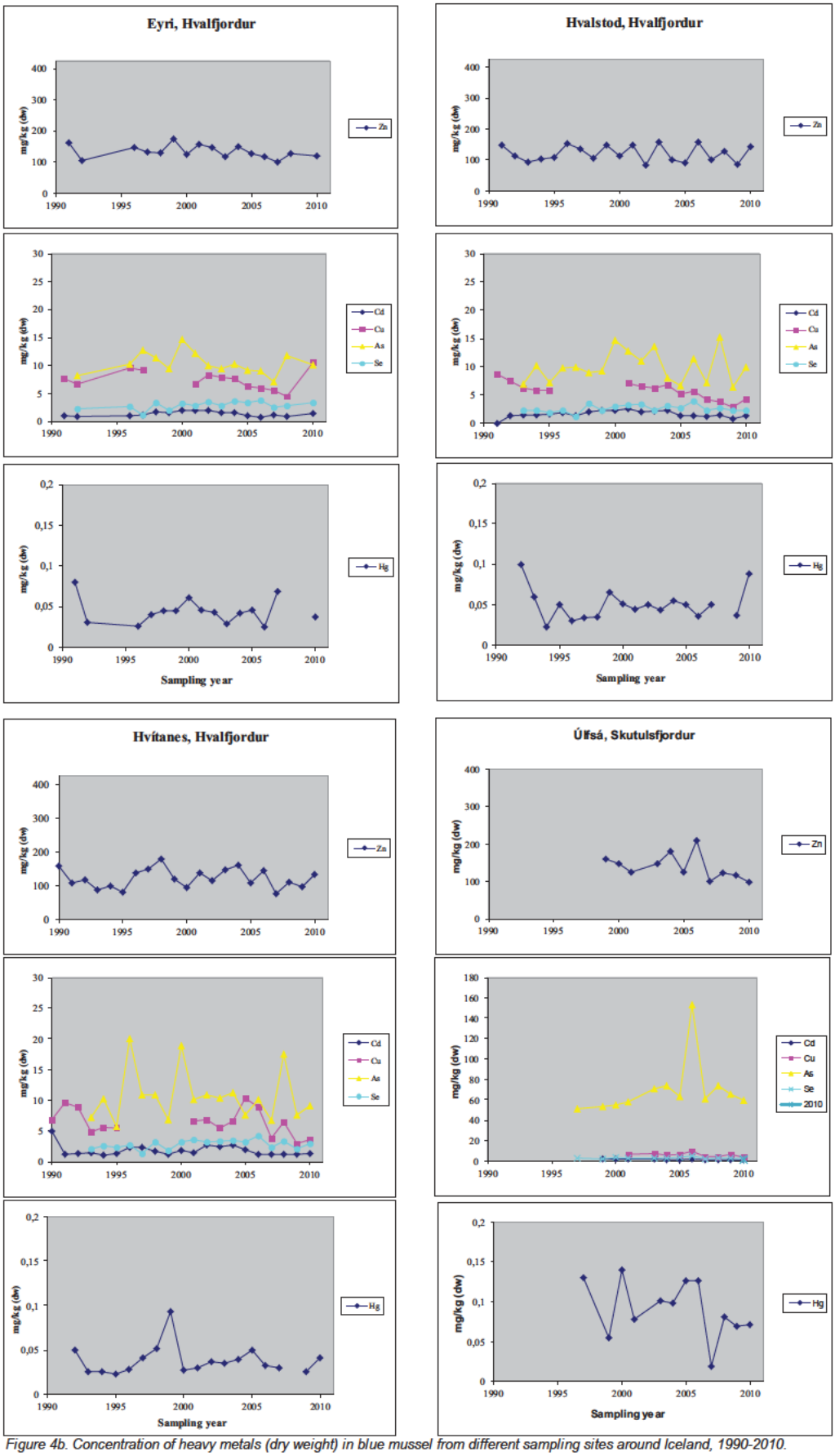

Figure 4b. Concentration of heavy metals (dry weight) in blue mussel from different sampling sites around Iceland, 1990-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

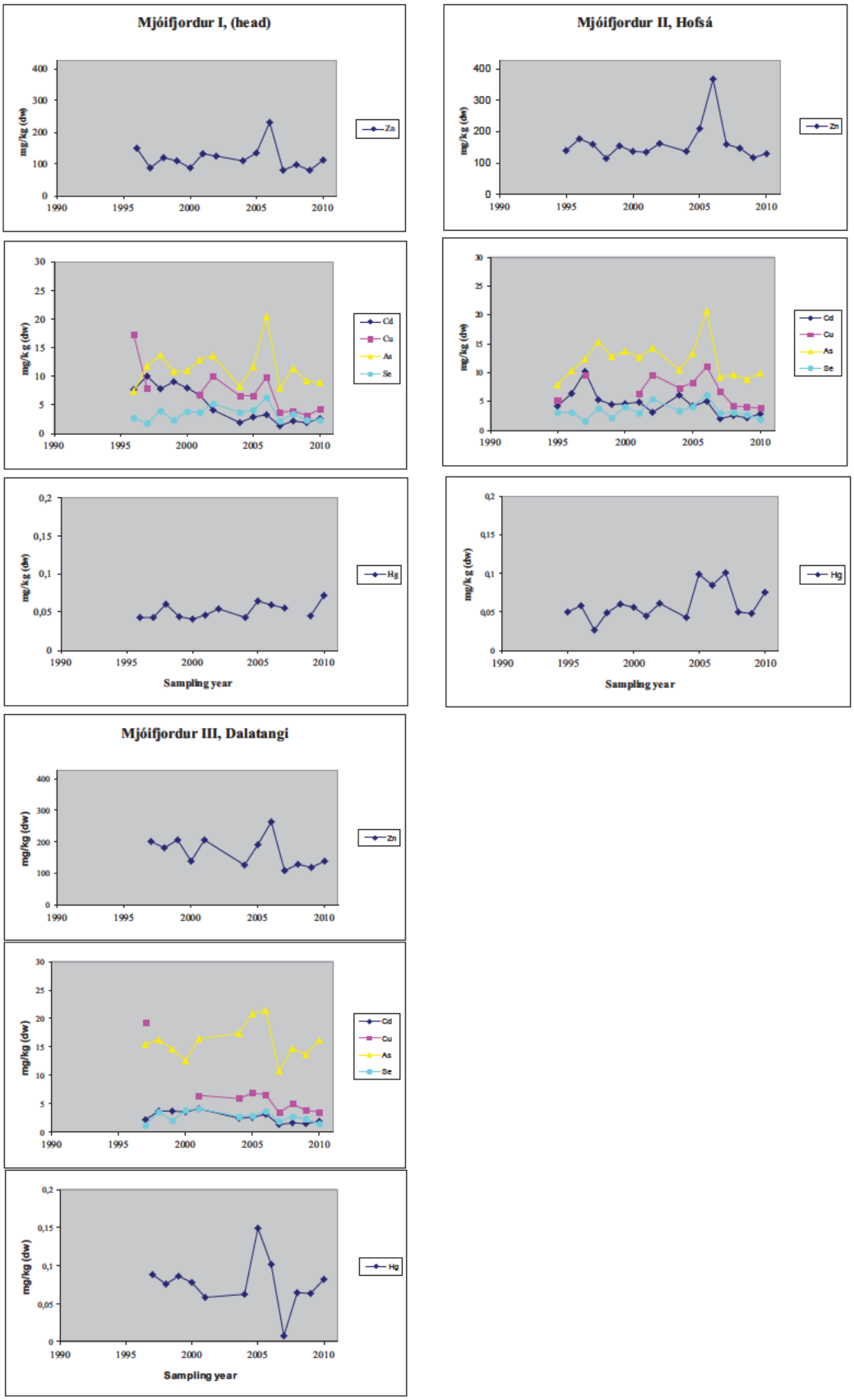

Figure 4c. Concentration of heavy metals (dry weight) in blue mussel from different sampling sites around Iceland, 1990-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

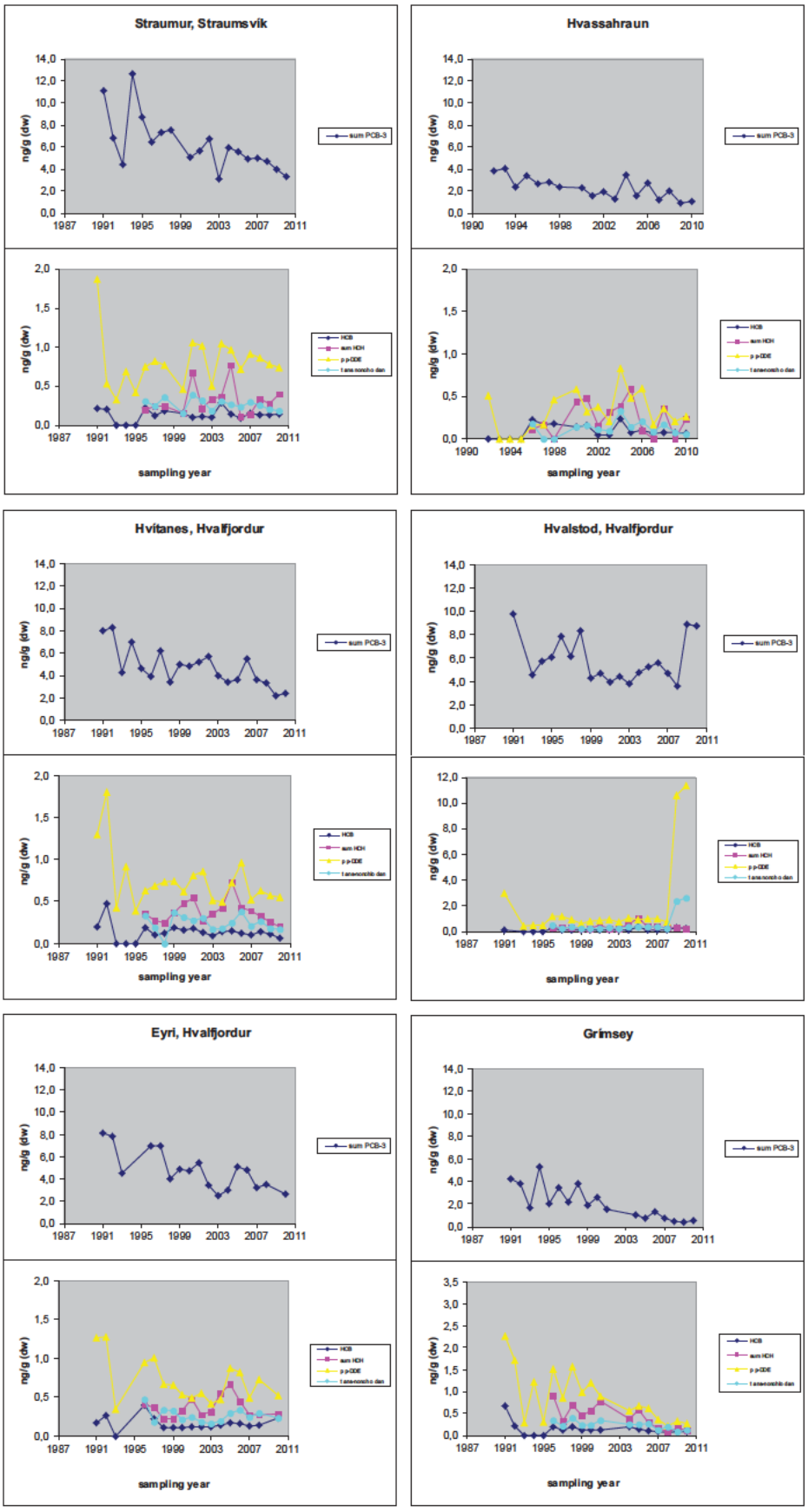

Figure 5a. Concentration of organochlorine compounds (dw) in Blue mussel (Mytilus edulis) at different locations 1991-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8152

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

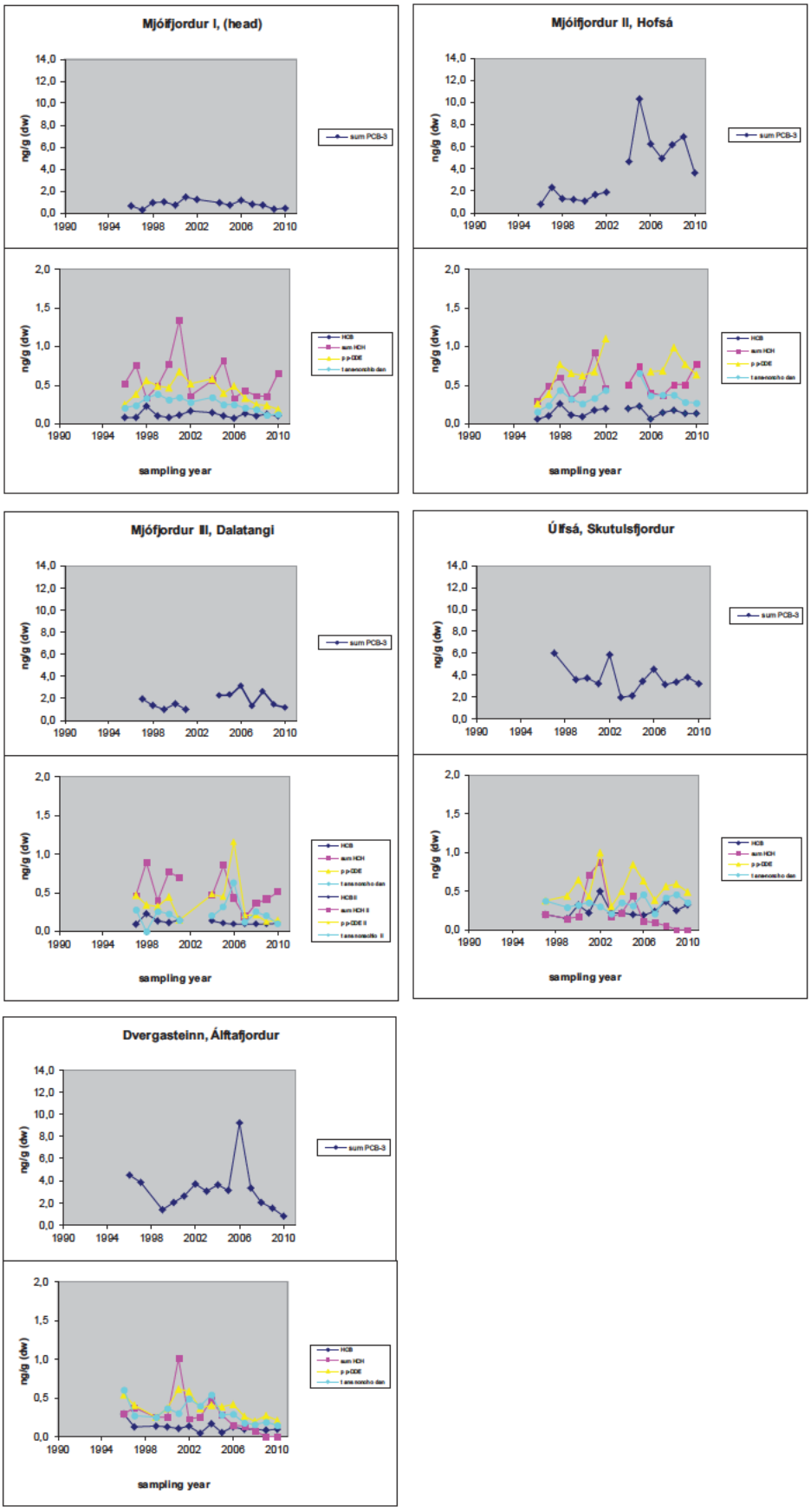

Figure 5b. Concentration of organochlorine compounds (dw) in Blue mussel (Mytilus edulis) at different locations 1991-2010.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8138

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix VIII.

Graphs of metals and organic compounds in Cod (*Gadus morhua*) 1990-2009

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

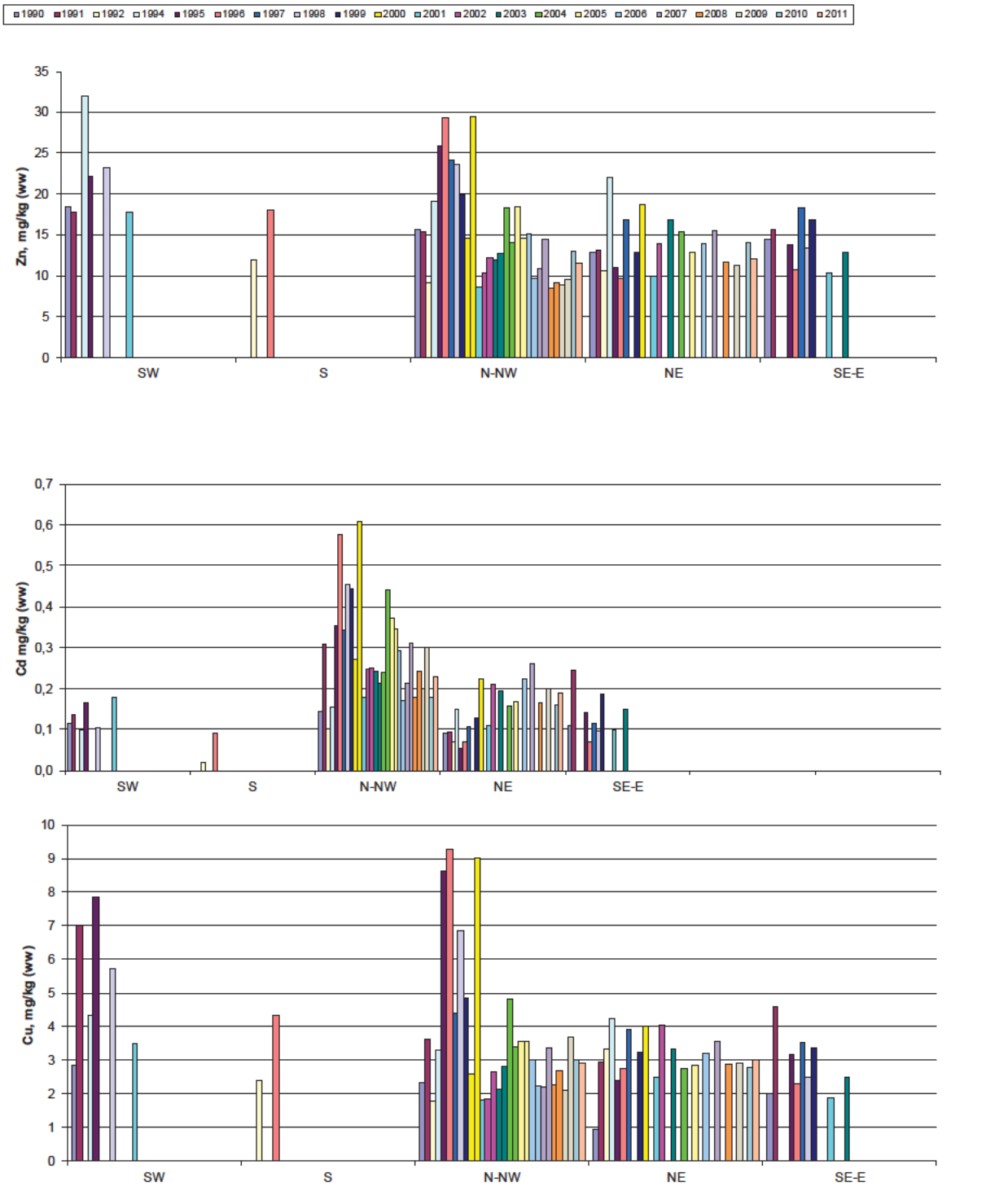

Figure 6a. Heavy metal concentration (ww) in livers of 30-45cm cod (Gadus morhua) from Icelandic waters in March 1990-2011.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

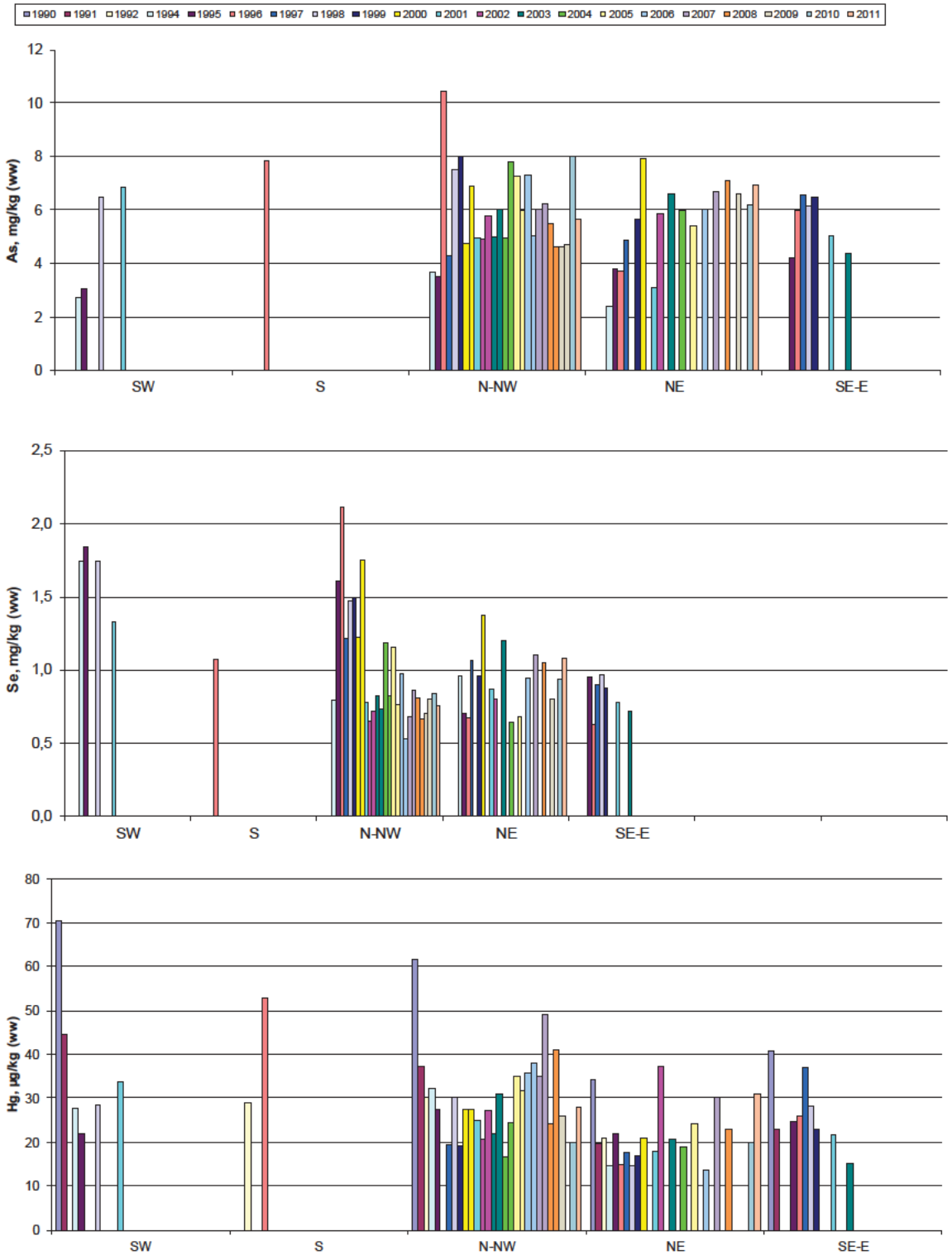

Figure 6b. Heavy metal concentration (ww) in livers of 30-45cm cod (Gadus morhua) from Icelandic waters in March 1990-2011 Mercury (Hg) was analysed in the flesh

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

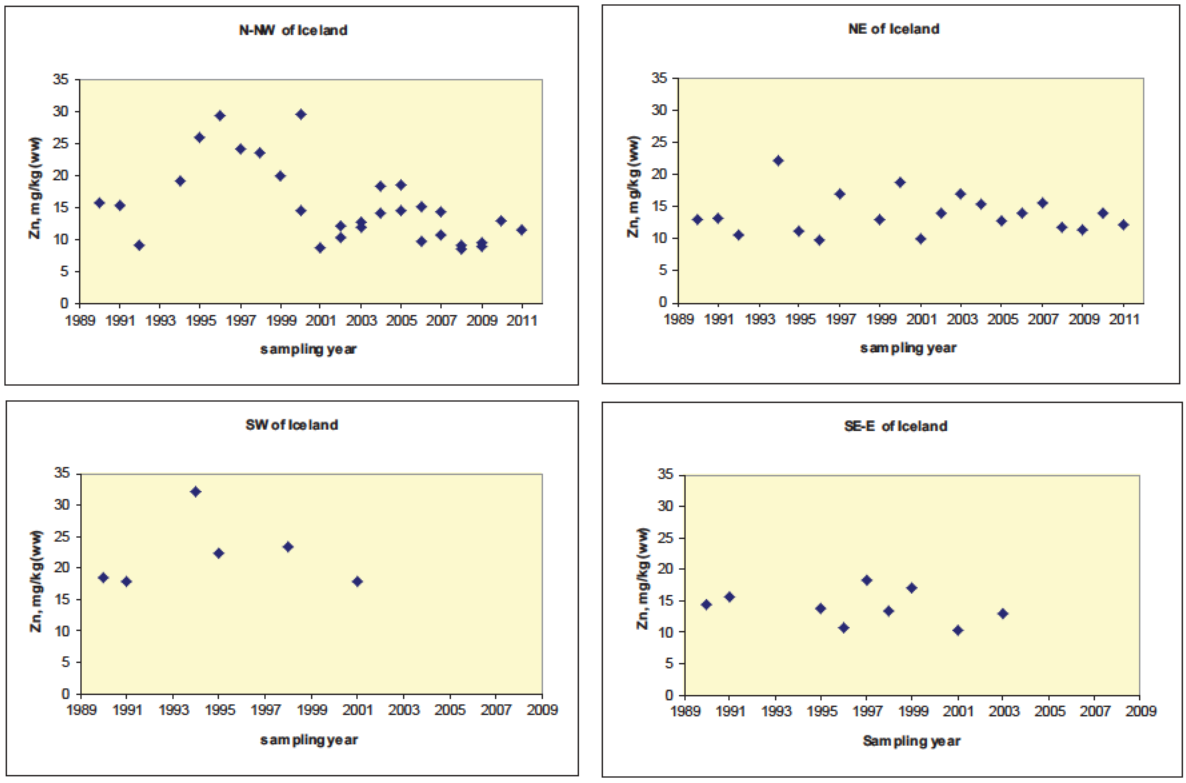

Figure 7a. Average concentration of Zinc (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

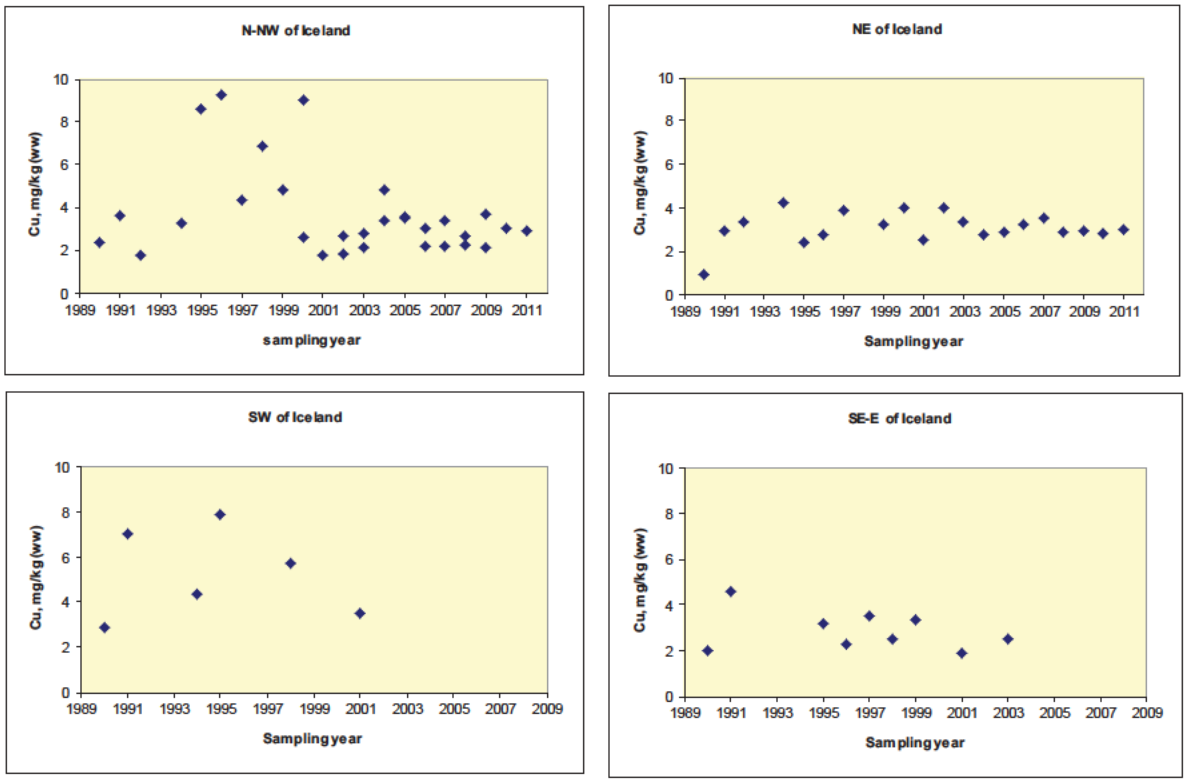

Figure 7b. Average concentration of Copper (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

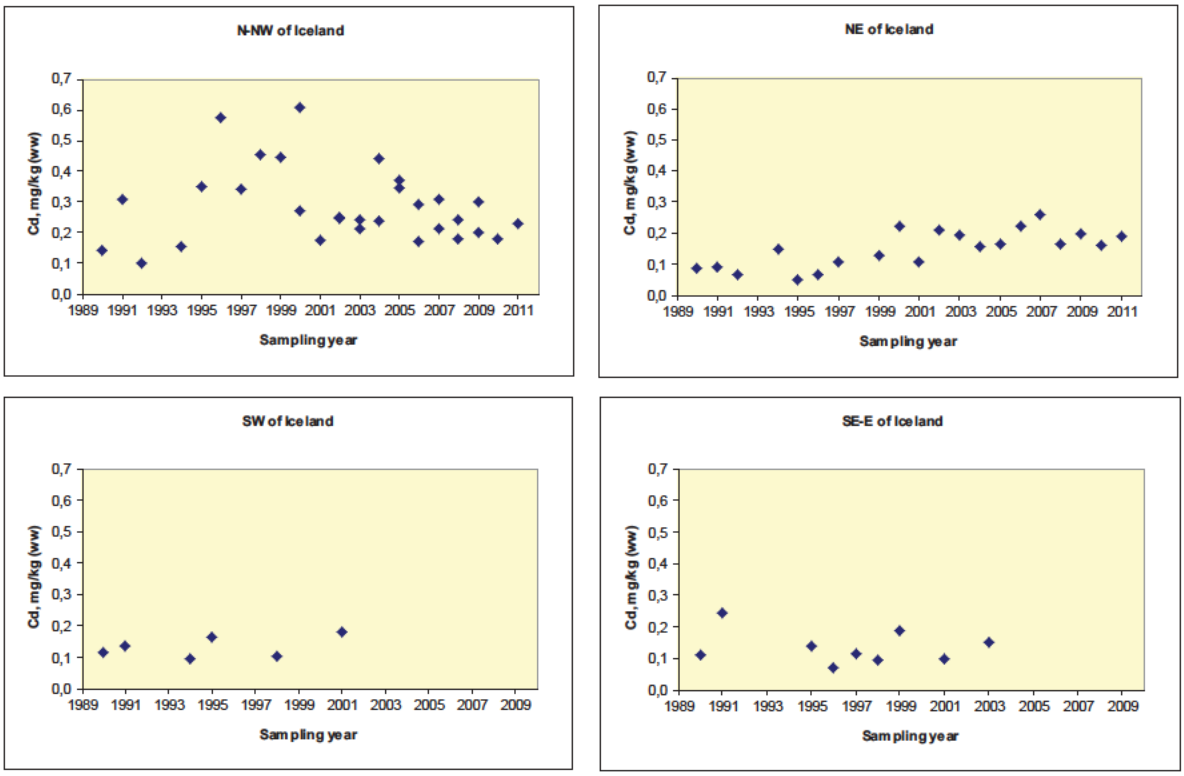

Figure 7c. Average concentration of Cadmium (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

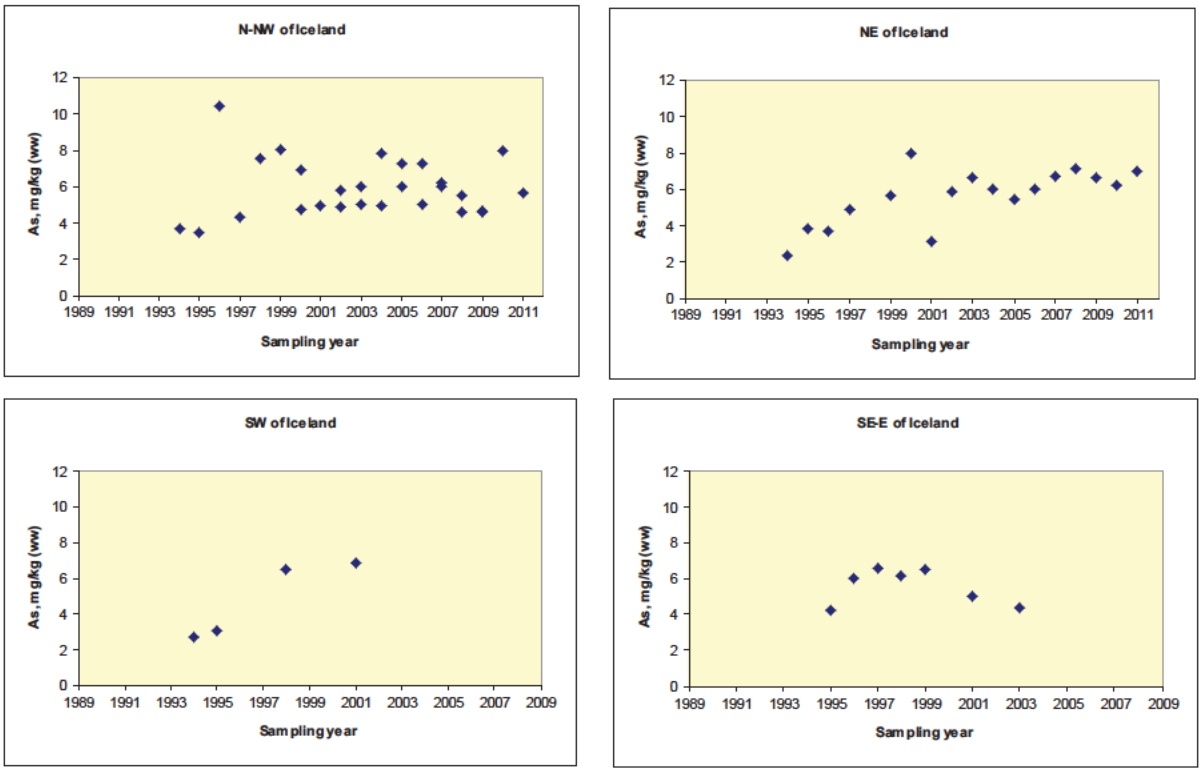

Figure 7d. Average concentration of Arsenic (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8158

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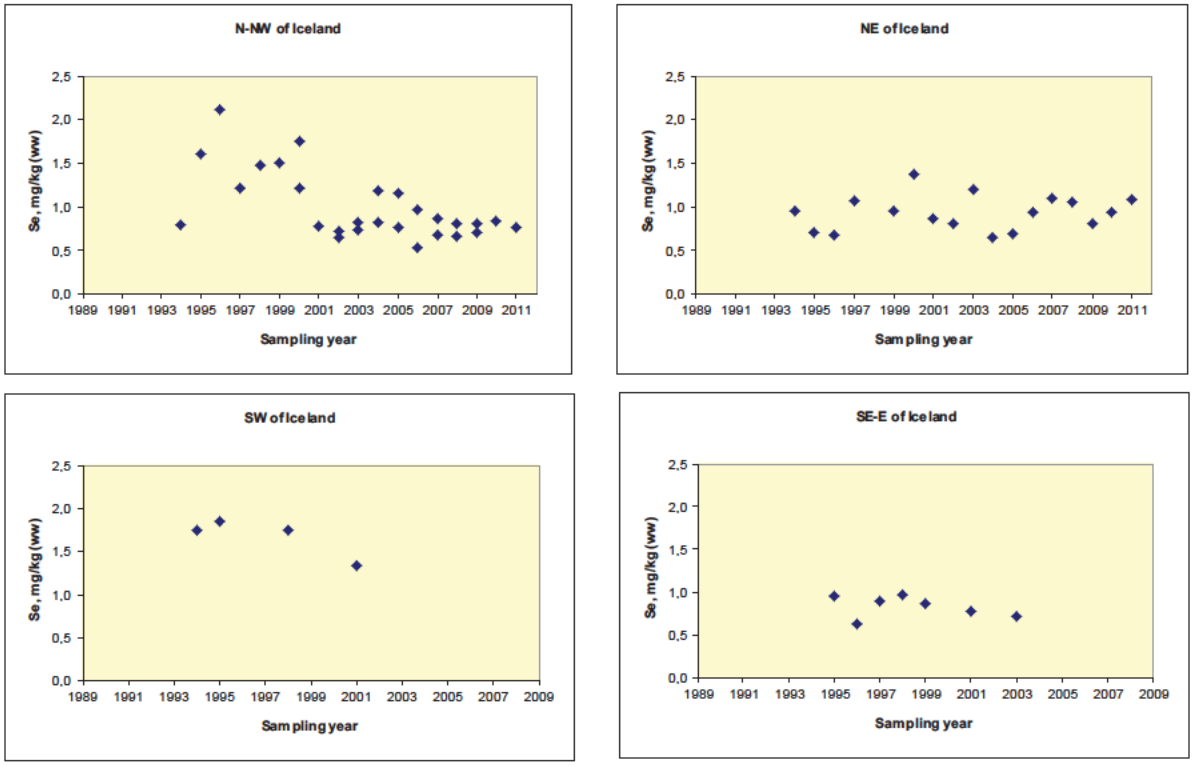

Figure 7e. Average concentration of Selenium (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

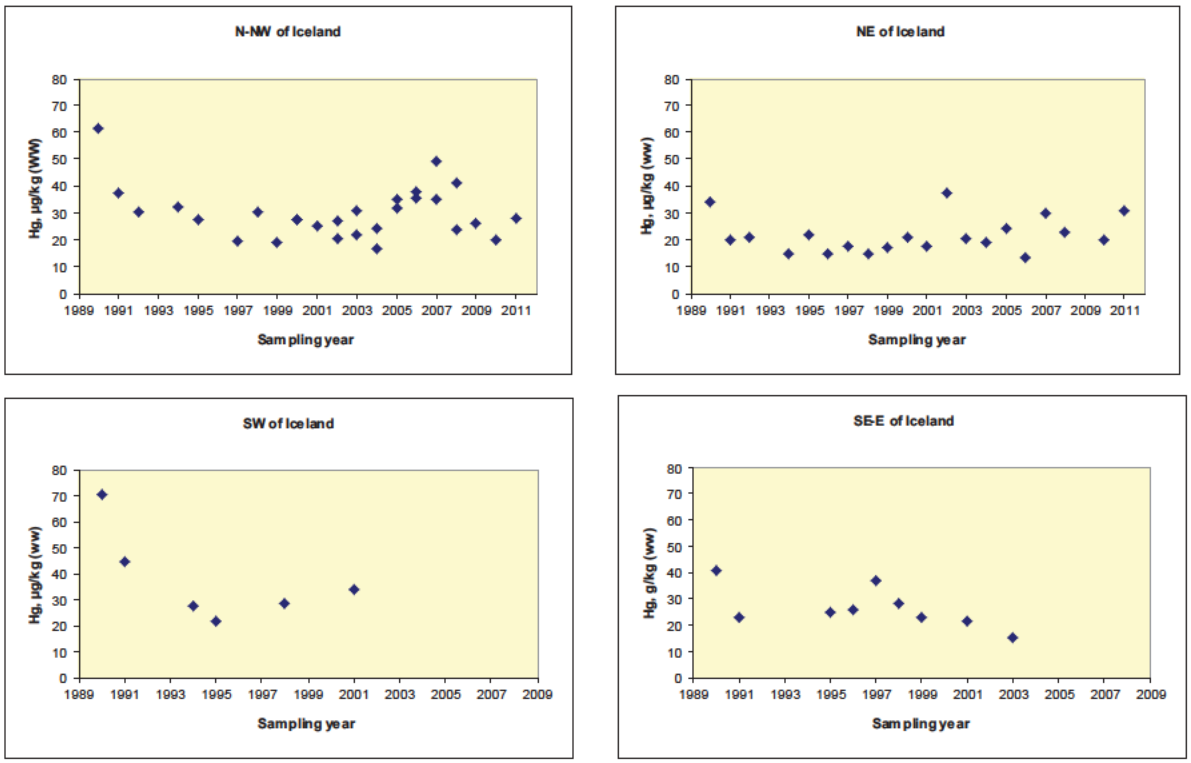

Figure 7f. Average concentration of Mercury (ww) in flesh of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1990-2011.

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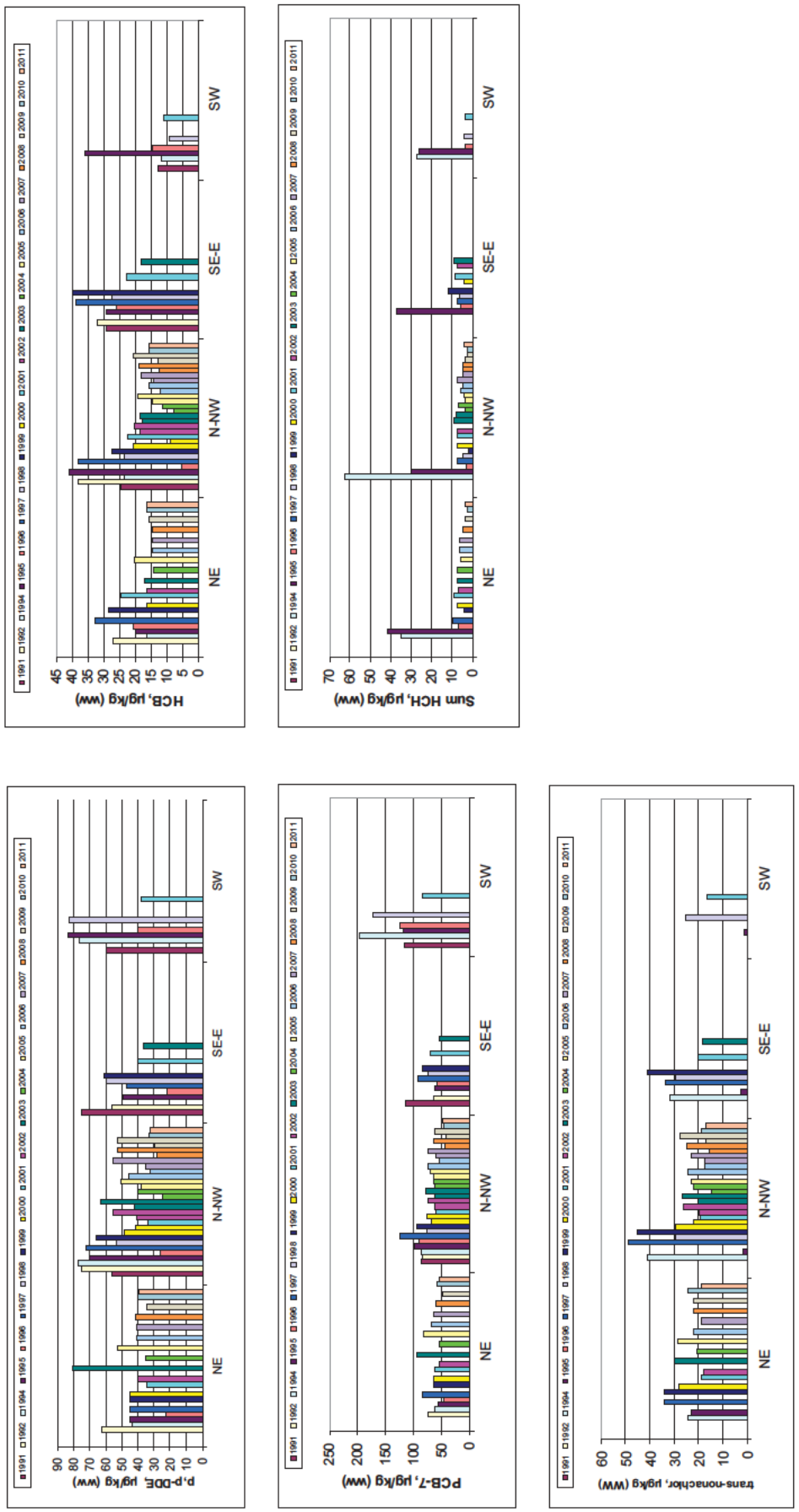

Figure 8. Average concentration of organochlorine compounds (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

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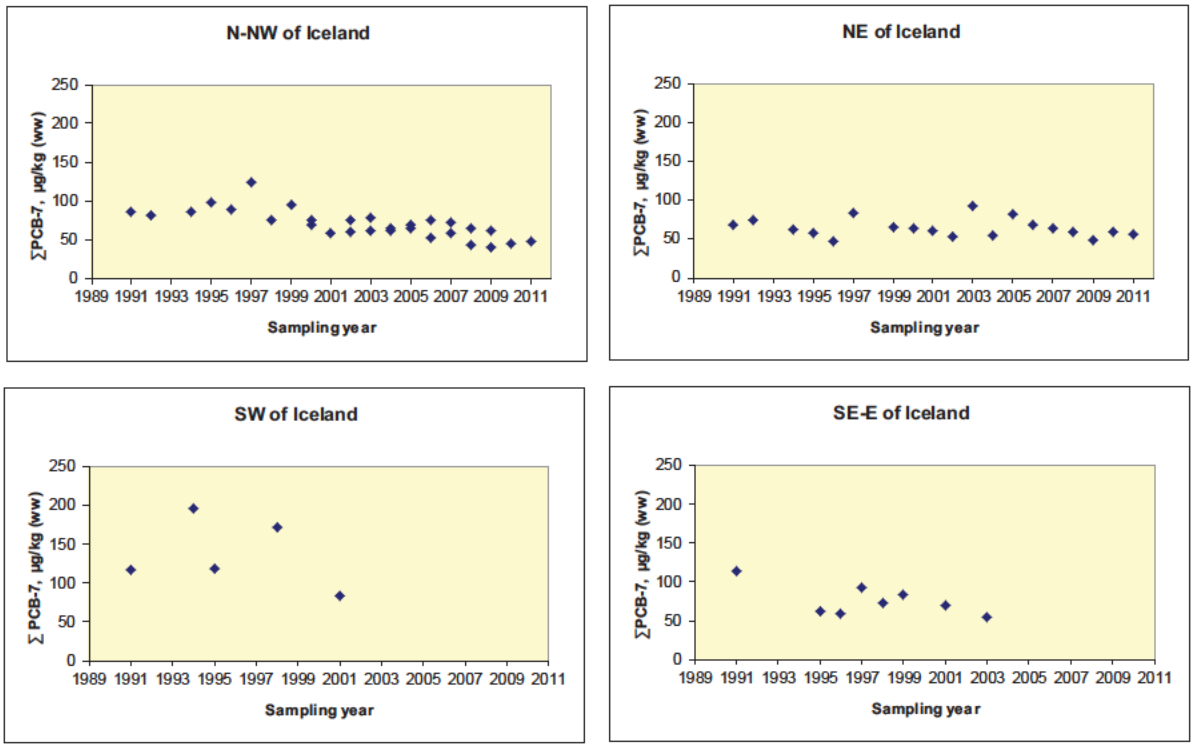

Figure 9a. Average concentration of ∑PCB-7 (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

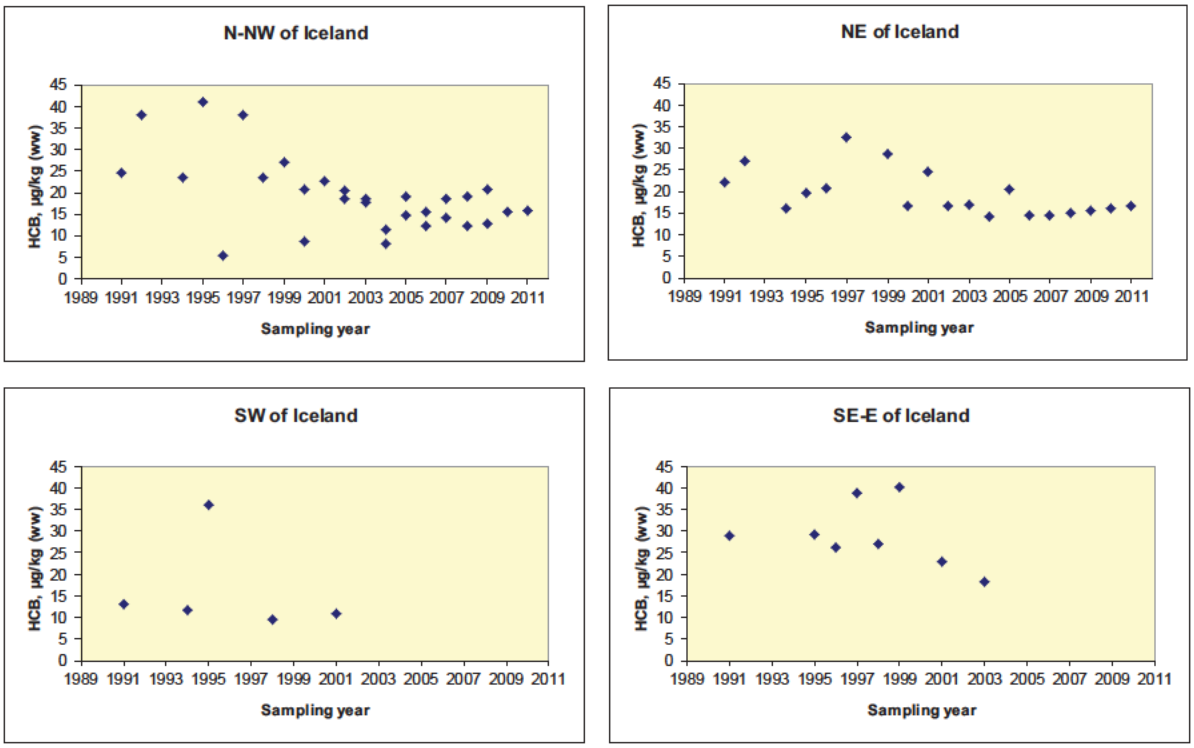

Figure 9b. Average concentration of HCB (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

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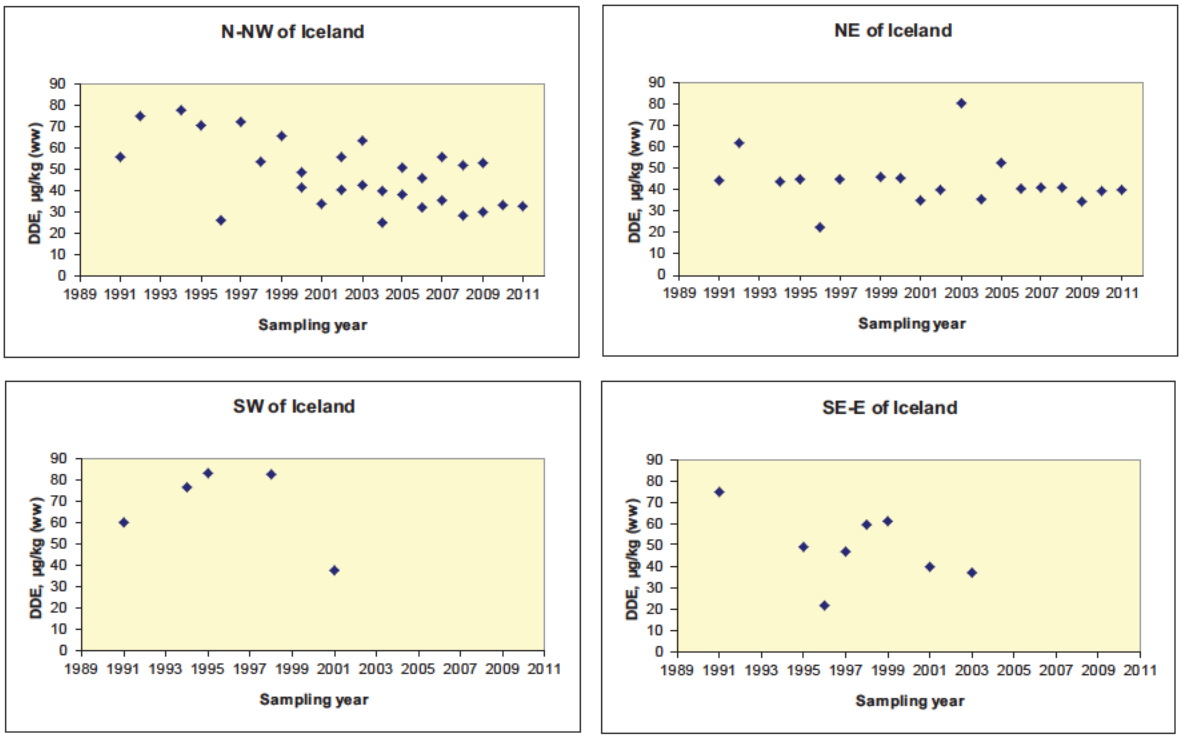

Figure 9c. Average concentration of DDE (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

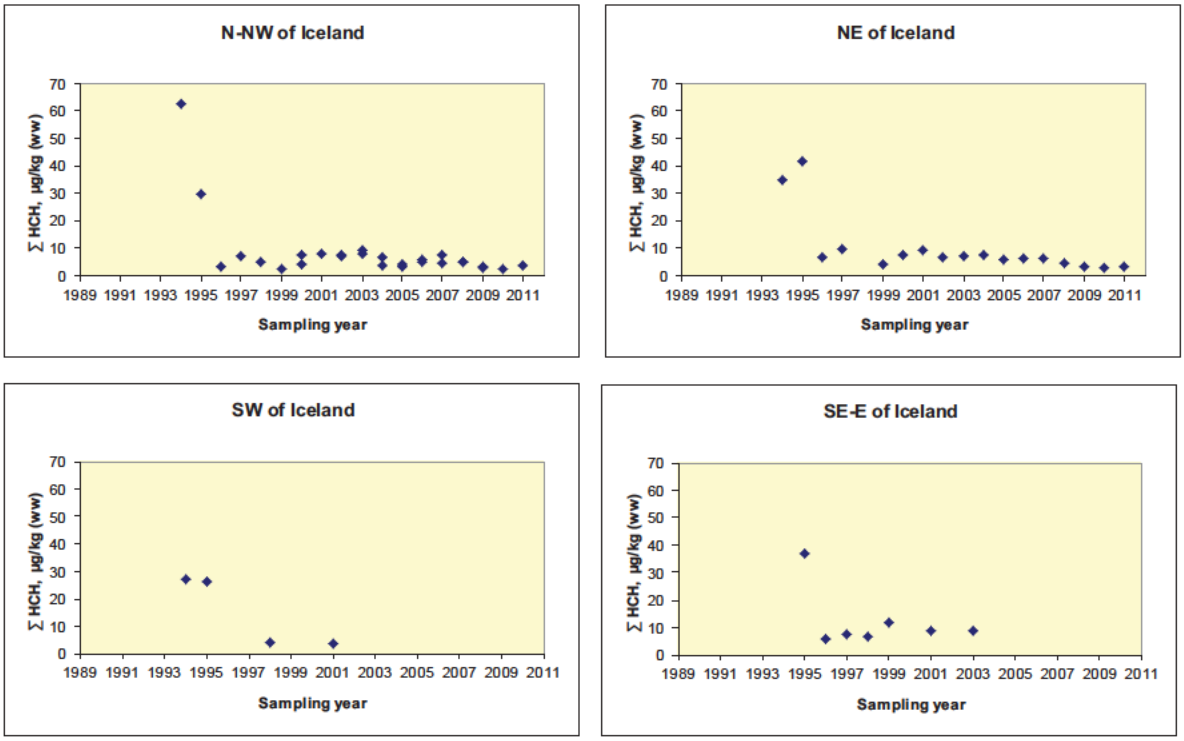

Figure 9d. Average concentration of ∑HCH (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

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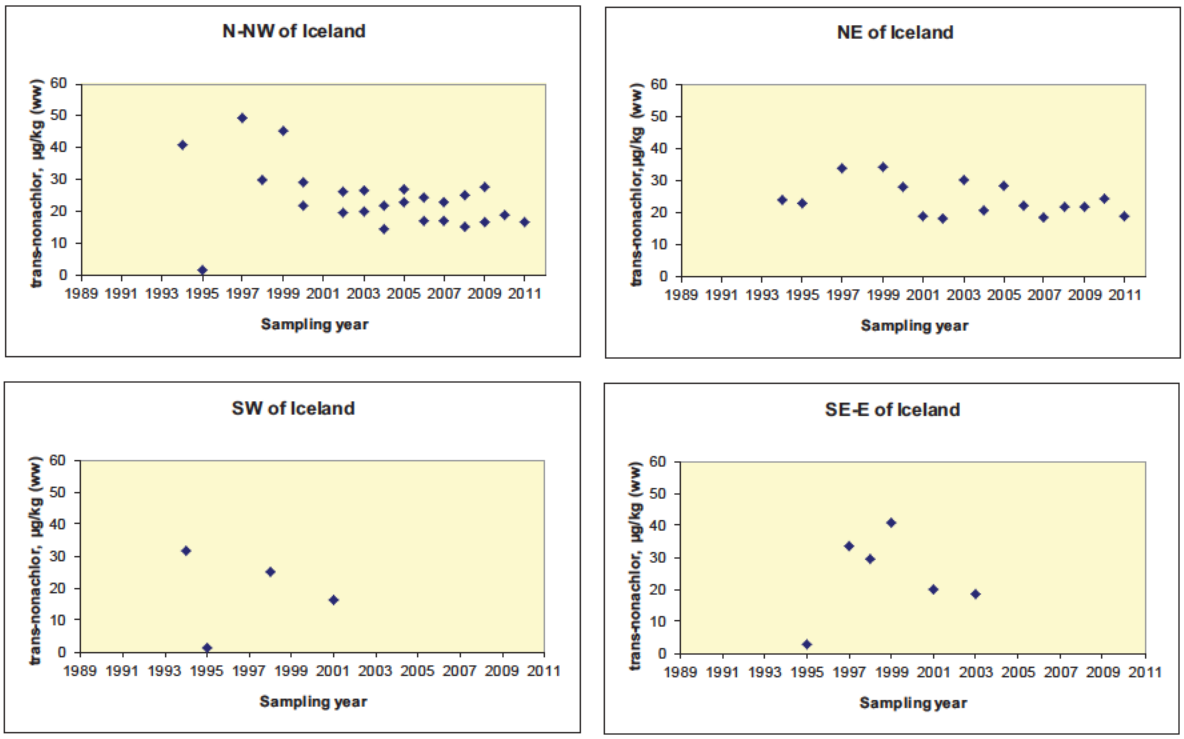

Figure 9e. Average concentration of transnonachlor (ww) in livers of 30-45 cm Cod (Gadus morhua) from different locations in Icelandic waters in March 1991-2011.

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Appendix 11-11
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Undesirable substances in seafood products – results from the Icelandic marine monitoring activities in the year 2011

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Skýrsluágrip Matís ohf
Icelandic Food and Biotech R&D

matís

Report summary

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Titill / Title	**Undesirable substances in seafood products – results from the Icelandic marine monitoring activities in the year 2011**		
Höfundar / Authors	Hrönn Ólína Jörundsdóttir, Vordís Baldursdóttir, Natasa Desnica, Þuríður Ragnarsdóttir, Helga Gunnlaugsdóttir		
Skýrsla / Report no.	17-12	*Útgáfudagur / Date:*	Maí 2012
Verknr. / Project no.	1687		
Styrktaraðilar / funding:	Ministry of Fisheries and Agriculture		
Ágrip á íslensku:	Árið 2003 hófst, að frumkvæði sjávarútvegsráðuneytisins, vöktun fyrir óæskilegum efnum í sjávarafurðum, bæði afurðum til manneldis sem afurðum til lýsis- og mjöliðnaðar. Matís hefur verið falin umsjón með vöktunarverkefninu. Tilgangur vöktunarinnar er að meta ástand íslenskra sjávarafurða með tilliti til magns aðskotaefna. Einnig er markmið að safna óháðum vísindagögnum um óæskileg efni í sjávarafurðum fyrir stjórnvöld, fiskiðnaðinn og kaupendur og neytendur íslensks sjávarfangs. Gögnin sem safnað er í vöktunarverkefninu verða einnig notuð í áhættumat og til að byggja upp gagnagrunn um aðskotaefni í íslensku lífríki. Umfjöllun um aðskotaefni í sjávarafurðum, bæði í almennum fjölmiðlum og í vísindaritum, hefur margoft krafist viðbragða íslenskra stjórnvalda. Nauðsynlegt er að hafa til taks vísindaniðurstöður sem sýna raunverulegt ástand íslenskra sjávarafurða til þess að koma í veg fyrir tjón sem af slíkri umfjöllun getur hlotist. Ennfremur eru mörk aðskotaefna í sífelldri endurskoðun og er mikilvægt fyrir Íslendinga að taka þátt í slíkri endurskoðun og styðja mál sitt með vísindagögnum. Þetta sýnir mikilvægi þess að regluleg vöktun fari fram og að á Íslandi séu stundaðar sjálfstæðar rannsóknir á eins mikilvægum málaflokki og mengun sjávarafurða er. Þessi skýrsla er samantekt niðurstaðna vöktunarinnar fyrir árið 2011. Mat á ástandi íslenskra sjávarafurða með tilliti til aðskotaefna er langtímaverkefni og verður einungis framkvæmt með sívirkri vöktun. Á hverju ári er því farið vandlega yfir hvaða gögn vantar og þannig stefnt að því að fylla inní eyðurnar. Árið 2011 voru í fyrsta skipti mæld svokölluð PFC efni í íslenskum sjávarafurðum sem ætlaðar eru til manneldis sem og afurðum til lýsis- og mjöliðnaðar, en PFC efni eru yfirborðsvirk efni sem hafa fengið aukna athygli vegna þrávirkni og eitrunaráhrifa þeirra. Einnig voru eftirfarandi efni mæld: dioxin, dioxinlík PCB og bendi PCB efni, PBDEs, málmar, auk þess 12 mismunandi tegundir varnarefna. Árið 2011 voru einnig mæld grásleppuhrogn ásamt þorskhrognum, svili og lifur til að meta dreifingu mengandi efna í þessi líffæri. Af PCF efnunum var PFOS eina PFC efnið sem greindist yfir greiningarmörkum og var styrkur PFOS yfirleitt lágur. Eins og áður mældist almennt lítið magn óæskilegra efna í íslensku sjávarfangi árið 2011 og ekkert sýni mældist með óæskileg efni yfir viðmiðunarmörkum.		
Lykilorð á íslensku:	*Sjávarfang, vöktun, Díoxín, díoxínlík PCB, PCB, varnarefni, PBDEs, málmar*		

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Icelandic Food and Biotech R&D

Report summary

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Summary in English:	This screening of undesirable substances in seafood products was initiated by the Icelandic Ministry of Fisheries and Agriculture in the year 2003. Until then, this type of monitoring had been limited in Iceland. Matis was assigned the responsibility of carrying out the surveillance program, which has now been ongoing for eight consecutive years. The purpose of the project is to gather information and evaluate the status of Icelandic seafood products in terms of undesirable substances. Further, the aim of the project is to provide independent scientific data on undesirable substances in Icelandic seafood for food authorities, fisheries authorities, industry, markets and consumers. The information will also be utilized for a risk assessment and gathering of reference data. This report summarizes the results obtained in the year 2011 for the screening of various undesirable substances in the edible part of marine catches, fish meal and fish oil for feed. The evaluation of the status of the Icelandic seafood products in terms of undesirable substances is a long term project which can only be reached through continuous gathering of data. For this reason, both the undesirable substances and seafood samples are carefully selected each year with the aim to fill in the gaps of the available data. Thus, the project fills in gaps of knowledge regarding the level of undesirable substances in economically important marine catches for Icelandic export. In the year 2011, PFCs were analyzed for the first time in the edible part of fish, fish oil and meal for feed from Icelandic fishing grounds but PFCs is a group of surfactants that have received increased attention due to their persistency and toxic effects. In addition, data was collected on dioxins, dioxin-like PCBs, marker PCBs, 12 different types of pesticides, PBDEs and trace metals. Samples collected in 2011 contained generally low concentrations of undesirable substances. The year 2011, lumpfish roes as well as roes, sperm and liver of cod were analyzed in order to estimate the organ distribution of pollutants. PFOS was the only PFC analyzed above limits of detection and its concentration was generally low. These results are in agreement with our previous results obtained in the monitoring program in the years 2003 to 2010. No sample contained undesirable compounds exceeding the maximum level set by the EU.
English keywords:	*Marine catches, monitoring, dioxin, PCB, pesticides, PBDEs, metals*

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Table of Contents

1 Introduction 2

2 Summary 3

3 Contaminants measured in the project 4

4 Sampling and analysis 5

4.1 Sampling 5
4.1.1 Seafood 5
4.1.2 Fish meal and fish oil for feed 6

4.2 Analysis 6

5 Results of monitoring of fish and seafood products in Iceland 7

5.1 Dioxins (PCDD/Fs) and dioxin like PCBs 7
5.1.1 Dioxins and dioxin like PCBs in seafood 7
5.1.2 Dioxins and dioxin like PCBs in fish oil for human consumption 8
5.1.3 Dioxins and dioxin like PCBs in liver, roes and sperm 8
5.1.4 Dioxins and dioxin like PCBs in fish meal and fish oil for feed 10

5.2 Marker PCBs 12
5.2.1 Marker PCBs in seafood 12
5.2.2 Marker PCBs in fish oil for human consumption 13
5.2.3 Marker PCBs in liver, roes and sperm 14
5.2.4 Marker PCBs in fish meal and fish oil for feed 16

5.3 Brominated flame retardants (BFRs) 17
5.3.1 PBDE in seafood 17
5.3.2 PBDEs in liver, roes and sperm 18
5.3.3 PBDEs in fish oil and fish meal for feed 18

5.4 PAH 19

5.5 Pesticides 19
5.5.1 Pesticides in seafood 20
5.5.2 Pesticides in fish oil for human consumption 21
5.5.3 Pesticides in fish meal and fish oil for feed 21

5.6 Inorganic trace elements 24
5.6.1 Inorganic trace elements in seafood 24
5.6.2 Inorganic trace elements in liver, roes and sperm 25
5.6.3 Inorganic trace elements in fish oil and fish meal 28

5.7 Poly- and perfluorinated compounds 29
5.7.1 PFCs in seafood 29
5.7.2 PFCs in liver, roes and sperm 29
5.7.3 PFC in fish meal and oil for feed 30

6 References 31

7 Appendix 34

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

1 Introduction

In 2003, the Icelandic Ministry of Fisheries initiated a project aimed at screening for undesirable substances in the edible portion of marine catches, as well as in fish meal and fish oil for feed, captured in Icelandic waters. Matis was assigned the responsibility of carrying out the surveillance programme, which has now been on-going for eight consecutive years. The goal of the surveillance programme is to gather information and evaluate the status of Icelandic seafood products regarding undesirable substances. The project is funded by the Ministry of Fisheries and Agriculture in Iceland. The project includes measurements on various undesirable substances in a number of economically important marine species from Icelandic fishing grounds in order to gather information for Icelandic export. Special emphasis was on poly- and perfluorinated compounds (PFC), where limited knowledge is available on levels and distribution of these compounds in the Icelandic marine environment. This is the first time PFCs are included in the present screening program. The substances investigated in this monitoring project are: poly- and perfluorinated compounds, polychlorinated dibenzo dioxins and dibenzo furans (commonly called dioxins), dioxin-like polychlorinated biphenyls (PCBs), marker PCBs, polybrominated flame retardants (PBDEs), 30 pesticides and breakdown products (i.e. HCB, DDTs, HCHs, dieldrin, endrin, chlordanes, toxaphenes and endosulfan substances) and inorganic trace elements such as heavy metals.

The purpose of this work is:

A) To gather information and evaluate the status of Icelandic seafood products in terms of undesirable substances.
B) Provide scientific evidence that Icelandic seafood products conform to regulations on seafood safety. That is, to evaluate how products measure up to limits currently in effect for inorganic trace elements, organic contaminants and pesticides in the EU (Regulation (EC) No 1881/2006, Commission Regulation (EC) No 629/2008, Commission Directive 2002/32/EC, Commission Directive 2003/100/EC).
C) To utilize the data gather in the programme for a risk assessment and the setting of maximum values that are now under consideration within EU e.g. for PAHs, PCBs, inorganic arsenic and brominated flame retardants, etc.
D) Provide independent scientific data on undesirable substances in Icelandic seafood for food authorities, fisheries authorities, industry, markets and consumers.

This report summarizes results from the screening programme in the year 2011. The results obtained in the years 2003 to 2010 have already been published and are accessible at the Matis website (http://www.matis.is: Auðunsson, 2004, Ásmundsdóttir *et al.*, 2005,

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Ásmundsdóttir and Gunnlaugsdóttir, 2006, Ásmundsdóttir *et al.*, 2008, Jörundsdóttir *et al.*, 2009, Jörundsdóttir *et al*., 2010a, Jörundsdóttir *et al*., 2010b, Baldursdóttir *et al.*, 2011). The above mentioned EU regulations have now been implemented in the Icelandic legal framework regarding undesirable substances in food and feed (Reglugerð 265/2010).

2 Summary

This report summarizes the results obtained in 2011 for the screening of various undesirable substances in the edible part of marine catches, fish meal and fish oil for feed. The surveillance program began in 2003 and has now been carried out for eight consecutive years. The project fills in gaps of knowledge regarding the level of undesirable substances in economically important marine catches for Icelandic export. It is considered to be a long-term project where extension and revision is constantly necessary.

In the year 2011 emphasis was laid on gathering information on the organic compounds PFCs and inorganic trace elements in the edible part of marine catches as well as in the fish meal and fish oil for feed. Generally, the results obtained in 2011 are in agreement with our previous results on undesirable substances in the edible part of marine catches, fish meal and fish oil for feed obtained in the monitoring years 2003 to 2010. The results show that the edible parts of Icelandic seafood products contain negligible amounts of persistent organic pollutants (POPs) such as; dioxins, dioxin like PCBs and pesticides. The results for PBDEs reveal that these compounds are also in very low amounts in fish and fish products. This is the first time PFCs are analysed in Icelandic seafood and fish products and the results show that the main PFC compound, perfluorooctane sulfonate (PFOS) was the only congener detected, all other congeners (10 in total) were under limit of detection (LOD). Emphasis was laid on studying the PFCs concentration in different cod organs, the results show that only PFOS was detected and that the highest concentration was measured in cod roes while sperm and liver have similar concentrations. Further, the concentration of marker PCBs was found to be low in the edible part of fish muscle, compared to the maximum limits in the European countries, where such limits exist. The results showed that the concentrations of heavy metals, e.g. cadmium (Cd), lead (Pb) and mercury (Hg) in Icelandic seafood products was always well below the maximum limits set by EU.

The samples of fish meal and fish oil for feed measured are subjected to different maximum limits by the EU. This year all samples measured were below the EU maximum limits for feed components of marine origin.

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3 Contaminants measured in the project

The following contaminants are measured in edible parts of seafood and fish oil for human consumption, as well as in fish meal and fish oils used as feed ingredients:

Dioxins, PCDD/Fs: Dioxins (dibenzo-p-dioxins) and dibensofurans (17 congeners according to WHO): 2.3.7.8-Tetra-CDD, 1.2.3.7.8-Penta-CDD, 1.2.3.4.7.8-Hexa-CDD, 1.2.3.6.7.8-Hexa-CDD, 1.2.3.7.8.9-Hexa-CDD, 1.2.3.4.6.7.8-Hepta-CDD, OCDD, 2.3.7.8-Tetra-CDF, 1.2.3.7.8-Penta-CDF, 2.3.4.7.8-Penta-CDF, 1.2.3.4.7.8-Hexa-CDF, 1.2.3.6.7.8-Hexa-CDF, 1.2.3.7.8.9-Hexa-CDF, 2.3.4.6.7.8-Hexa-CDF, 1.2.3.4.6.7.8-Hepta-CDF, 1.2.3.4.7.8.9-Hepta-CDF, OCDF.

Dioxin like PCB (12 congeners according to WHO):
non-ortho (CB-77, CB-81, CB-126, CB-169) and mono-ortho (CB-105, CB-114, CB-118, CB-123, CB-156, CB-157, CB-167, CB-189).

Marker- PCB (7 congeners):
CB-28, CB-52, CB-101, CB-118, CB-138, CB-153, CB-180.

Pesticides:
DDT-substances (6 congeners: pp-DDT, op-DDT, pp-DDD, op-DDD, pp-DDE and op-DDE), HCH-substances (4 isomers: α-, β-, γ-(Lindane), and δ-hexachlorocyclohexan), HCB, chlordanes (4 congeners and isomers: α- and γ-chlordane, oxychlordane and trans-nonachlor), toxaphenes (3 congeners, P 26, 50 and 62), aldrin, dieldrin, endrin, endosulfan (3 congeners and isomers: α- and β-endosulfan and endosulfansulfat) and heptachlor (3 congeners: heptachlor, cis-hepatchlorepoxid, trans-heptachlorepoxid).

PBDEs (10 congeners):
BDE-28, BDE-47, BDE-66, BDE-100, BDE-99, BDE-85, BDE-154, BDE-153, BDE-183, BDE-209.

Inorganic trace elements:
Hg (mercury), Cd (cadmium), Pb (lead), total As (organic and inorganic arsenic), chromium (Cr), iron (Fe), copper (Cu), zinc (Zn) and selenium (Se).

PFCs (11 congeners):
Perfluorobutane sulfonat (PFBS), Perfluorodecanoate (PFDA), Perfluorodecane sulfonate (PFDS), Perfluorododecanate (PFDoA), Perfluoroheptanoate (PFHpA), Perfluorohexanoate (PFHxA), Perfluorohexane sulfonate (PFHxS), Perfluorononaoate

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(PFNA) Perfluoroctanoate (PFOA), Perfluoroctane sulphonamide (PFOSA), Perfluoroctane sulfonate (PFOS).

4 Sampling and analysis

4.1 Sampling

The collection of samples and the quality criteria for the analytical methods were in accordance with conditions set out by the EU for the information gathering campaign on dioxins and dioxin-like PCBs as well as for metals (Commission Directive 2001/22/EC, Commission directive 2002/69/EC). Fish samples were collected by the Marine Research Institute (MRI) in Iceland. Mackerel (*Scomber scombrus*) samples were gathered from commercial industrial fish processor. Fish meal and fish oil were gathered by collaborating partners in the industry.

4.1.1 Seafood

All the analysis was done on the edible parts of the seafood products. The fish was collected from the fishing grounds around Iceland which are divided into five areas, as illustrated on
Figure 1. All samples were identified with the location of the fishing area, except when the sample contained individuals from more than one area. Each seafood sample consisted of a pooled sample from the entire edible part (e.g. skinless fish fillet) from at least ten individuals of a specific length distribution. For the internal organs the livers consisted of a pooled sample from 10 individuals, while number of roes and sperm in the pooled samples depended on the ratio of males and females. Cod roe sample no 1 and cod sperm sample no 3 (see Table 2 in the Appendix) consisted of five individuals each. Cod roe sample no 4 and cod sperm sample no 6 consisted of two and eight individuals, respectively. Lumpfish roe samples no 7, 8 and 9 consisted of 10 individuals each.

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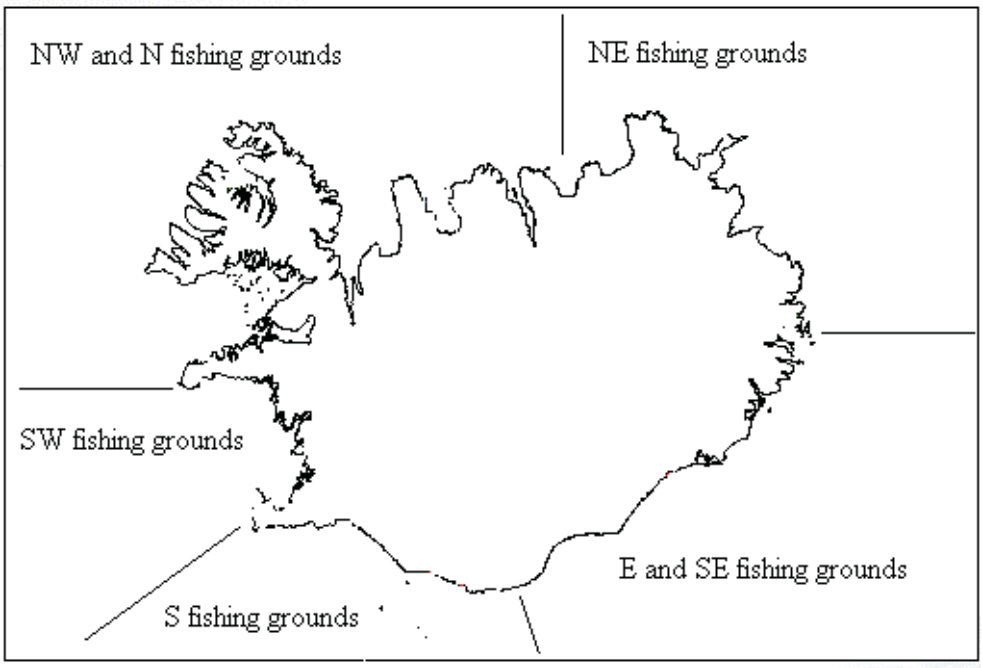

Figure 1: The division of the fishing grounds around Iceland used in this research.

4.1.2 Fish meal and fish oil for feed

The fish meal and fish oil samples were taken at the production sites and, when possible, sampling was distributed over the year. When possible, the fish meal and fish oil samples originate from the same batch.

4.2 Analysis

The organic contaminants were measured by Eurofins, Hamburg, Germany. Eurofins has taken part in international inter-laboratory quality control study organized by WHO and EU and uses accredited methods for analyzing dioxin, WHO-PCBs, marker-PCBs, pesticides and PBDEs.

Results are expressed as upper bond level, which means that when the concentration of a substance is measured to be below limit of detection (LOD) or limit of quantification (LOQ) of the analytical method, the concentration is set to be equal to the LOD/LOQ. In the case of dioxins and dioxin-like PCBs, the analytical data are converted to pg/g WHO-TEQ where the toxicity of each congener has been calculated using WHO-TEF (Toxic Equivalence Factor) based on the existing knowledge of its toxicity (Van den Berg et al., 1998). WHO-TEQ values have been adapted by the World Health Organization (WHO) in 1997 and by EU in its legislations.

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5 Results of monitoring of fish and seafood products in Iceland

All results of the monitoring program in 2011 are listed in Tables 1-16 in the Appendix.

5.1 Dioxins (PCDD/Fs) and dioxin like PCBs

5.1.1 Dioxins and dioxin like PCBs in seafood

All the fish species measured are far below the limits set by EU for the sum of dioxins and dioxin like PCBs (Figure 2 and Table 1 in the Appendix). As in previous years, a considerable difference was observed in the dioxin content between different fish species. The species that accumulate fat in the muscle, like for example Greenland halibut (sample no. 4), contain more dioxins and dioxin like PCBs than species which accumulate fat in the liver and thus have almost no fat in the muscle. Mackerel and lumpfish have also higher lipid content in the muscle and therefore higher dioxin and dioxin like PCB concentrations. The level of dioxin in the edible part of the fish increases as the fat percentage in the muscle increases, but other important variables are age (length) and habitat. Greenland halibut can become quite old, which probably contributes considerably to the high dioxins and dioxin-like PCBs value obtained for this species (Figure 2).

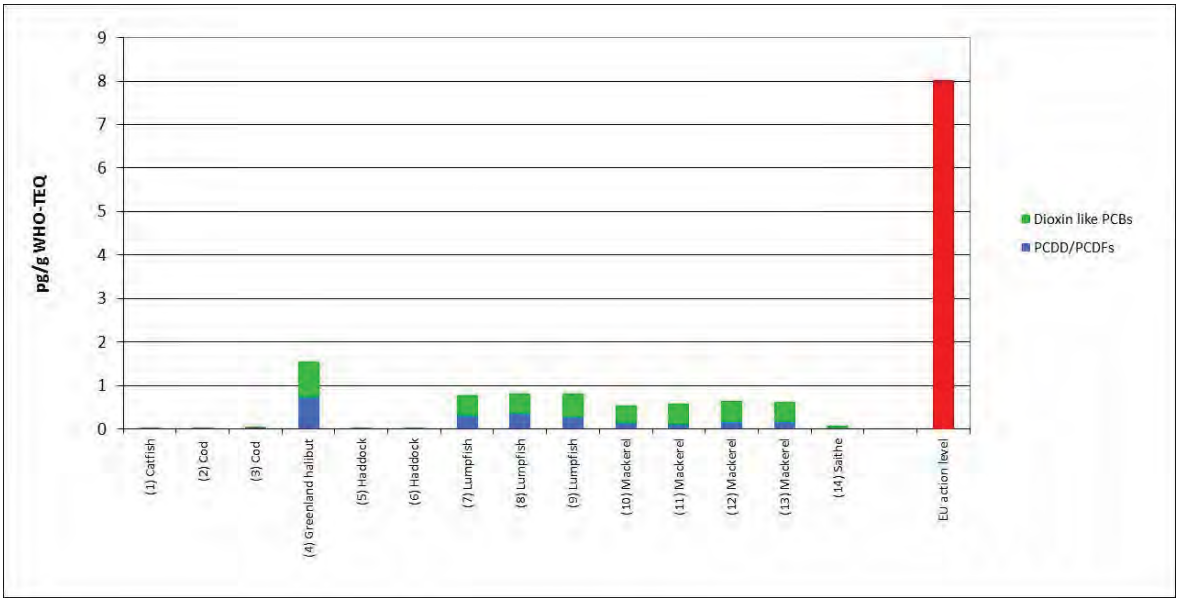

Figure 2: Dioxins and dioxin-like PCBs in the edible part of fish muscle from Icelandic fishing grounds in 2011 in relation to maximum EU limit in WHO-TEQ pg/g wet weight. The number within parenthesis is the sample number indicated in Table 1.

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5.1.2 Dioxins and dioxin like PCBs in fish oil for human consumption

There were no samples of fish oil for human consumption analysed or collected from the fish oil industry this year. Earlier results from 2005 and 2006 showed concentrations below the EU maximum limit of 2 pg/g WHO-TEQ for dioxins or the EU maximum limit of 10 pg/g WHO-TEQ for the sum of dioxins and dioxin like PCBs (Ásmundsdóttir and Gunnlaugsdóttir, 2006, Ásmundsdóttir et al., 2008, Regulation (EC) No 1881/2006).

5.1.3 Dioxins and dioxin like PCBs in liver, roes and sperm

Two pooled samples of each of the following cod organs; cod livers, roes and sperm were collected and analysed this year. The reason for this selection was that these organs are all used for human consumption and limited data is available regarding the content of undesirable substances in them. Samples no. 1-3 in Table 2 correspond to cod sample no. 2 in Table 1 in the Appendix, samples no. 4-6 in Table 2 correspond to cod sample no. 3 in Table 1 in the Appendix. Concentrations of dioxins and dioxin like PCBs are below the EU maximum limit of 25 pg/g WHO-TEQ for cod liver.

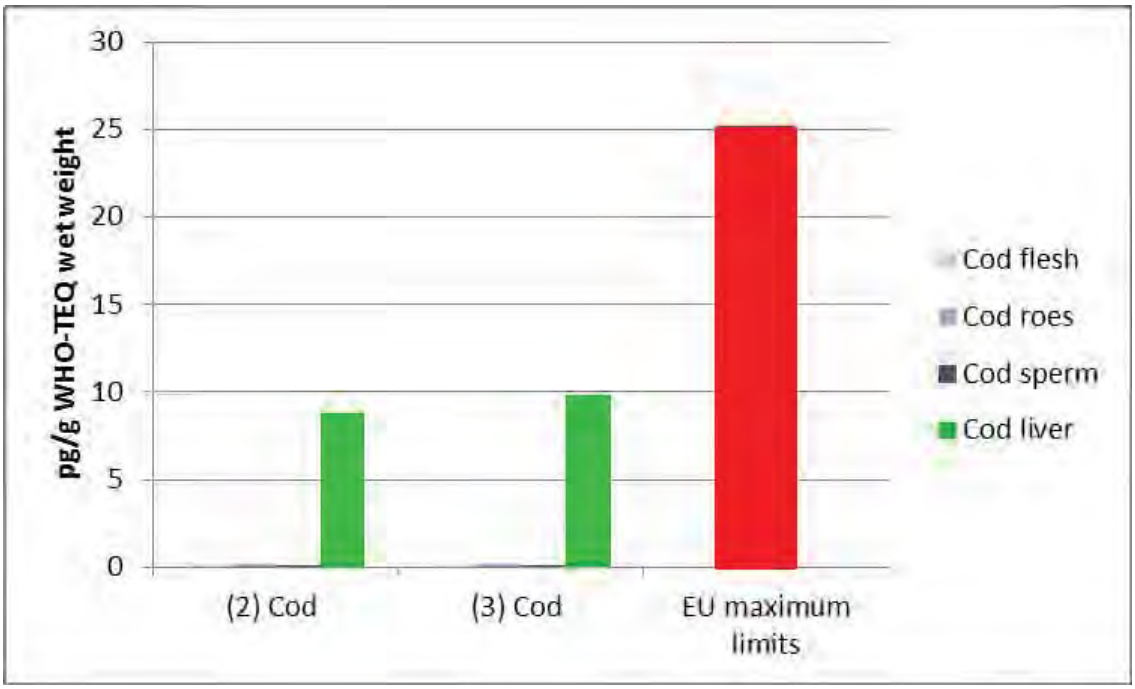

Figure 3: Comparison of sum of dioxins and dioxin like PCBs between different organs from of cod in pg/g WHO-TEQ wet weight.

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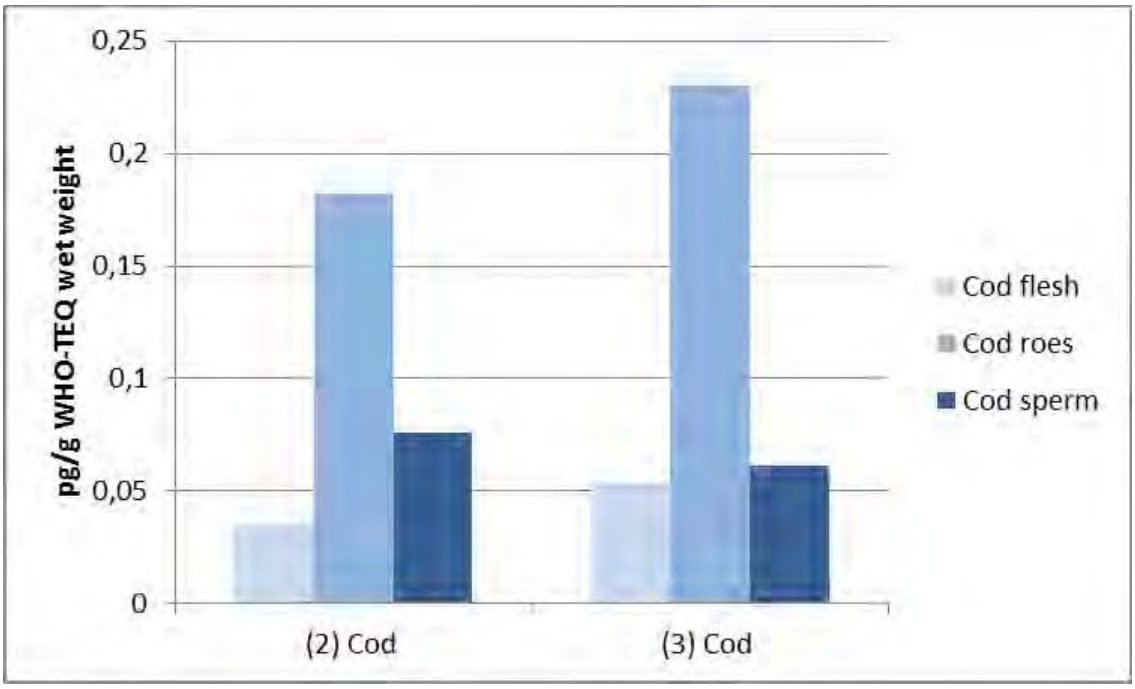

Figure 4: Comparison of sum of dioxins and dioxin like PCBs between cod flesh, cod roes and sperm excluding the results for cod liver in pg/g WHO-TEQ wet weight.

Figure 3 and Figure 4 show comparison of sum of dioxin and dioxin like PCB levels in different organs from cod. Cod accumulates fat in the liver which is clearly reflected in the dioxin and dioxin like PCB concentration. Lumpfish roes were also collected (Table 2 in the Appendix. Lumpfish roe no. 7 in Table 2 corresponds to lumpfish sample no. 7 in Table 1, lumpfish roe sample no. 8 in Table 2 corresponds to lumpfish sample no. 8 in Table 1 and lumpfish roe sample no. 9 Table 2 corresponds to lumpfish sample no. 9 in Table 1.

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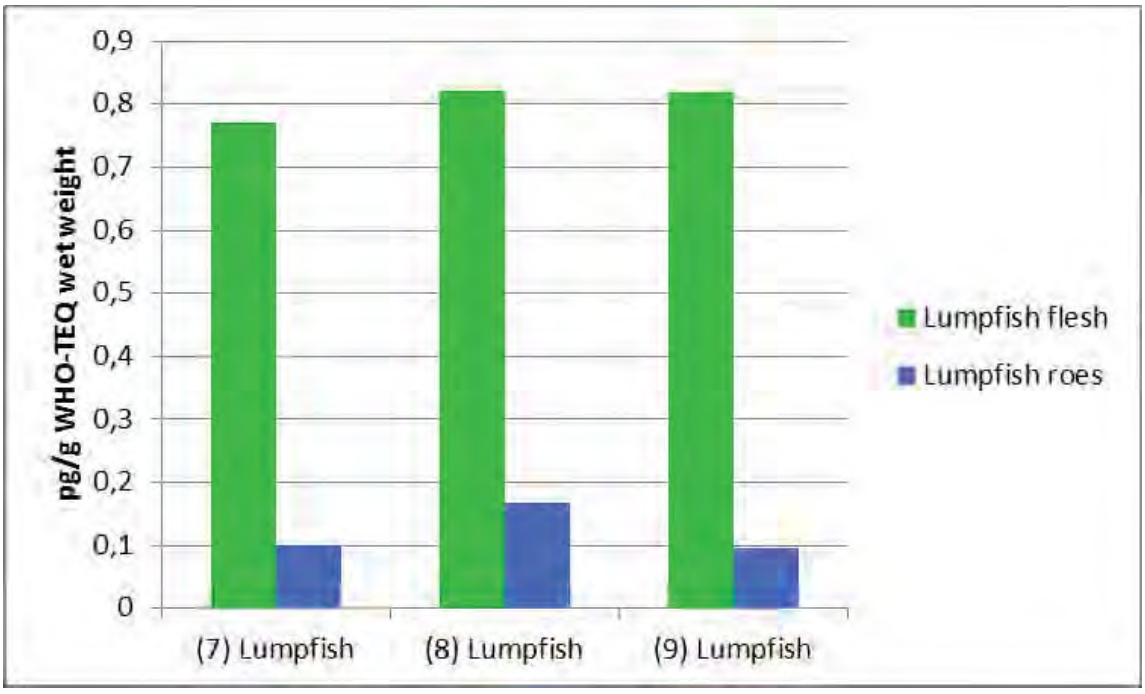

Figure 5: Comparison of sum of dioxin and dioxin like PCB between lumpfish flesh and lumpfish roes.

Figure 5 shows comparison in sum of dioxin and dioxin like PCBs between lumpfish flesh and lumpfish roes. The flesh has higher lipid content compared to the roes, 15% compared to 6.1%, respectively. This only explains a part of the difference in dioxin and dioxin like PCB concentration between the two organs where the dioxin concentration is almost seven times higher in flesh compared to roes, but the lipid content is only 2-3 times higher in flesh compared to roes.

5.1.4 Dioxins and dioxin like PCBs in fish meal and fish oil for feed

Samples of fish meal and fish oil are taken annually. The samples taken in the year 2011 consisted of capelin meal and herring meal and corresponding capelin oil. Concentration of dioxins and dioxin like PCBs are shown in Tables 3 and 4 in the Appendix. The EU maximum limits for dioxins and dioxin-like PCBs in fish meal and fish oil for feed are set relatively low in order to prevent the accumulation of these toxic substances in the food chain (Commission Directive 2006/13/EC). For this reason, results for these products are closer to the maximum limits than in the edible part of the fish muscle discussed in chapter 5.1.1.

The sum of dioxin and dioxin-like PCB was lower than the EU maximum limit in all fish meals tested (Figure 6). The same was observed for the fish oil (Figure 7).

All fish oil samples measured in this study are can be paired with specific fish meal samples, i.e. these fish oil and meal samples were obtained from the same original raw

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material and samples of the oil and meal were taken during production of this raw material. The fish oil samples correspond to the fish meal sample with the same number.

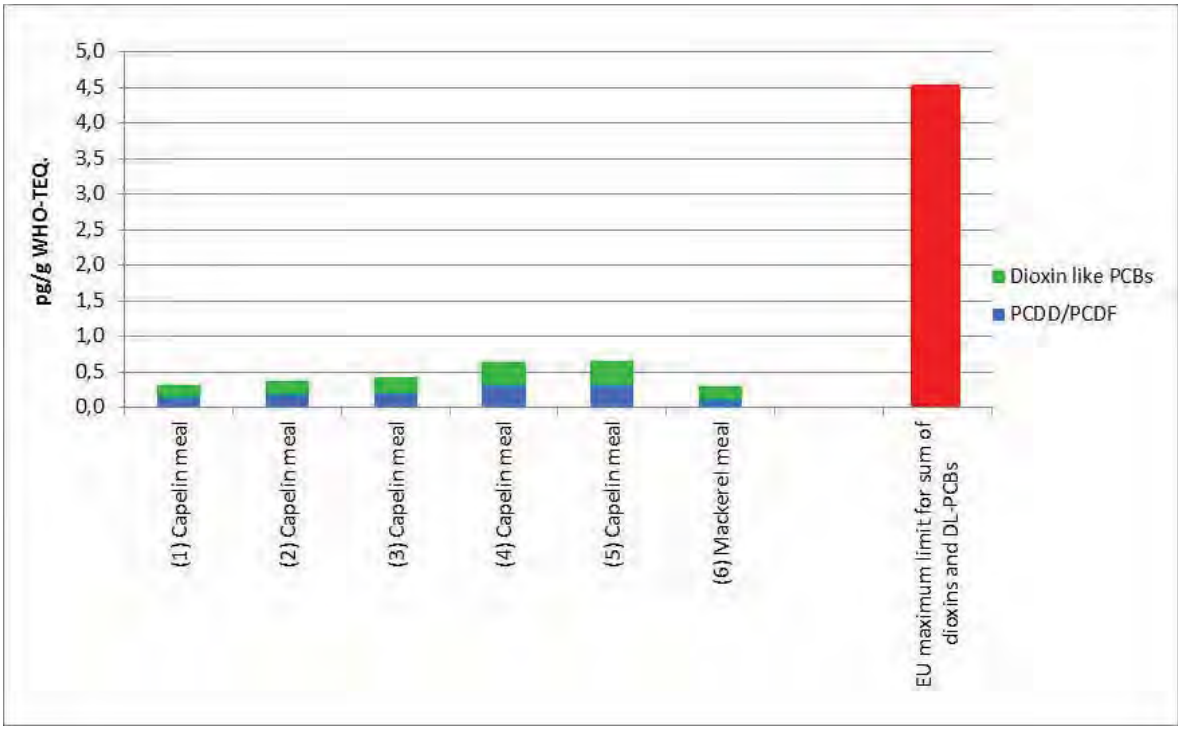

Figure 6: Dioxins and dioxin-like PCBs (in pg/g WHO-TEQ) in samples of fish meal from Iceland 2011 calculated in relation to 12% moisture compared to the EU maximum limit.

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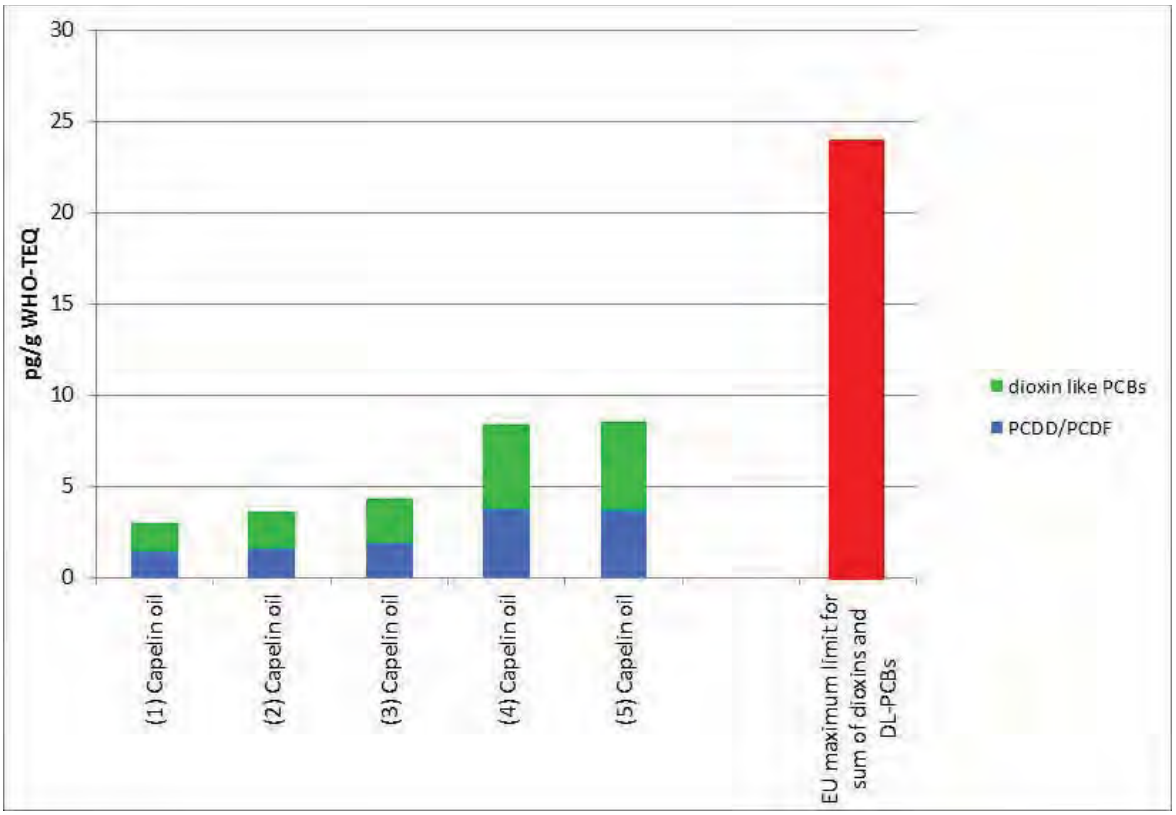

Figure 7: Dioxins and dioxin-like PCBs in samples of fish oil for feed from Iceland in 2011 (in pg/g WHO-TEQ) compared to the EU maximum limit.

5.2 Marker PCBs

Marker PCBs, sometimes called "Dutch seven" or ICES7, are seven PCBs that have been measured for many years as an indication of the total PCB contamination. One of these seven, PCB-118, is classified as a dioxin-like PCB, but the toxicity factor of the other six has not yet been estimated. The EU is working on a risk assessment for marker PCBs in order to establish a maximum level in the nearest future. Maximum levels of marker PCBs exist for some or all seven marker PCBs in several European countries and in USA.

5.2.1 Marker PCBs in seafood

The results obtained for the majority of the Icelandic fish species are well below the available limits for marker PCBs mentioned above. The maximum level of each of the individual PCB congeners range from 40 µg/Kg to 120 µg/Kg in Germany, Holland and Sweden. In this research, the highest total concentration for the sum of all seven marker PCBs was measured in Greenland halibut (sample no. 4, Figure 8), a total of 6.7 µg/kg wet weight, the highest individual PCB congener measured in the halibut was PCB-153 with 1.9 µg/kg wet weight, or approximately one third of the total. As for the dioxins and dioxin-like PCBs, the highest concentrations of PCBs are found in fish with high lipid content in the filet. For details, see Table 1 in the Appendix.

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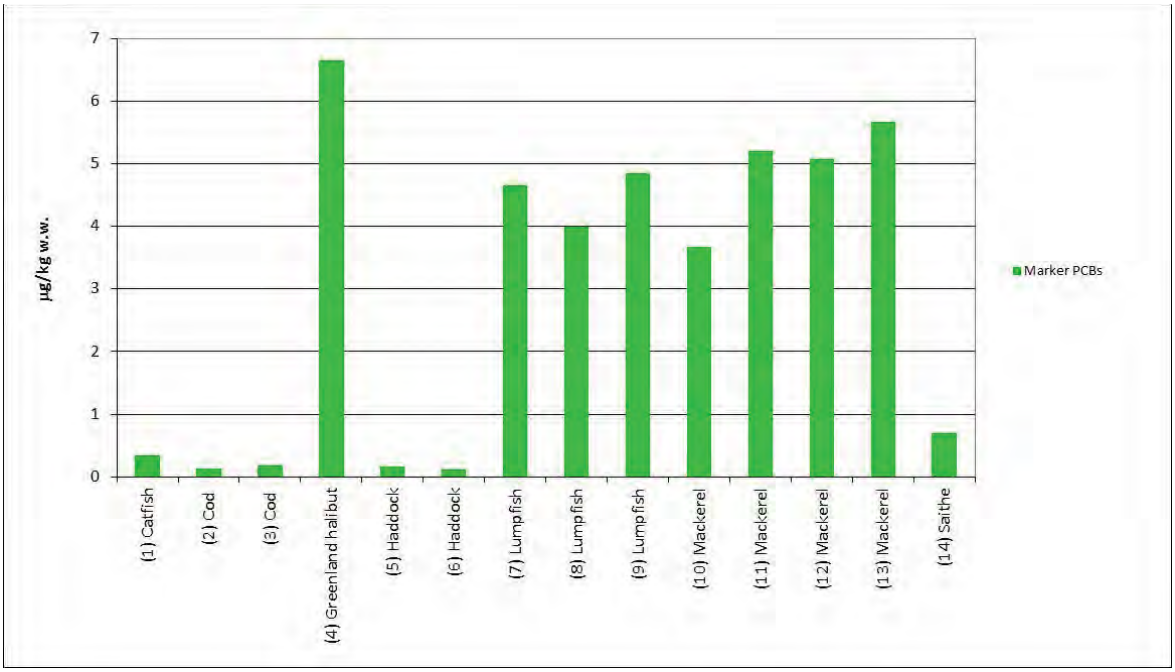

Figure 8: Marker PCBs in the edible part of fish muscle from Iceland in 2011 (in µg/kg wet weight). Number in parenthesis is the sample number designated to each sample, see Table 1 in Appendix.

5.2.2 Marker PCBs in fish oil for human consumption

There were no samples of fish oil for human consumption analysed this year. Earlier results from 2005 and 2006 were reported in previous reports from the Icelandic monitoring program (Ásmundsdóttir and Gunnlaugsdóttir, 2006, Ásmundsdóttir et al., 2008).

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5.2.3 Marker PCBs in liver, roes and sperm

Figure 9 shows a comparison between the sum of all seven marker PCBs concentrations measured in different cod organs. As for the dioxin and dioxin like PCBs, the highest concentration is measured in the liver, which also contains the highest lipid content. When the results for the cod liver are excluded, Figure 10, the highest marker PCBs concentration is measured in the cod roes. Of these three organs, the cod roes have the highest lipid content, but the difference in the marker PCB concentration is nevertheless greater than can be accounted for by the difference in lipid content in these organs i.e. cod roes 2,7% lipid vs. cod sperm 2,4% lipid. The reason for this difference in marker PCB concentration between cod roes and sperm could be due to difference in their lipid composition e.g. lipid classes in these organs, but this needs to be investigated further. Further details can be found in Table 2 in the Appendix.

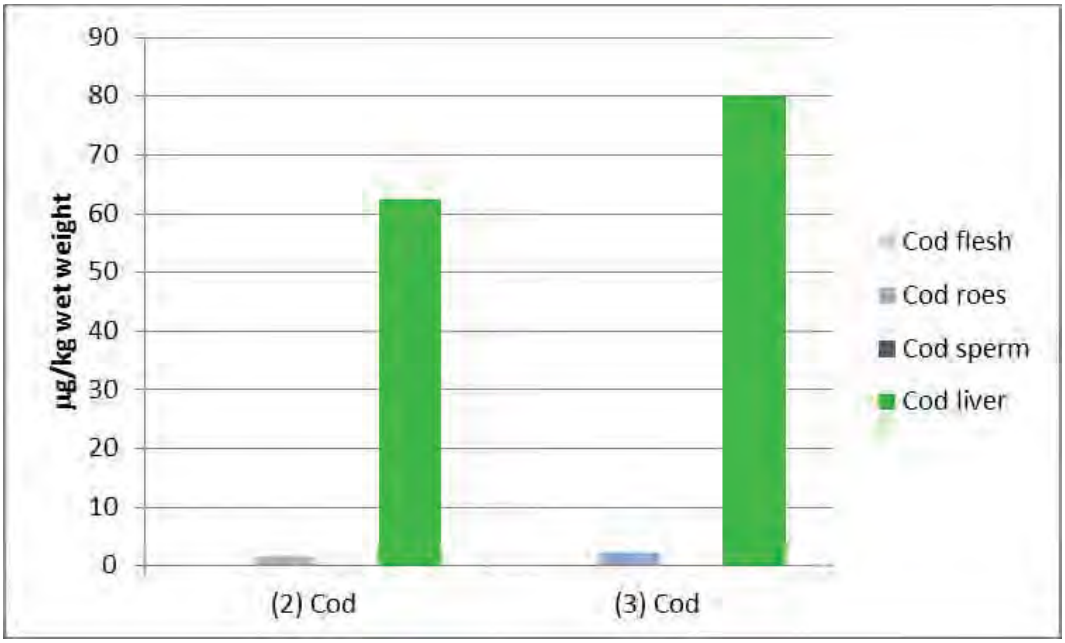

Figure 9: Marker PCBs concentration in different cod organs in µg/kg wet weight

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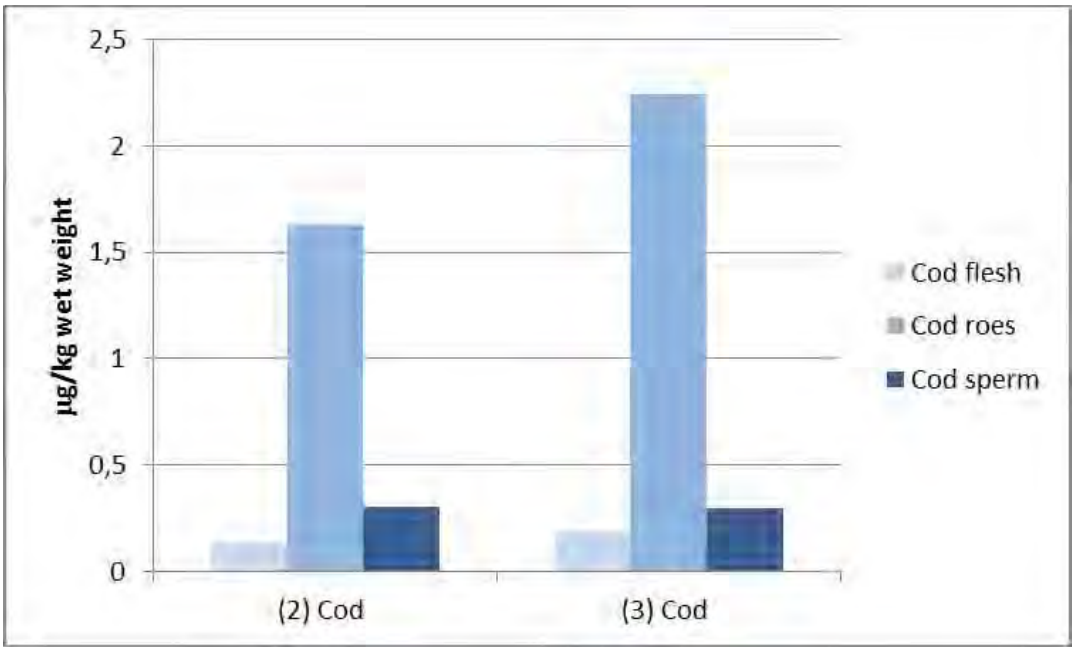

Figure 10: Marker PCBs concentration in different cod organs excluding cod liver in µg/kg wet weight

Figure 11 shows a comparison between the sum of all seven marker PCBs concentration measured in different lumpfish organs. As for the dioxins and dioxin like PCBs, the marker PCBs concentration is higher in the flesh compared to the roes and this is most likely due to difference in lipid content. For details refer to Table 1 and 2 in the Appendix.

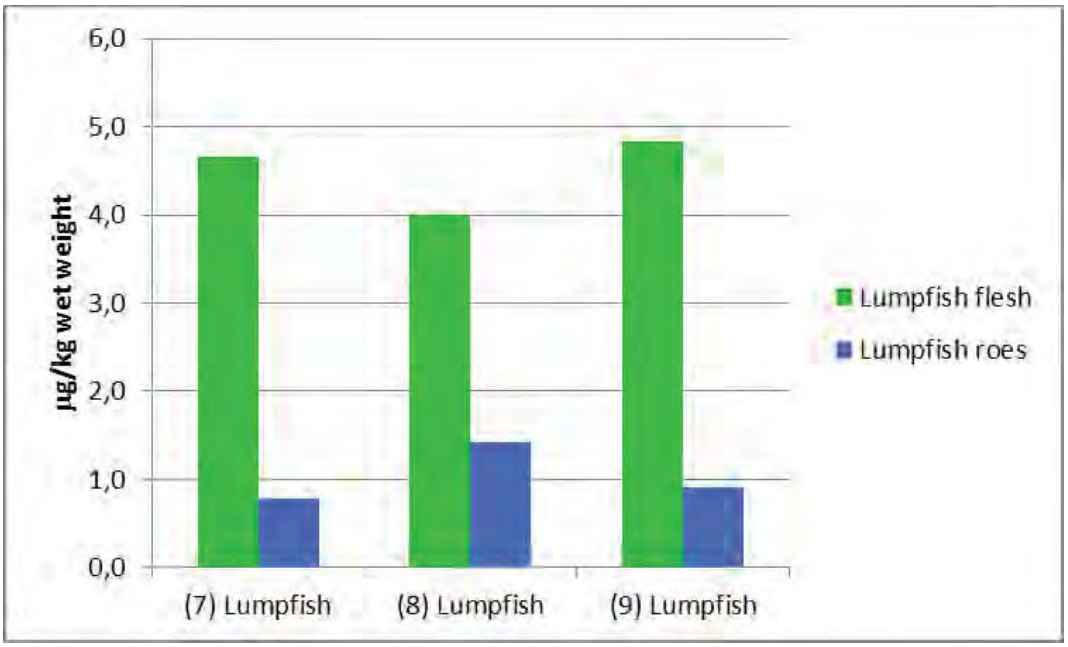

Figure 11: Marker PCBs concentration in different lumpfish organs in µg/kg wet weight

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

5.2.4 Marker PCBs in fish meal and fish oil for feed

The results for the marker PCBs in fish meal and fish oil samples measured in this study are shown in Tables 3 and 4 in the Appendix and in Figure 12 and Figure 13 below. No limits have yet been set for these substances in fish meal and fish oil for feed in the EU. The same patterns that are seen in different capelin meal samples are observed in the corresponding capelin oil.

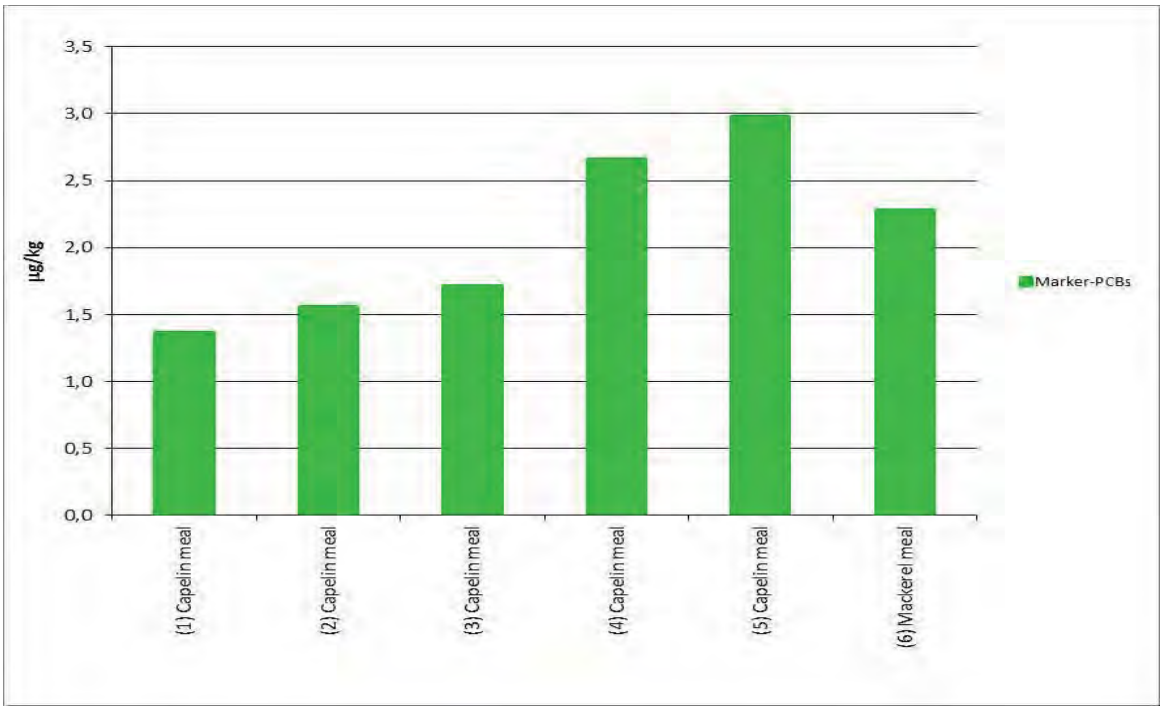

Figure 12: Marker PCBs in fish meal from Iceland in 2011 calculated in relation to 12% moisture

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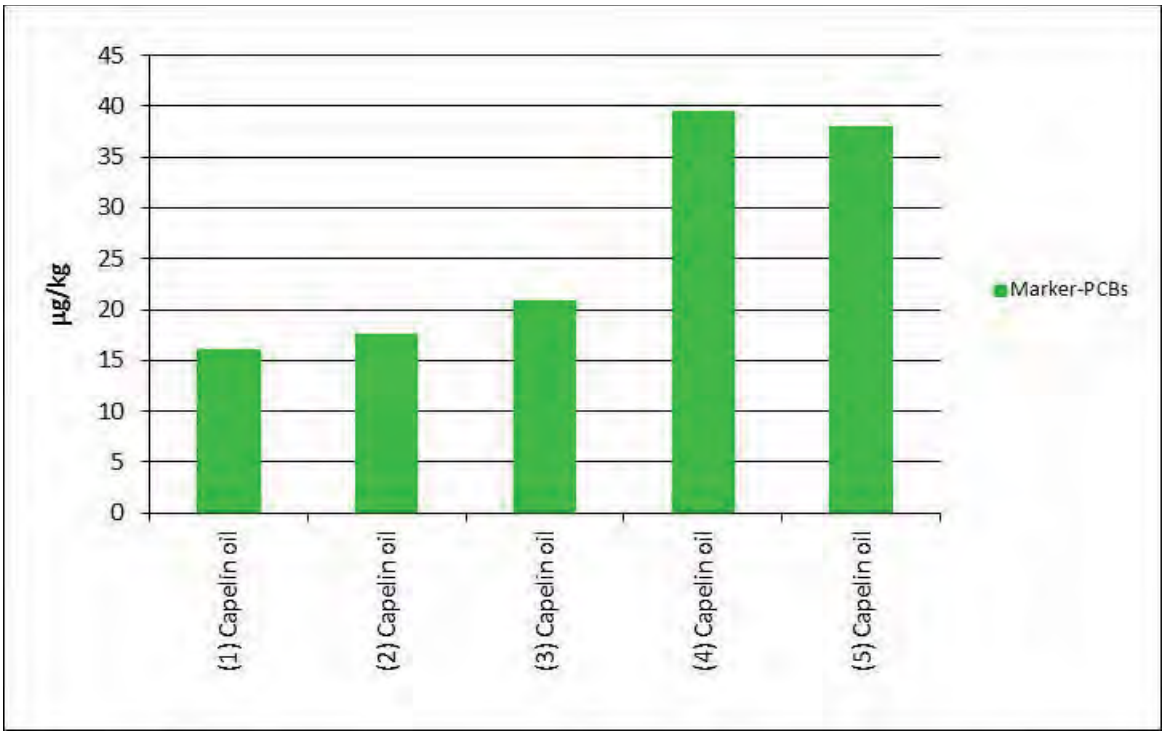

Figure 13: Marker PCBs in fish oils from Iceland in 2011.

5.3 Brominated flame retardants (BFRs)

Brominated diphenyl ethers (BFRs) have been accumulating in the environment over the last decade as their use in industry has increased. One group of BFR is Polybrominated dipheynyl ethers (PBDEs). No maximum limits have yet been set in the EU, but they have been estimated to be ten times less toxic than the pesticide DDT (Scientific Advisory Committee on Nutrition (SACN, 2005). There were three major PBDE products (PentaBDE, OctaBDE and DecaBDE) available on the global market and two of them, PentaBDE and OctaBDE, have been banned in the EU and all use of PBDEs has been restricted by the RoHS directive (Restriction of the use of certain Hazardous substances in electrical and electronic equipment).

5.3.1 PBDE in seafood

There is still limited data available on PBDEs in seafood from Iceland (Ásmundsdóttir et al., 2008; Rabieh et al., 2008, Jörundsdóttir et al., 2010 a, Jörundsdóttir *et al*., 2010b). Therefore a special emphasis was laid on gathering information on PBDE in 2009, 2010 and again in 2011. PBDEs were measured in 9 samples of fish muscle and three different cod organs and lumpfish roes. The PBDE are reported here as the upper bound sum of BDE-28, BDE-47, BDE-66, BDE-100, BDE-99, BDE-85, BDE-154, BDE-153 and BDE-

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

183. BDE-209 is not included in the sum as it was only detected in three of four mackerel samples tested but not in any other fish muscle or fish organs investigated in this study. No maximum limits have been set for PBDEs in seafood.

The results in Figure 14 showed in general very low level of PBDEs in fish muscle from Icelandic fishing grounds except for the species that accumulate fat in the muscle, like the lumpfish and mackerel. The results are reported in detail in Table 1 in the Appendix.

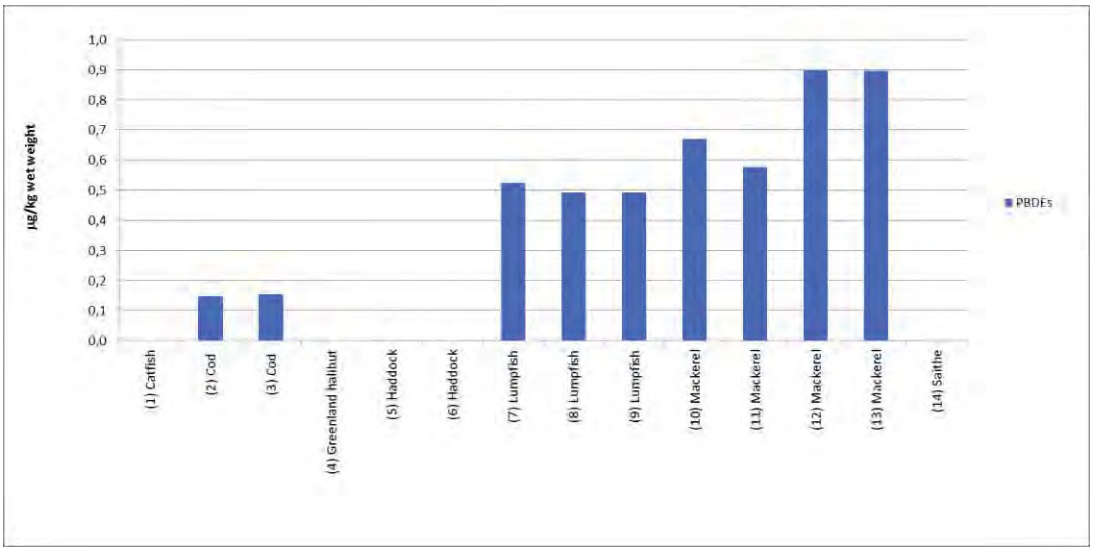

Figure 14: PBDE in fish muscle from Icelandic fishing ground in 2011 in µg/kg wet weight sum of: BDE-28, BDE-47, BDE-66, BDE-100, BDE-99, BDE-85, BDE-154, BDE-153 and BDE-183.

5.3.2 PBDEs in liver, roes and sperm

Concentrations of PBDEs in different fish organs are shown in Table 2 in Appendix. The concentration trend of PBDEs is the same as for dioxins and PBCs i.e. highest in cod liver of the four cod organs investigated, and higher in lumpfish flesh compared to lumpfish roes.

5.3.3 PBDEs in fish oil and fish meal for feed

PBDEs were only analysed in the mackerel meal where the sum concentration is 0.91 µg/kg wet weight, Table 3 in the Appendix. PBDE in Table 3 is the upper bound sum of BDE-28, BDE-47, BDE-66, BDE-100, BDE-99, BDE-85, BDE-154, BDE-153 and BDE-183. BDE-209 is not included in the sum as it was not detected in most samples.

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

5.4 PAH

PAHs were not analysed in the samples this year. Results on PAHs in Icelandic seafood have been published in previous reports (Jörundsdóttir et al., 2010).

5.5 Pesticides

In this chapter, the results for 12 different classes of pesticides are discussed. Results are shown in Tables 5 to 8 in the Appendix. Without exception, the fish muscle samples contained negligible amount of pesticides (Regulation (EC) No 396/2005). All samples of seafood contained pesticides below the EU maximum limits (Commission Directive 2002/32/EC, Commission Directive 2003/100/EC).

12 different pesticides or groups of pesticides were measured in the monitoring program.

DDT (dichloro diphenyl trichloroethan) is probably the best known insecticide. The technical product DDT is fundamentally composed of p,p'-DDT (80%) (Buser, 1995). DDT breaks down in nature, mostly to DDE but also to DDD. The concentration of DDT presented in this report is the sum of p,p'-DDT, o,p´-DDT, p,p'-DDE, o,p´-DDE, p,p´-DDD and o,p´-DDD.

HCH (hexachlorocyclohexan) is an insecticide which has been used since 1949. It is still produced and used in many countries, although it has been banned in many other countries since the 1970s. Technical-grade HCH is a mixture of mainly four isomers: α-, β-, γ-(Lindane), and δ-HCH. Of these, only Lindane is an active substance comprising of approximately 15% of the total mixture, while α-HCH is 60-70% of the mixture. The Food and Agriculture Organization of the UN (FAO) has prohibited the use of the HCH mixture since in the 1980s, after that it was only allowed to use 99% pure Lindane. In this report the concentration of α-, β-, γ-(Lindane), and δ-HCH in the samples are reported.

HCB (hexachlorobenzene) is a fungicide, but it has also been used for industrial purpose and was e.g. produced in Germany until 1993. Today, HCB is mainly a by-product in different industrial processes, as production of pesticides but also from waste incineration and energy production from fossil fuel.

Chlordanes is a group of compounds and isomers where α- and γ-chlordane, oxychlordane and trans-nonachlor are the most common, but over 140 different Chlordanes were produced from 1946 until 1988 when the production was banned. Chlordanes have been widely used all over the world as insecticides. In this report the

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

concentration of Chlordanes is reported as the sum of α-chlordane, γ-chlordane and oxychlordane. trans-Nonachlor is reported separately.

The **Toxaphenes** measured in the samples are the so-called parlar 26, 50 and 62. Toxaphene was used as an insecticide after the use of DDT was discontinued. Toxaphenes use was widespread and the toxaphene congeners are numerous. Several hundred have been analyzed but they are thought to be tens of thousands. The substances measured, i.e. the parlar 26, 50 and 62, are the most common toxaphenes (about 25% of the total amount in nature) and these are used as indicators of toxaphene pollution. In this report the concentration of toxaphenes is reported as the sum of toxaphene 26, 50 and 62.

Aldrin and Dieldrin are widely used insecticides, but in plants and animals aldrin is transformed to dieldrin. Hence, the concentration of aldrin was below LOD in all the samples measured, while dieldrin was always above LOD. The maximum value in the EU is set for the sum of aldrin and dieldrin and the results are therefore presented as the sum of these two.

Two E**ndosulfans** were measured, α- and β-endosulfan, as well as endosulfansulfat which is the breakdown product of endosulfan. Endosulfans are not as persistent as the other insecticides measured in this project. In this report the concentration of endosulfans is reported as the sum of α-endusulfan, β-endusulfan and endosulfansulfat.

Other pesticides measured were **Endrin**, the sum of **Heptachlores** (cis-heptachlorepoxide, trans-heptachlorepoxide and heptachlor), **Pentachlorobenzene**, **Mirex** and **Octachlorostyrene**.

5.5.1 Pesticides in seafood

The results showed very low concentration of all pesticide groups measured in fish muscle from Icelandic waters (see Table 5 in the Appendix). As mentioned before, the results are expressed as upper bond, but most of the pesticides were below the limit of detection and therefore the results presented are likely to be an overestimation. Negligible amounts of ΣDDT, Pentachlorobenzene, HCB, Heptachlores, Aldrin/Dieldrin, Toxaphene, Chlordane and *trans*-Nonachlore were measured in almost all fish species and δ-HCH was always below LOQ except in one sample of mackerel. Figure 15 shows the level of DDT in fish muscle. All fish samples have ΣDDT concentration lower than the EU maximum limit of 500 µg/kg w.w. Of the fish species analysed, Greenland halibut, lumpfish and mackerel have the highest concentrations of all the pesticides investigated.

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

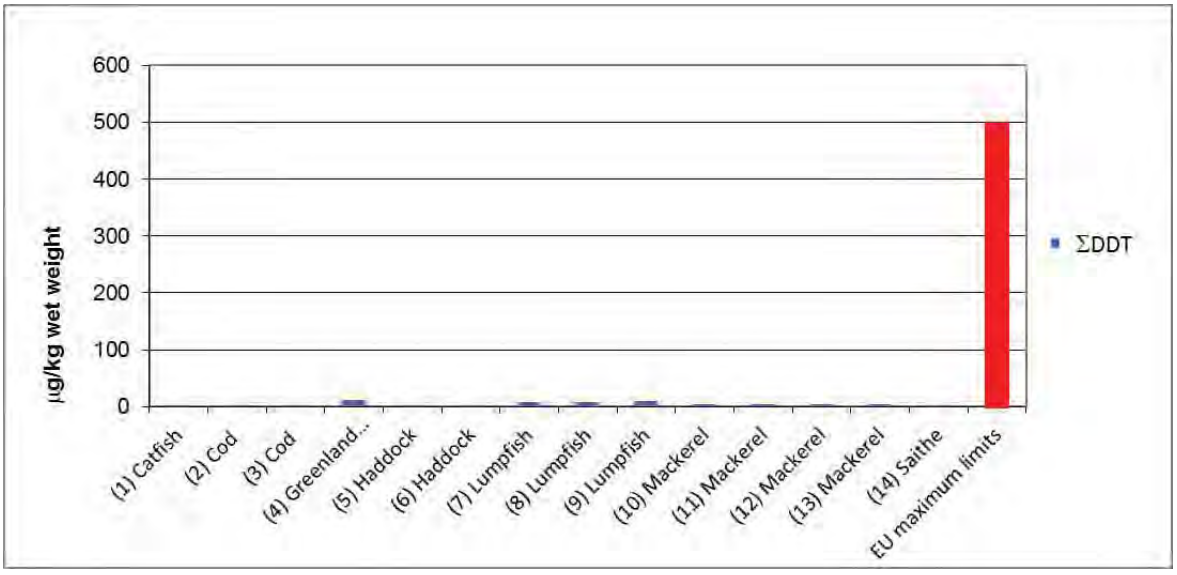

Figure 15: ΣDDT in fish muscle from Icelandic fishing grounds in 2011 in µg/kg wet weight.

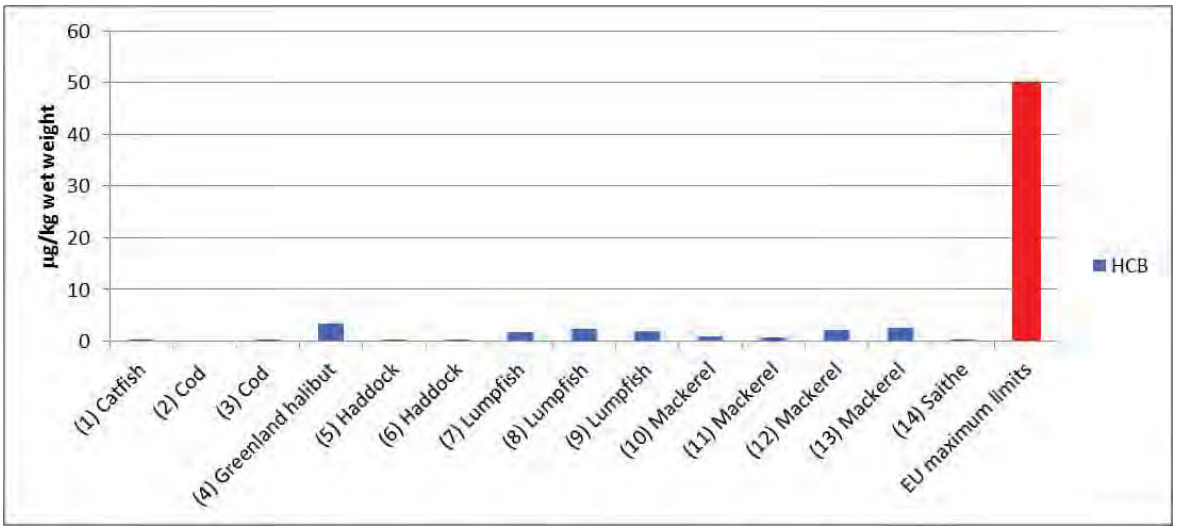

Figure 16: HCB in fish muscle from Icelandic fishing grounds in 2011 in µg/kg wet weight.

5.5.2 Pesticides in fish oil for human consumption

There were no samples of fish oil for human consumption analysed in the monitoring program in the year 2011.

5.5.3 Pesticides in fish meal and fish oil for feed

Several pesticides were measured in fish meal and fish oil for feed (see Tables 7 and Table 8 in the Appendix). There is some variation in the pesticide concentration in different capelin meal samples and the pesticide concentration is generally lower in the

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

mackerel meal sample. No mackerel oil sample was analysed, but similar variation is seen in the pesticide concentration in different capelin oil samples. No meal or oil samples exceed the maximum allowed pesticide level according to EU regulations.

As shown in Figure 17 and Figure 18, there is a difference in concentration of DDT and HCB in the fishmeal samples originating from different fish species. It is difficult to determine why the concentration of these substances varies in the capelin meal (Figure 17, Figure 18 and Figure 19), but factors such as season and condition of the fish are likely contributors.

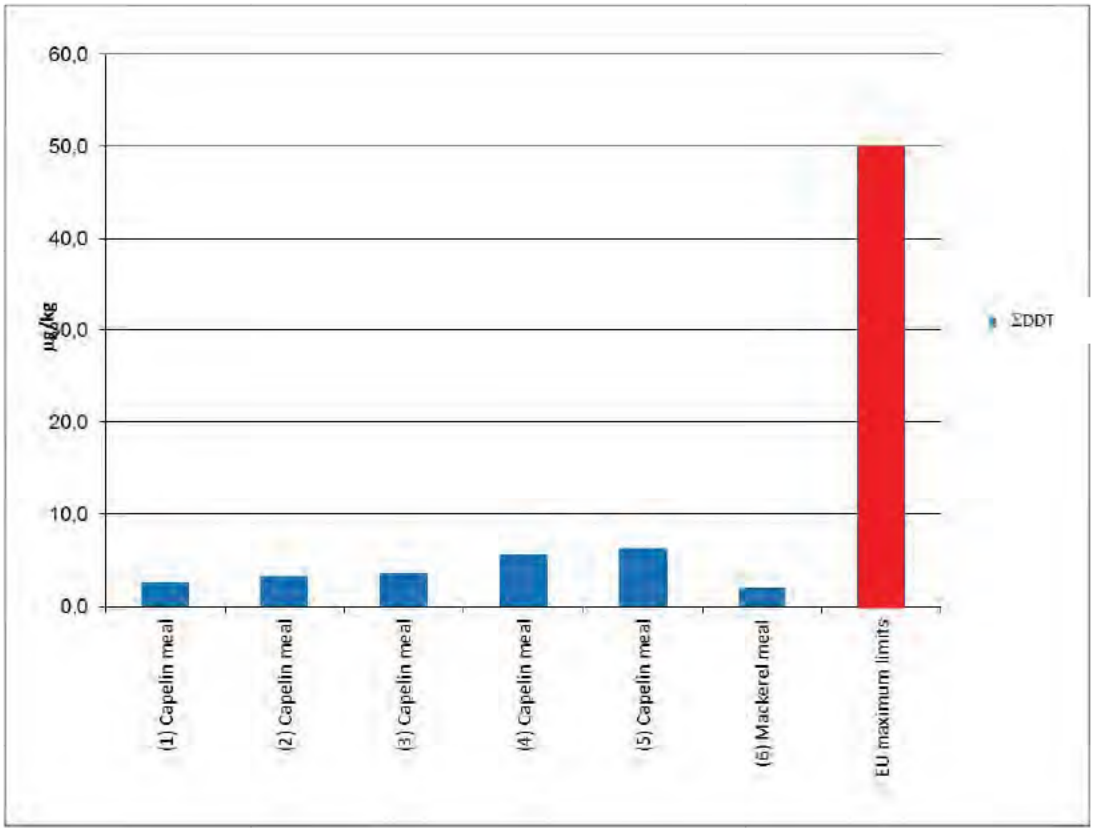

Figure 17: ΣDDT in samples of fish meal from Iceland 2011 calculated in relation to 12% moisture compared to the EU maximum limit.

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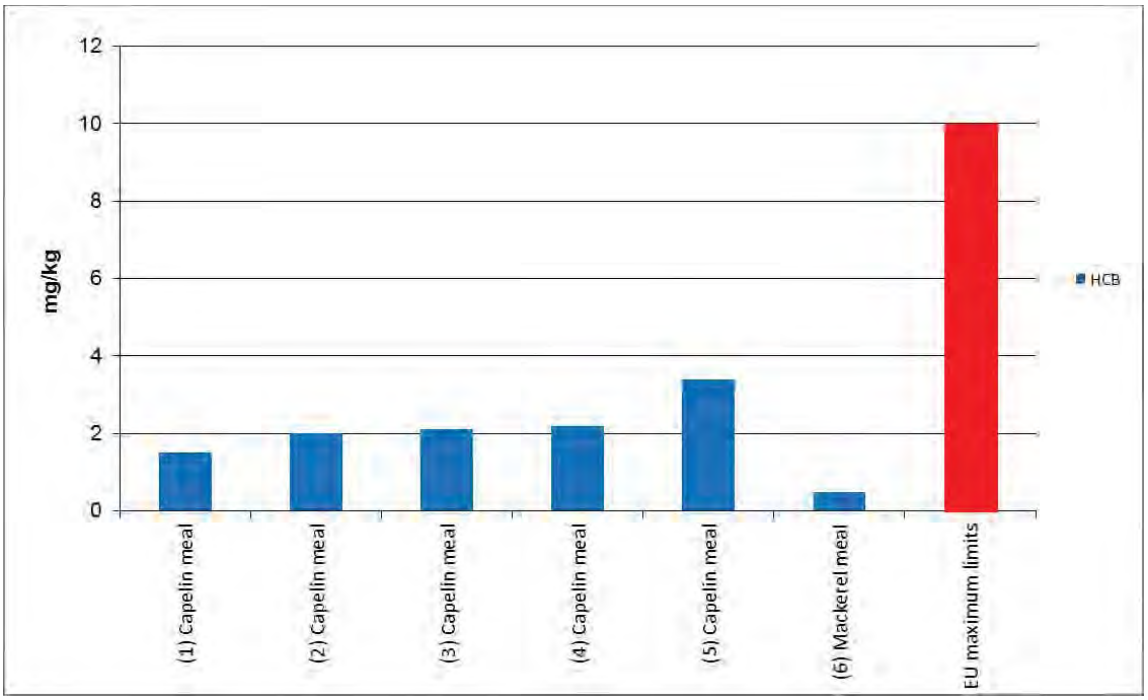

Figure 18: HCB in samples of fish meal from Iceland 2011 calculated in relation to 12% moisture compared to the EU maximum limit.

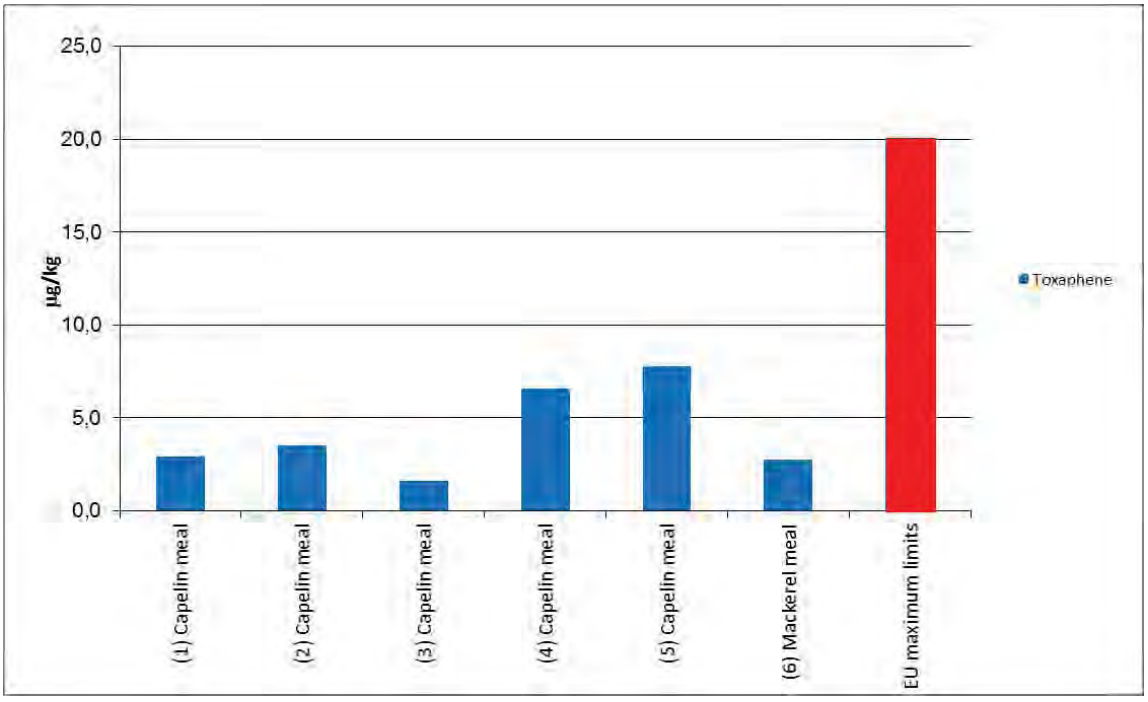

Figure 19: Toxaphene in samples of fish meal from Iceland 2011 calculated in relation to 12% moisture compared to the EU maximum limit.

Concentration of pesticides in fish oil were below EU maximum limits all cases (Commission Directive 2006/77/EC, Table 8 in Appendix).

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5.6 Inorganic trace elements

Inorganic trace elements were analysed in all samples from the year 2011. The following inorganic trace elements were analysed: Hg (mercury), Cd (cadmium), Pb (lead), As (arsenic), Se (selenium), Zn (zinc), Cu (copper) and Fe (iron). Some of the elements like Se, Zn, Cu and Fe are essential minerals and thus do not fall into the category undesirable substances, however, the ICP-MS technology used to measure the trace elements enables us to measure these elements as well for relatively little extra cost. Therefore, all the previously mentioned trace elements are reported in Table 9-12 in Appendix.

5.6.1 Inorganic trace elements in seafood

In short, the concentration of heavy metals like Hg, Pb and Cd in all the samples of the edible part of fish muscle was well below the maximum limits set by EU (Commission regulation 1881/2006, Commission Regulation (EC) No 629/2008). The concentration of mercury (Hg) in the fish samples is shown in Figure 20.

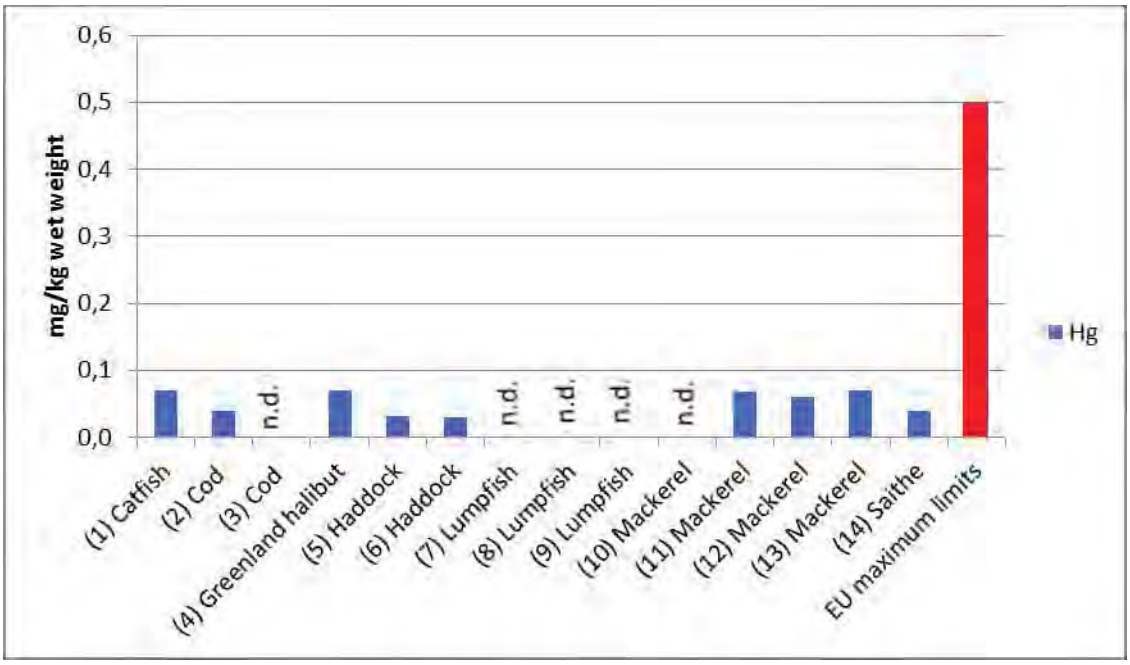

Figure 20: Hg in fish muscle from Icelandic fishing grounds in 2011 in mg/kg wet weight.

The concentration of lead (Pb) in fish muscle was very low as can be seen in Table 9 in the Appendix, in fact only two samples contained lead in concentrations above limits of detection, Greenland halibut and haddock.

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

No limits have yet been set for arsenic, but results from the monitoring in 2011, which are shown in Figure 21 were in agreement with earlier measurements (Auðunsson, 2004, Ásmundsdóttir et al. 2005, Ásmundsdóttir and Gunnlaugsdóttir, 2006, Jörundsdóttir et al., 2009, Baldursdóttir, 2011). The results obtained this year showed that the level of arsenic was well below 25 mg/kg and in all cases below 4 mg/kg except for catfish and haddock with concentrations around 9-11 mg/kg (Table 9). The total arsenic concentration was measured in the samples, but not the concentration of the toxic form i.e. inorganic arsenic.

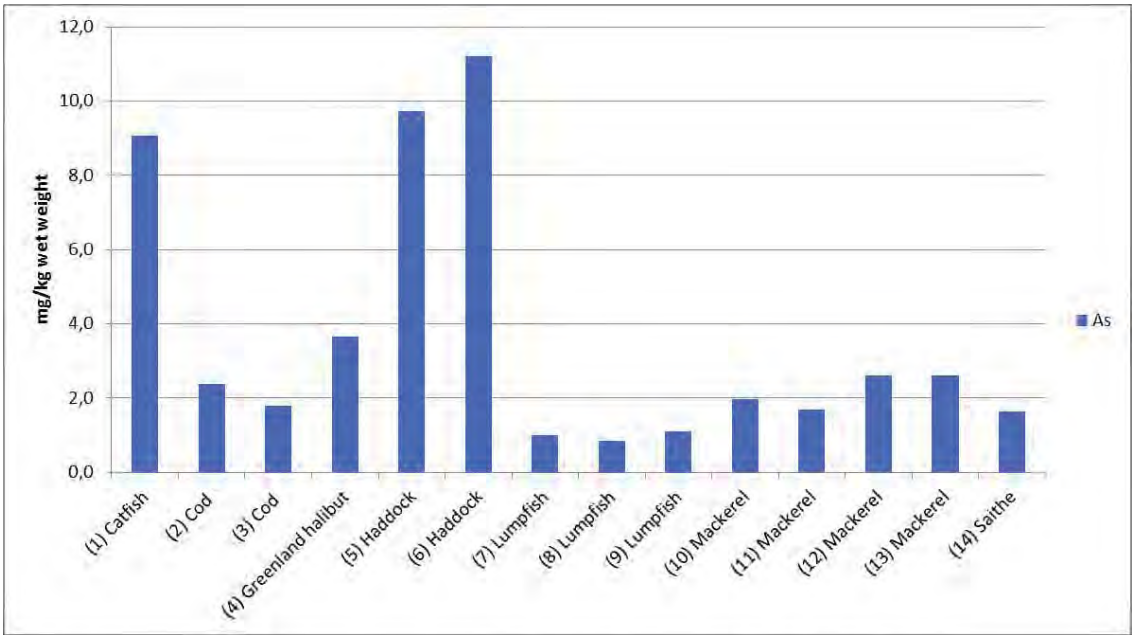

Figure 21: As in fish muscle from Icelandic fishing grounds in 2011 in mg/kg wet weight.

5.6.2 Inorganic trace elements in liver, roes and sperm

Results for inorganic trace elements in liver, roes and sperm are presented in Table 10 in the Appendix. For simplicity the results and discussion about the results obtain for inorganic trace elements in the internal fish organs (liver, roes and sperm) are grouped together in this section. Nevertheless, it is not possible to state that all these elements behave in a similar manner, as can be done for the organic compounds. This can be seen in Figure 22 and Figure 23. Roes have high iron content but low arsenic content compared to other organs investigated.

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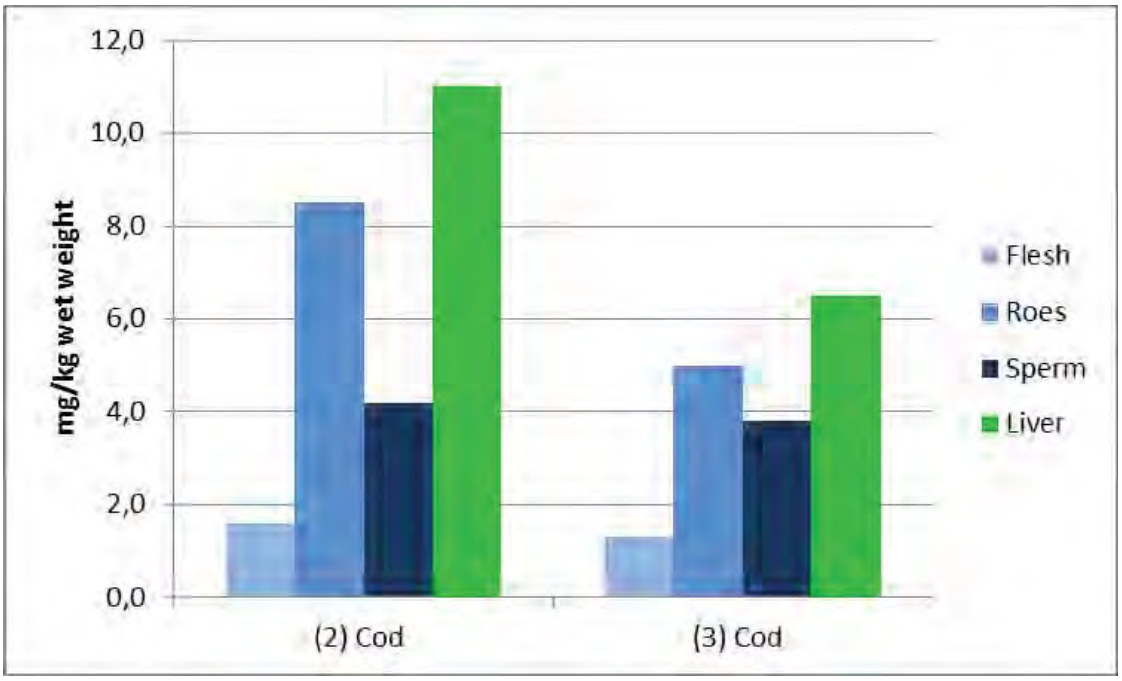

Figure 22: Iron in different organs from cod in mg/kg wet weight.

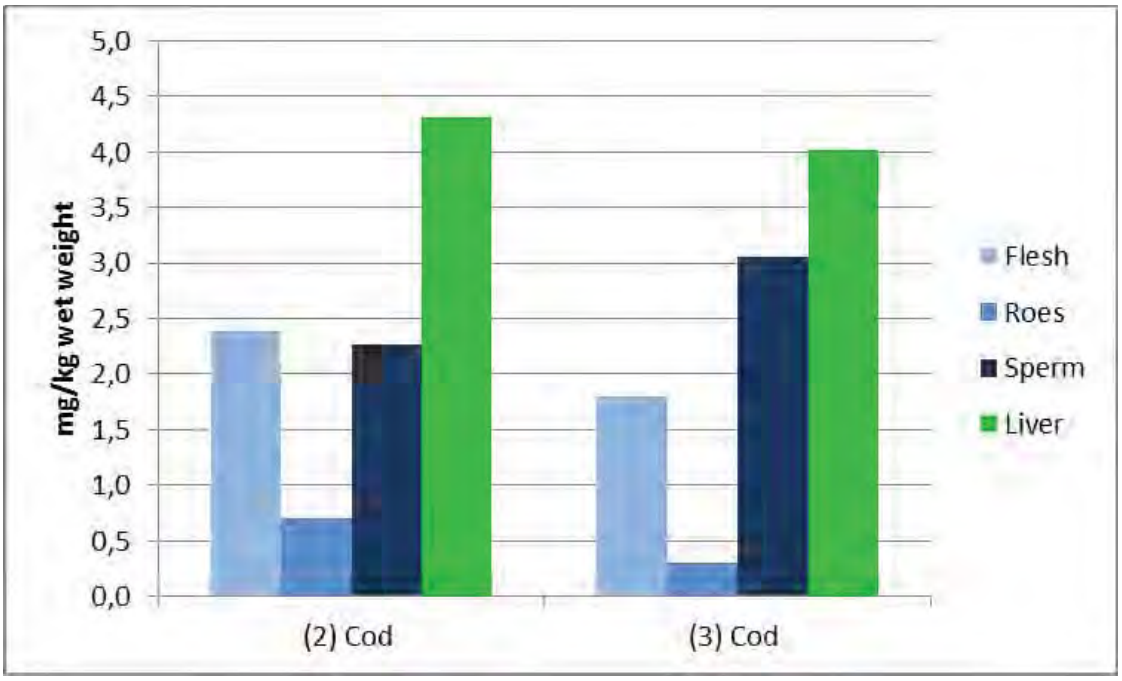

Figure 23: Arsenic in different organs from cod in mg/kg wet weight.

Generally, the cod liver seems to contain the highest concentration of most inorganic trace elements on wet weight basis (for details refer to Table 10 in the Appendix)

Same trend was observed for iron and arsenic content in lumpfish flesh and roes as for the cod, i.e. higher concentration of iron in roes and lower in flesh, and vice versa for

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arsenic, Figure 24 and Figure 25. The difference in inorganic trace element concentration between these two organs is greater in cod compared to lumpfish.

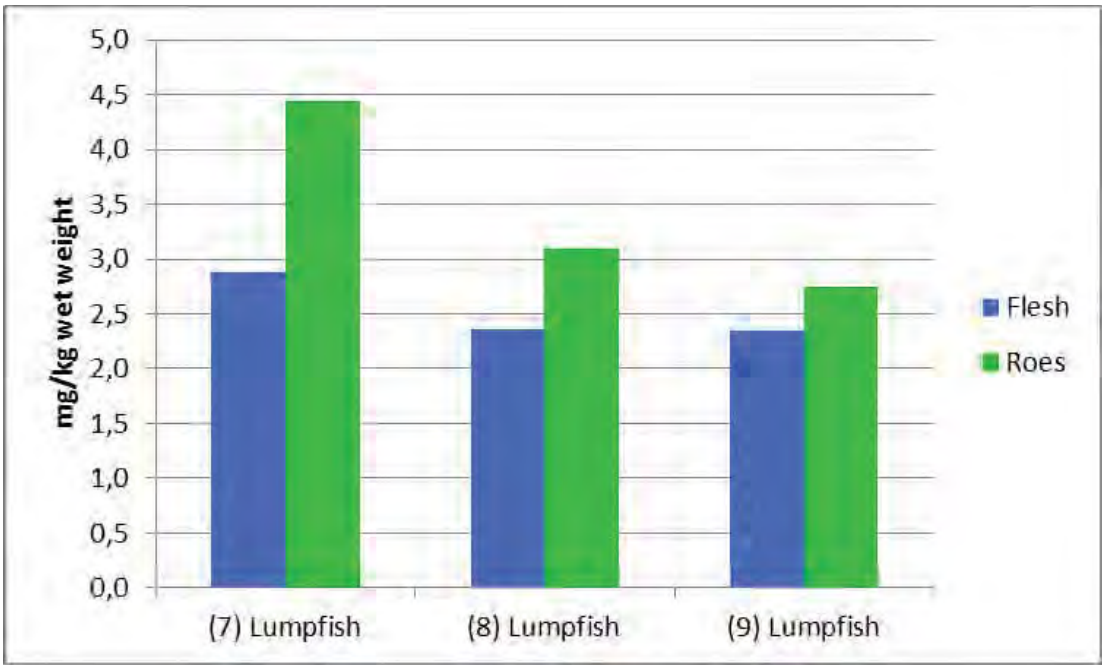

Figure 24: Iron in lumpfish flesh and roes in mg/kg wet weight.

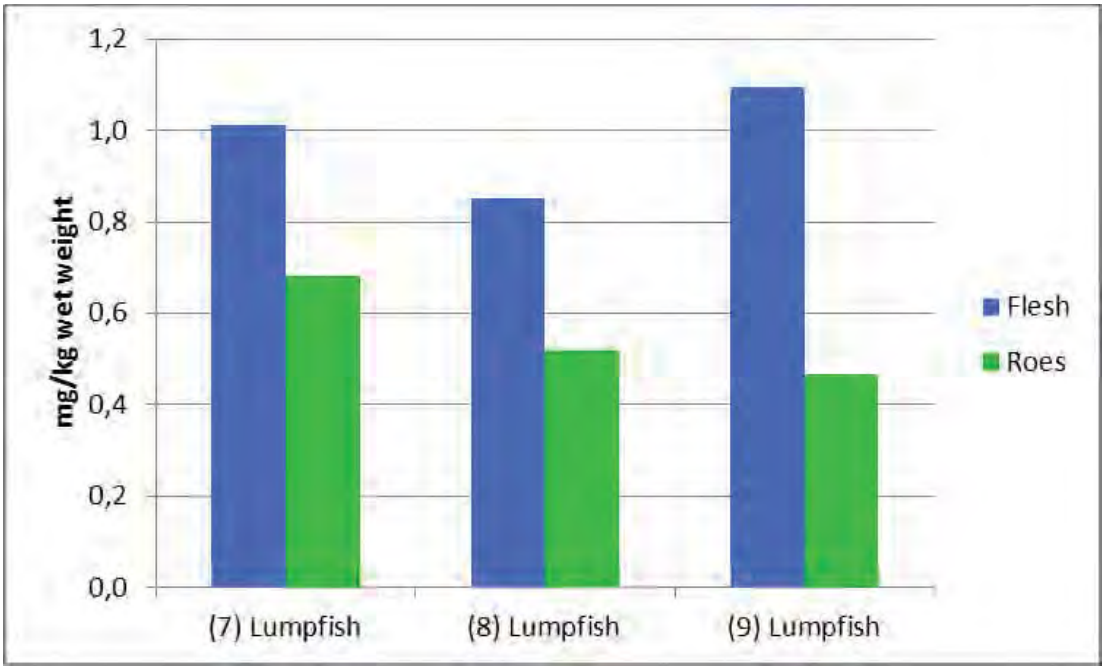

Figure 25: Arsenic in lumpfish flesh and roes in mg/kg wet weight.

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5.6.3 Inorganic trace elements in fish oil and fish meal

Inorganic trace elements were analysed in fish oil and fish meal as shown in Table 11 and 12 in the Appendix. Both undesirable and essential metals as well as metalloids were analysed. Maximum limits exist for arsenic, cadmium, mercury and lead in fish meal and oil (Directive 2002/32/EC, Commission Directive 2003/100/EC, Commission Directive 2005/87/EC, Commission Directive 2009/141/EC). Levels of these metals were low in both meal and oil samples and in all cases well below the EU maximum level (Figure 26 and Figure 27).

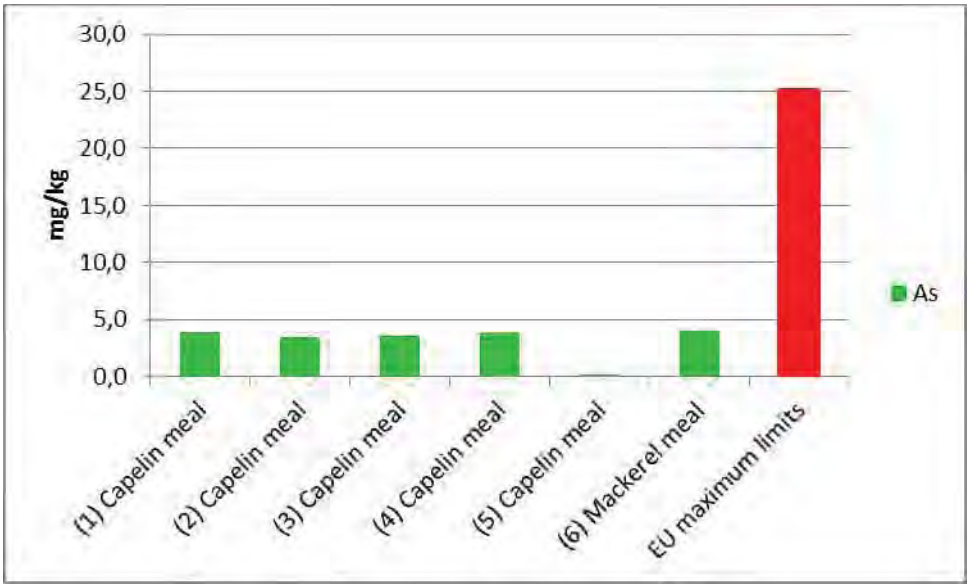

Figure 26: As in fish meal from Icelandic fishing grounds in 2011 in mg/kg wet weight (i.e. meal measured as received from industrial partner)

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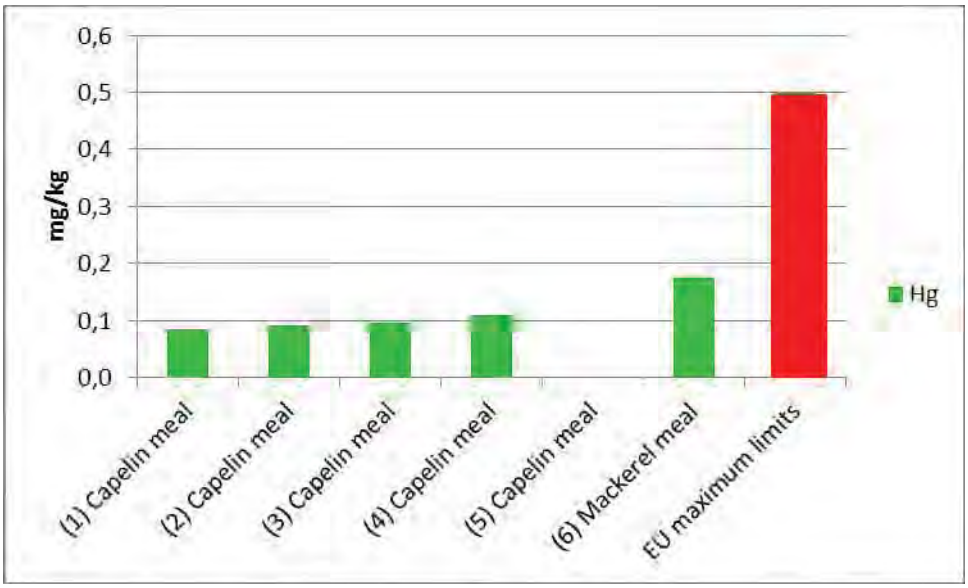

Figure 27: Hg in fish meal from Icelandic fishing grounds in 2011 in mg/kg wet weight (i.e. meal measured as received from industrial partner)

5.7 Poly- and perfluorinated compounds

Poly- and perfluorinated compounds (PFC) are receiving more and more attention since they were first analysed in environmental samples (Giesy and Kannan, 2001; Hansen *et al.*, 2001). The group consists of long chain alkane compounds where most or all chain hydrogens have been exchanged for fluorine. One of the major compound, perfluorooctane sulfonate (PFOS) has been included into the Stockholm Convention on persistent organic pollutants. Very limited information is available on PFCs in Icelandic environment and this is the first data on the concentration of these undesirable substances in Icelandic fish and seafood products. For this reason we laid emphasis on gathering information about PFCs in the edible part of marine catches as well as in the fish meal and fish oil for feed in the year 2011. No maximum levels have yet been issued for PFCs by the EU in food or feed products.

5.7.1 PFCs in seafood

PFCs were not detected in the muscle tissue of any of the fish species origination from Icelandic waters and investigated 2011 as shown in Table 13 in the Appendix.

5.7.2 PFCs in liver, roes and sperm

PFOS was the only PFC above limit of quantification as shown in Table 14 in the Appendix. Further, PFOS was only detected in cod organs, but not in lumpfish roes.

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Figure 28 shows the PFOS concentration in different cod organs. Highest concentration was measured in cod roes while sperm and liver have similar concentrations. PFOS is not lipophilic and does therefore not follow the lipids in organs and tissues like the persistent organic pollutants. PFOS has a known protein binding ability and it is therefore most likely that the different distribution of PFOS to organs is due to protein binding of PFOS to different proteins in these organs (Jones *et al.*, 2003).

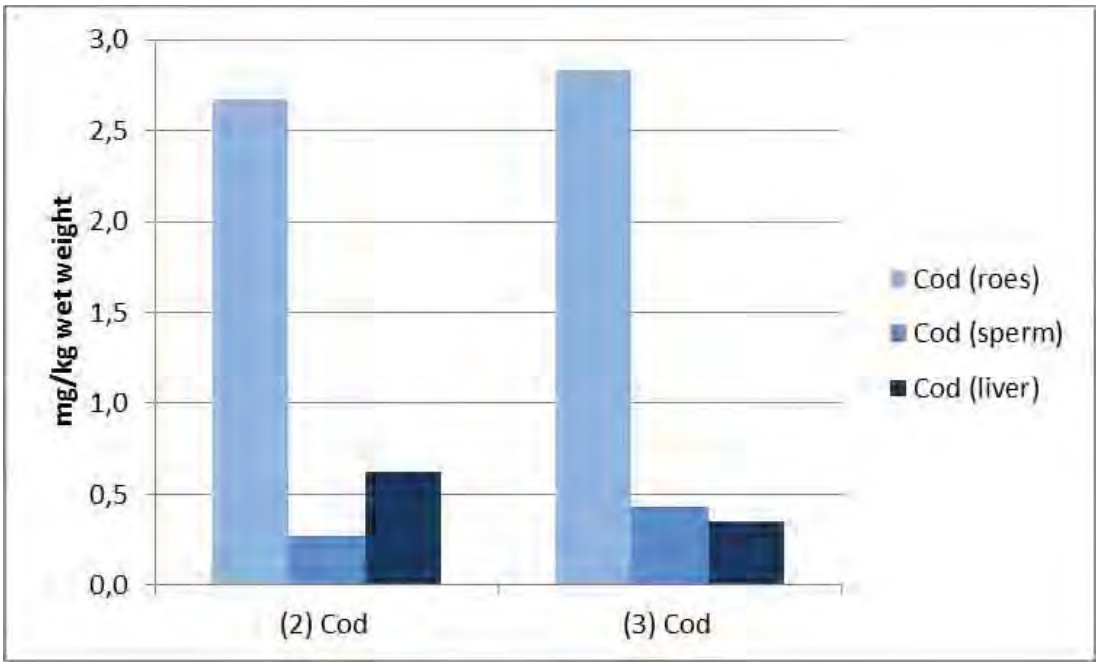

Figure 28: PFOS in different organs from cod in mg/kg wet weight.

5.7.3 PFC in fish meal and oil for feed

Table 15 and 16 in the Appendix show PFC concentrations in fish meal and oil for the year 2011 calculated in relation to 12% moisture. PFCs were not detected in any of the fish oil for feed samples analysed in this study and PFOS was the only compound detected in fish meal. The absence of PFCs in fish oil is due to the fact that and PFCs are not lipophilic and bind to proteins (Jones *et al.*, 2003) and the fish oil contains virtually no proteins. Mackerel meal contained lower levels of PFOS compared to capelin meal, even though there is some variation between capelin meal samples, however only one Mackerel meal was included in this study and therefore more data is need to confirm these results.

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Commission Directive 2005/87/EC of 5th December 2005

Commission Directive 2006/13/EC of 3th February 2006

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Commission Regulation (EC) No 629/2008 of 2nd of July 2008

Directive 2002/32/EC of the European Parliament and of the Council of 7 May 2002

Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 of February 2005

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Reglugerð um gildistöku reglugerðar framkvæmdastjórnarinnar (EB) nr. 1881/2006 um hámarksgildi fyrir tiltekin aðskotaefni í matvælum. Nr 265/2010.

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7 Appendix

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Table 1 Dioxins PCBs and PBDE in fish muscle on wet weight

Sample code	Fish sample no.	Sample name	Latin name	Fishing ground	Size [cm]	Lipid content %	PCDD/PCDFs pg/g WHO-TEQ	Dioxin like PCBs pg/g WHO-TEQ	Sum of Dioxins and DL-PCBs pg/g WHO-TEQ	Marker PCBs µg/kg	PBDEs µg/kg	BDE-209 µg/kg
R11-994-3	1	Catfish	*Anarhichas lupus*	*NW*	30-50	0,55	0,020	0,018	0,038	0,35	n.a.	n.a.
R11-710-1	2	Cod	*Gadus morhua*	*SW*	60-74	0,41	0,018	0,017	0,035	0,131	0,15	< 1
R11-782-1	3	Cod	*Gadus morhua*	*SW*	75+	0,93	0,034	0,020	0,054	0,18	0,15	< 0,6
R11-994-4	4	Greenland halibut	*Reinhardtius hippoglossoides*	*N*	50-60	13	0,74	0,82	1,6	6,7	n.a.	n.a.
R11-994-1	5	Haddock	*Melanogrammus aeglefinus*	*NE*	50-60	0,53	0,020	0,021	0,041	0,17	n.a.	n.a.
R11-994-2	6	Haddock	*Melanogrammus aeglefinus*	*NE*	40-50	0,47	0,021	0,017	0,038	0,12	n.a.	n.a.
R11-666-1	7	Lumpfish	*Cyclopterus lumpus*	*NW*	35-45	20	0,30	0,47	0,77	4,7	0,52	< 0,7
R11-932-1	8	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	14	0,36	0,46	0,82	4,0	0,49	< 0,5
R11-1276-1	9	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	12	0,27	0,55	0,82	4,8	0,49	< 0,4
R11-2567-1	10	Mackerel	*Scomber scombrus*	*S*	33-35	12	0,15	0,39	0,54	3,7	0,67	0,22
R11-2567-2	11	Mackerel	*Scomber scombrus*	*SE*	30-36	12	0,11	0,49	0,60	5,2	0,58	0,20
R11-2567-3	12	Mackerel	*Scomber scombrus*	*NE*	33-37	25	0,16	0,50	0,65	5,1	0,90	< 0,3
R11-2567-4	13	Mackerel	*Scomber scombrus*	*NE*	33-37	21	0,16	0,46	0,62	5,7	0,90	0,48
R11-747-1	14	Saithe	*Pollachius virens*	*SW*	60-70	0,89	0,025	0,058	0,08	0,69	n.a.	n.a.
		EU action level					3,00	3,00	*	*	*	*
		EU maximum limits					4,00	*	8,00	*	*	*

*No maxinmum limits exist in the EU for the substances

n.a. Not analysed

PCDD/PCDFs are 2,3,7,5,8-PCDDs and PCDFs.

DL-PCBs are CB-77, -81, -126, -169, -105, -114, -118, -123, -156, -157, -167 and -189

Marker PCBs are CB-28, -52, -101, -118, -138, -153 and -180

PBDEs are BDE-170, -28, -47, -49, -66, -71, -85, --99, -100, -119, -126, -138, -153, -154, -183, -184, -196, -197, -206 and -207. BDE-209 was not detected in any sample.

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 2: Dioxins, PCBs and PBDE in different fish organs on wet weight

Sample code	Sample no.	Sample name	Latin name	Fishing ground	Size [cm]	Lipid content %	PCDD/PCDFs pg/g WHO-TEQ	Dioxin like PCBs pg/g WHO-TEQ	Sum of Dioxins and DL-PCBs pg/g WHO-TEQ	Marker PCBs µg/kg	PBDEs µg/kg
R11-710-2	1	Cod (roes)	*Gadus morhua*	*SW*	60-74	2,5	0,070	0,11	0,18	1,6	0,28
R11-710-3	2	Cod (liver)	*Gadus morhua*	*SW*	60-74	82	2,8	6,0	8,8	62	1,3
R11-710-4	3	Cod (sperm)	*Gadus morhua*	*SW*	60-74	2,2	0,053	0,023	0,076	0,31	0,1
R11-782-3	4	Cod (roes)	*Gadus morhua*	*SW*	75+	2,8	0,074	0,16	0,23	2,2	0,33
R11-782-2	5	Cod (liver)	*Gadus morhua*	*SW*	75+	86	2,9	7,0	9,9	80	7,5
R11-782-4	6	Cod (sperm)	*Gadus morhua*	*SW*	75+	2,6	0,030	0,031	0,061	0,30	0,14
R11-666-2	7	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	6,3	0,049	0,052	0,10	0,78	0,22
R11-932-2	8	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	8,4	0,073	0,094	0,17	1,4	0,29
R11-1276-2	9	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	3,7	0,041	0,055	0,096	0,91	0,20
		EU action level for cod liver							25		
		EU maximum limits for cod liver									

* No maximum limits exist in the EU for the substance

N/A Not analysed

PCDD/PCDFs are 2,3,7,8-PCDDs and PCDFs.

DL-PCBs are CB -77, -81, -126, -169, -105, -114, -118, -123, -156, -157, -167 and -189.

Marker PCBs are CB -28, -52, -101, -118, -138, -153 and 180.

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Table 3: Dioxins and PCBs in fish meal for feed calculated in relation to 12% moisture

Sample code	Meal sample no.	Sample name	Latin name	PCDD/PCDF pg/g WHO-TEQ	Dioxin like PCBs pg/g WHO-TEQ	Sum of Dioxins and DL-PCBs pg/g WHO-TEQ	Marker-PCBs µg/kg	PBDEs µg/kg
R11-1335-1	1	Capelin meal	*Mallotus villosus*	0,15	0,16	0,30	1,4	n.a.
R11-1335-3	2	Capelin meal	*Mallotus villosus*	0,17	0,19	0,36	1,6	n.a.
R11-1335-5	3	Capelin meal	*Mallotus villosus*	0,20	0,22	0,42	1,7	n.a.
R11-1335-7	4	Capelin meal	*Mallotus villosus*	0,32	0,31	0,63	2,7	n.a.
R11-593-1	5	Capelin meal	*Mallotus villosus*	0,31	0,35	0,66	3,0	n.a.
R11-2732-1	6	Mackerel meal	*Scomber scombrus*	0,11	0,19	0,30	2,3	0,91
		EU action level		1,00	2,50	3,50	*	*
		EU maximum limits		1,25		4,50	*	*

* No maximum limits exist in the EU for substances

PCDD/PCDFs are 2,3,7,8-PCDDs and PCDFs.
DL-PCBs are CB -77, -81, -126, -169, -105, -114, -118, -123, -156, -157, -167 and -189.
Marker PCBs are CB -28, -52, -101, -118, -138, -153 and 180.
PBDEs are BDE -170, -28, -47, -49, -66, -71, -77, -85, -99, -100, -119, -126, -138, -153, -154, -183, -184, -196, -197, -206, and -207. BDE-209 was not detected in any sample

Table 4: Dioxin, PCB and PBDE in fish oil for feed

Sample code	Fish oil sample no.	Sample name	Latin name	PCDD/PCDF pg/g WHO-TEQ	dioxin like PCBs pg/g WHO-TEQ	Sum of Dioxins and DL-PCBs pg/g WHO-TEQ	Marker-PCBs µg/kg	PBDEs µg/kg
R11-1335-2	1	Capelin oil	*Mallotus villosus*	1,4	1,6	3,0	16	n.a.
R11-1335-4	2	Capelin oil	*Mallotus villosus*	1,6	2,1	3,6	18	n.a.
R11-1335-6	3	Capelin oil	*Mallotus villosus*	1,9	2,4	4,3	21	n.a.
R11-1335-8	4	Capelin oil	*Mallotus villosus*	3,7	4,6	8,4	40	n.a.
R11-593-2	5	Capelin oil	*Mallotus villosus*	3,7	4,8	8,5	38	n.a.
		EU action level		5,0	14		*	*
		EU maximum limits		6,0		24	*	*

* No maxinum limits exist in the EU for the substances.

PCDD/PCDFs are 2,3,7,8-PCDDs and PCDFs.
DL-PCBs are CB -77, -81, -126, -169, -105, -114, -118, -123, -156, -157, -167 and -189.
Marker PCBs are CB -28, -52, -101, -118, -138, -153 and 180.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 5 Pesticides in fish mucle on wet weight

Sample code	Fish sample no.	Sample name	Latin name	Fishing ground	Size [cm]	Lipid content %	β-HCH µg/kg	α-HCH µg/kg	γ-HCH µg/kg	δ-HCH µg/kg	Σ DDT µg/kg	Pentachlor benzene µg/kg	HCB µg/kg	Σ Heptachlores µg/kg
R11-994-3	1	Catfish	*Anarhichas lupus*	*NW*	30-50	0,55	< 0,0020	0,0027	< 0,0030	< 0,0020	0,21	0,0063	0,079	0,30
R11-710-1	2	Cod	*Gadus morhua*	*SW*	60-74	0,41	0,03	< 0,0020	< 0,010	< 0,0020	0,15	0,032	< 0,0020	0,22
R11-782-1	3	Cod	*Gadus morhua*	*SW*	75+	0,93	< 0,0020	< 0,0020	< 0,0047	< 0,0020	0,24	0,010	0,19	0,44
R11-994-4	4	Greenland halibut	*Reinhardtius hippoglossoides*	*N*	50-60	13	0,14	0,42	0,14	< 0,020	12	0,33	3,4	16
R11-994-1	5	Haddock	*Melanogrammus aeglefinus*	*NE*	50-60	0,53	< 0,0020	0,0046	< 0,0032	< 0,0020	0,064	0,0066	0,23	0,30
R11-994-2	6	Haddock	*Melanogrammus aeglefinus*	*NE*	40-50	0,47	< 0,0020	0,0034	< 0,0034	< 0,0020	0,038	0,0062	0,19	0,23
R11-666-1	7	Lumpfish	*Cyclopterus lumpus*	*NW*	35-45	20	0,20	0,39	0,11	< 0,023	7,4	0,070	1,8	9,3
R11-932-1	8	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	14	0,14	0,28	< 0,069	< 0,020	7,9	0,060	2,4	10
R11-1276-1	9	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	12	0,095	0,23	0,047	< 0,020	9,6	0,046	2,0	12
R11-2567-1	10	Mackerel	*Scomber scombrus*	*S*	33-35	12	0,10	0,27	0,054	< 0,013	3,6	0,13	0,91	0,44
R11-2567-2	11	Mackerel	*Scomber scombrus*	*SE*	30-36	12	0,075	0,24	< 0,034	< 0,013	4,2	0,10	0,73	0,40
R11-2567-3	12	Mackerel	*Scomber scombrus*	*NE*	33-37	25	0,21	0,72	0,24	< 0,020	5,0	0,22	2,1	0,66
R11-2567-4	13	Mackerel	*Scomber scombrus*	*NE*	33-37	21	0,21	0,62	0,20	< 0,020	4,8	0,20	2,5	0,69
R11-747-1	14	Saithe	*Pollachius virens*	*SW*	60-70	0,89	0,0047	0,0047	< 0,0052	< 0,0020	0,80	0,014	0,28	1,1
		EU maximum limits					50	50	50		500		50	50

Table 5 (cont) Pesticides in fish muscle on wet weight

Sample code	Fish sample no.	Sample name	Date of catch	Fishing ground	Size [cm]	Lipid content %	Aldrin/ dieldrin µg/kg	Toxaphene µg/kg	Octachloro styrene µg/kg	Endrin µg/kg	Endo-sulfane µg/kg	Chlordane µg/kg	*trans*-Nonachlor µg/kg	Mirex µg/kg
R11-994-3	1	Catfish	*Anarhichas lupus*	*NW*	30-50	0,55	0,10	0,21	0,0026	0,0050	0,065	0,031	0,078	0,03
R11-710-1	2	Cod	*Gadus morhua*	*SW*	60-74	0,41	0,078	0,094	0,0045	0,0067	0,069	0,028	0,030	0,0086
R11-782-1	3	Cod	*Gadus morhua*	*SW*	75+	0,93	0,074	0,18	0,0031	0,012	0,1	0,04	0,036	0,0028
R11-994-4	4	Greenland halibut	*Reinhardtius hippoglossoides*	*N*	50-60	13	3,5	11	0,097	0,53	0,7	3,17	2,7	0,13
R11-994-1	5	Haddock	*Melanogrammus aeglefinus*	*NE*	50-60	0,53	0,040	0,036	0,0041	< 0,0020	0,08	0,01	0,015	< 0,0020
R11-994-2	6	Haddock	*Melanogrammus aeglefinus*	*NE*	40-50	0,47	0,034	0,031	0,0027	< 0,0020	0,07	0,01	0,011	< 0,0020
R11-666-1	7	Lumpfish	*Cyclopterus lumpus*	*NW*	35-45	20	4,3	9,0	0,057	0,92	0,8	2,6	1,4	0,036
R11-932-1	8	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	14	4,0	9,3	0,059	0,73	0,694	2,4	1,7	0,041
R11-1276-1	9	Lumpfish	*Cyclopterus lumpus*	*NW*	39-45	12	4,2	8,3	0,071	0,86	0,78	2,8	1,6	0,053
R11-2567-1	10	Mackerel	*Scomber scombrus*	*S*	33-35	12	1,3	6,0	0,03	0,28	0,52	1,11	0,75	0,03
R11-2567-2	11	Mackerel	*Scomber scombrus*	*SE*	30-36	12	1,1	5,8	0,03	0,29	0,52	1,03	0,94	0,02
R11-2567-3	12	Mackerel	*Scomber scombrus*	*NE*	33-37	25	2,5	5,0	0,05	0,36	1,00	1,44	1,30	< 0,020
R11-2567-4	13	Mackerel	*Scomber scombrus*	*NE*	33-37	21	1,9	4,3	0,05	0,55	0,90	1,25	1,10	0,02
R11-747-1	14	Saithe	*Pollachius virens*	*SW*	60-70	0,89	0,20	0,8	0,012	0,02	0,07	0,2	0,18	0,011
		EU maximum limits					50			50		100		

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

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Table 6: Pesticides in different fish organs on wet weight

Sample code	Fish sample no.	Sample name	Latin name	Fishing ground	Size [cm]	Lipid content %	β-HCH µg/kg	α-HCH µg/kg	γ-HCH µg/kg	δ-HCH µg/kg	Σ DDT µg/kg	Pentachlorbenzene µg/kg	HCB µg/kg	Σ Heptachlores µg/kg
R11-710-2	1	Cod (roes)	*Gadus morhua*	*SW*	60-74	2,5	0,013	0,028	0,012	< 0,0040	2,1	0,079	1,1	3,2
R11-710-3	2	Cod (liver)	*Gadus morhua*	*SW*	60-74	82	0,70	2,3	0,32	< 0,080	88	1,2	24	113
R11-710-4	3	Cod (sperm)	*Gadus morhua*	*SW*	60-74	2,2	< 0,0040	< 0,0040	< 0,0062	< 0,0040	0,41	0,014	0,22	0,65
R11-782-3	4	Cod (roes)	*Gadus morhua*	*SW*	75+	2,8	0,013	0,045	0,019	< 0,0040	2,8	0,094	1,4	4,3
R11-782-2	5	Cod (liver)	*Gadus morhua*	*SW*	75+	86	0,91	2,7	0,40	< 0,080	130	1,7	29	161
R11-782-4	6	Cod (sperm)	*Gadus morhua*	*SW*	75+	2,6	0,0048	0,0059	< 0,0087	< 0,0040	0,46	0,011	0,20	0,67
R11-666-2	7	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	6,3	0,049	0,18	0,052	< 0,010	1,5	0,048	0,80	2,4
R11-932-2	8	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	8,4	0,059	0,19	0,045	< 0,010	2,6	0,16	1,5	4,3
R11-1276-2	9	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	3,7	0,026	0,077	0,023	< 0,010	1,9	0,061	0,70	2,7
		EU maximum limits												

N/A Not analysed

Table 6 (cont): Pesticides in different fish organs on wet weight

Sample code	Fish sample no.	Sample name	Date of catch	Fishing ground	Size [cm]	Lipid content %	Aldrin/dieldrin µg/kg	Toxaphene µg/kg	Octachlorostyrene µg/kg	Endrin µg/kg	Endosulfane µg/kg	Chlordane µg/kg	*trans*-Nonachlor µg/kg	Mirex µg/kg
R11-710-2	1	Cod (roes)	*Gadus morhua*	*SW*	60-74	2,5	1,7	1,5	0,016	0,61	0,13	1,82	1	0,018
R11-710-3	2	Cod (liver)	*Gadus morhua*	*SW*	60-74	82	23	83	0,55	2,9	2,58	21,5	22	0,97
R11-710-4	3	Cod (sperm)	*Gadus morhua*	*SW*	60-74	2,2	0,21	0,29	0,0048	0,025	0,13	0,1	0,078	0,0046
R11-782-3	4	Cod (roes)	*Gadus morhua*	*SW*	75+	2,8	2,2	2,1	0,78	3,8	4,7	28,80	31	1,3
R11-782-2	5	Cod (liver)	*Gadus morhua*	*SW*	75+	86	29	109	0,023	0,71	0,2	2,26	1,4	0,024
R11-782-4	6	Cod (sperm)	*Gadus morhua*	*SW*	75+	2,6	0,20	0,33	< 0,0040	0,021	0,1	0,09	0,07	0,0063
R11-666-2	7	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	6,3	1,3	1,5	0,013	0,20	0,38	0,63	0,32	< 0,010
R11-932-2	8	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	8,4	1,9	3,4	0,025	0,33	0,30	0,780	0,55	0,013
R11-1276-2	9	Lumpfish (roes)	*Cyclopterus lumpus*	*NW*	N/A	3,7	1,2	1,8	0,016	0,19	0,33	0,6	0,29	< 0,010
		EU maximum limits												

N/A Not analysed

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

Table 7: Pesticides in fish meal for feed on wet weight

Sample code	Meal sample no.	Sample name	β-HCH µg/kg	α-HCH µg/kg	γ-HCH µg/kg	δ-HCH µg/kg	Σ DDT µg/kg	Pentachlor benzene µg/kg	HCB µg/kg	Σ Heptachlores µg/kg
R11-1335-1	1	Capelin meal	0,10	0,14	0,073	< 0,020	2,6	0,15	1,5	0,52
R11-1335-3	2	Capelin meal	0,13	0,098	0,071	< 0,020	3,3	0,15	2,0	0,56
R11-1335-5	3	Capelin meal	0,083	0,094	< 0,020	< 0,020	3,5	0,18	2,1	0,59
R11-1335-7	4	Capelin meal	0,055	0,038	0,025	< 0,020	5,7	0,15	2,2	0,62
R11-593-1	5	Capelin meal	0,048	0,089	0,037	< 0,020	6,4	0,22	3,4	0,67
R11-2732-1	6	Mackerel meal	0,076	0,43	0,035	< 0,013	2,0	0,099	0,49	0,30
EU maximum limits			10	20	200		50		10	

Table 7 (cont.): Pesticides in fish meal for feed on wet weight.

Sample code	Meal sample no.	Sample name	Aldrin/ dieldrin µg/kg	Toxaphene µg/kg	Octachlor o styrene µg/kg	Endrin µg/kg	Endo- sulfane µg/kg	Chlordane µg/kg	*trans*- Nonachlor µg/kg	Mirex µg/kg
R11-1335-1	1	Capelin meal	2,2	2,9	< 0,020	0,33	0,65	1,2	0,72	< 0,020
R11-1335-3	2	Capelin meal	2,8	3,5	0,028	0,41	0,65	1,5	0,76	0,021
R11-1335-5	3	Capelin meal	2,8	1,6	0,03	0,41	0,66	1,7	0,94	< 0,020
R11-1335-7	4	Capelin meal	3,1	6,6	0,042	0,51	0,65	2,2	1,3	0,039
R11-593-1	5	Capelin meal	3,8	7,8	0,064	0,63	0,65	2,7	1,5	0,040
R11-2732-1	6	Mackerel meal	0,9	2,7	0,0	0,2	0,4	0,6	0,6	0,0
EU maximum limits			10	20		10	100	20		

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 8: Pesticides in fish oil for feed

Sample code	Fish oil no.	Sample name	β-HCH µg/kg	α-HCH µg/kg	γ-HCH µg/kg	δ-HCH µg/kg	Σ DDT µg/kg	Pentachlor benzene µg/kg	HCB µg/kg	Σ Heptachlores µg/kg
R11-1335-2	1	Capelin oil	1,1	3,9	3,0	< 0,10	33	2,5	21	4,4
R11-1335-4	2	Capelin oil	1,2	3,4	2,9	< 0,10	37	2,8	25	4,5
R11-1335-6	3	Capelin oil	1,1	2,5	4,1	< 0,10	43	2,9	28	5,6
R11-1335-8	4	Capelin oil	1,0	1,8	7,2	< 0,10	88	2,9	42	6,6
R11-593-2	5	Capelin oil	0,87	1,8	6,2	< 0,10	80	3,0	41	6,5
		EU maximum limits	100	200	2000		500		200	

Table 8 (cont): Pesticides in fish oil for feed

Sample code	Fish oil no.	Sample name	Aldrin/ dieldrin µg/kg	Toxaphene µg/kg	Octachloro styrene µg/kg	Endrin µg/kg	Endo-sulfane µg/kg	Chlordane µg/kg	*trans*-Nonachlor µg/kg	Mirex µg/kg
R11-1335-2	1	Capelin oil	26	45	0,26	4,2	3,4	15	8,4	0,28
R11-1335-4	2	Capelin oil	27	48	0,37	4,1	7,4	16	9,8	0,33
R11-1335-6	3	Capelin oil	35	52	0,39	5,0	3,3	20	12	0,36
R11-1335-8	4	Capelin oil	49	117	0,74	6,4	4,0	36	22	0,78
R11-593-2	5	Capelin oil	40	96	0,62	5,2	4,3	32	19	0,65
		EU maximum limits	100	200		50	100	50		

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

Table 9: Trace elements in fish muscle on wet weight

Sample code	Fish sample no.	Sample name	Latin name	Fe mg/kg	Cu mg/kg	Zn mg/kg	As mg/kg	Se mg/kg	Cd mg/kg	Hg mg/kg	Pb mg/kg
R11-994-3	1	Catfish	*Anarhichas lupus*	1,5	0,1	6,3	9,1	0,6	<0,006	0,07	<0,007
R11-710-1	2	Cod	*Gadus morhua*	1,6	0,2	3,6	2,4	0,3	<0,006	0,04	<0,008
R11-782-1	3	Cod	*Gadus morhua*	1,3	0,2	2,5	1,8	0,3	<0,006	<0,006	<0,008
R11-994-4	4	Greenland halibut	*Reinhardtius hippoglossoides*	1,0	0,1	4,0	3,7	0,3	<0,03	0,07	0,14
R11-994-1	5	Haddock	*Melanogrammus aeglefinus*	1,0	0,1	2,6	9,7	0,4	<0,006	0,03	0,09
R11-994-2	6	Haddock	*Melanogrammus aeglefinus*	1,2	0,1	2,7	11,2	0,5	<0,006	0,03	<0,008
R11-666-1	7	Lumpfish	*Cyclopterus lumpus*	2,9	0,2	2,7	1,0	0,1	<0,03	<0,08	<0,04
R11-932-1	8	Lumpfish	*Cyclopterus lumpus*	2,4	0,2	3,0	0,9	0,1	<0,03	<0,06	<0,04
R11-1276-1	9	Lumpfish	*Cyclopterus lumpus*	2,3	0,2	3,3	1,1	0,1	<0,03	<0,06	<0,04
R11-2567-1	10	Mackerel	*Scomber scombrus*	7,9	0,8	7,2	2,0	0,4	<0,03	<0,06	<0,04
R11-2567-2	11	Mackerel	*Scomber scombrus*	8,7	0,7	8,4	1,7	0,4	<0,03	0,07	<0,04
R11-2567-3	12	Mackerel	*Scomber scombrus*	9,0	0,7	8,1	2,6	0,5	<0,03	0,06	<0,04
R11-2567-4	13	Mackerel	*Scomber scombrus*	9,7	0,90	9,4	2,6	0,4	<0,03	0,07	<0,04
R11-747-1	14	Saithe	*Pollachius virens*	2,7	0,35	3,0	1,6	0,2	<0,006	0,04	<0,008
		EU maximum limits, flesh							0,05	0,5	0,3

Table 10: Trace elements in different fish organs on wet weight

Sample code	Fish sample no.	Sample name	Latin name	Fe mg/kg	Cu mg/kg	Zn mg/kg	As mg/kg	Se mg/kg	Cd mg/kg	Hg mg/kg	Pb mg/kg
R11-710-2	1	Cod (roes)	*Gadus morhua*	8,5	0,7	37,3	0,7	1,2	<0,009	<0,02	<0,01
R11-710-3	2	Cod (liver)	*Gadus morhua*	11,0	3,0	9,7	4,3	4,3	0,23	0,04	<0,04
R11-710-4	3	Cod (sperm)	*Gadus morhua*	4,2	0,3	6,7	2,3	0,4	0,01	0,01	<0,006
R11-782-3	4	Cod (roes)	*Gadus morhua*	5,0	0,4	19,3	0,3	0,6	<0,009	<0,02	<0,01
R11-782-2	5	Cod (liver)	*Gadus morhua*	6,5	2,2	6,9	4,0	0,5	0,19	0,09	<0,04
R11-782-4	6	Cod (sperm)	*Gadus morhua*	3,8	0,3	7,9	3,1	0,4	<0,005	0,01	<0,006
R11-666-2	7	Lumpfish (roes)	*Cyclopterus lumpus*	4,4	0,5	14,9	0,7	0,9	<0,007	<0,02	<0,009
R11-932-2	8	Lumpfish (roes)	*Cyclopterus lumpus*	3,1	0,3	13,1	0,5	0,6	<0,006	<0,01	0,01
R11-1276-2	9	Lumpfish (roes)	*Cyclopterus lumpus*	2,7	0,4	15,1	0,5	0,5	<0,006	<0,01	<0,007

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Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Table 11: Trace elements in fish meal for feed on wet weight.

Sample code	**Meal sample no.**	**Sample name**	**Fe mg/kg**	**Cu mg/kg**	**Zn mg/kg**	**As mg/kg**	**Se mg/kg**	**Cd mg/kg**	**Hg mg/kg**	**Pb mg/kg**
R11-1335-1	1	Capelin meal	72	2,0	68	3,9	1,3	0,15	0,085	0,046
R11-1335-3	2	Capelin meal	71	2,2	59	3,4	1,2	0,14	0,091	0,0075
R11-1335-5	3	Capelin meal	91	1,7	65	3,5	1,2	0,15	0,095	0,0091
R11-1335-7	4	Capelin meal	56	1,6	69	3,7	1,0	0,13	0,11	0,059
R11-593-1	5	Capelin meal	21	0,57	12	0,0014	0,23	0,0014	<0,08	0,0014
R11-2732-1	6	Mackerel meal	187	3,5	66	4,0	5,0	0,62	0,17	0,039
		EU maximum limits				25		2	0,5	10

Table 12: Trace elements in fish oil for feed

Sample code	Fish oil sample no.	Sample name	Fe mg/kg	Cu mg/kg	Zn mg/kg	As mg/kg	Se mg/kg	Cd mg/kg	Hg mg/kg	Pb mg/kg
R11-1335-2	1	Capelin oil	0,55	0,0028	0,0069	10	0,055	0,003	<0,08	0,025
R11-1335-4	2	Capelin oil	0,56	0,057	<0,002	9,9	0,092	0,021	<0,08	0,0021
R11-1335-6	3	Capelin oil	1,2	0,059	0,18	11	0,10	0,019	<0,08	0,016
R11-1335-8	4	Capelin oil	1,3	0,0026	0,0025	14	0,098	0,024	<0,08	0,0078
R11-593-2	5	Capelin oil	1,9	0,11	0,20	19	0,098	0,0029	0,098	0,0029
		EU maximum limits				25		2	0,5	10

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

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Table 13: Perfluorminated compounds in fish muscle on wet weight

Sample code	Fish sample no.	Sample name	PFBS µg/kg	PFDA µg/kg	PFDS µg/kg	PFDoA µg/kg	PFHpA µg/kg	PFHxA µg/kg	PFHxS µg/kg	PFNA µg/kg	PFOA µg/kg	PFOSA µg/kg	PFOS µg/kg
R11-994-3	1	Catfish	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-710-1	2	Cod	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-782-1	3	Cod	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-994-4	4	Greenland halibut	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	0,26
R11-994-1	5	Haddock	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-994-2	6	Haddock	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-666-1	7	Lumpfish	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-932-1	8	Lumpfish	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-1276-1	9	Lumpfish	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-2567-1	10	Mackerel	< 0,1	< 0,2	< 0,1	< 0,2	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1
R11-2567-2	11	Mackerel	< 0,1	< 0,2	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1
R11-2567-3	12	Mackerel	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1
R11-2567-4	13	Mackerel	< 0,1	< 0,3	< 0,1	< 0,3	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1	< 0,1
R11-747-1	14	Saithe	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15

Table 14: Perfluorminated compounds in different fish organs on wet weight

Sample code	Fish sample no.	Sample name	PFBS µg/kg	PFDA µg/kg	PFDS µg/kg	PFDoA µg/kg	PFHpA µg/kg	PFHxA µg/kg	PFHxS µg/kg	PFNA µg/kg	PFOA µg/kg	PFOSA µg/kg	PFOS µg/kg
R11-710-2	1	Cod (roes)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,20	< 0,10	< 0,15	2,7
R11-710-3	2	Cod (liver)	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	< 0,30	0,62
R11-710-4	3	Cod (sperm)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	0,27
R11-782-3	4	Cod (roes)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	2,83
R11-782-2	5	Cod (liver)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,20	< 0,10	< 0,15	0,35
R11-782-4	6	Cod (sperm)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	0,43
R11-666-2	7	Lumpfish (roes)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-932-2	8	Lumpfish (roes)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15
R11-1276-2	9	Lumpfish (roes)	< 0,15	< 0,20	< 0,15	< 0,20	< 0,10	< 0,10	< 0,15	< 0,10	< 0,10	< 0,15	< 0,15

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

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Table 15: Perfluorinated compounds in fish meal for feed

Sample code	Meal sample no.	Sample name	PFBS µg/kg	PFDA µg/kg	PFDS µg/kg	PFDoA µg/kg	PFHpA µg/kg	PFHxA µg/kg	PFHxS µg/kg	PFNA µg/kg	PFOA µg/kg	PFOSA µg/kg	PFOS µg/kg
R11-1335-1	1	Capelin meal	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	6,5
R11-1335-3	2	Capelin meal	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	7,5
R11-1335-5	3	Capelin meal	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	2,3
R11-1335-7	4	Capelin meal	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	13
R11-593-1	5	Capelin meal	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	6,9
R11-2732-1	6	Mackerel meal	< 0,2	< 0,2	< 0,2	< 0,2	< 0,2	< 0,2	< 0,2	< 0,2	< 0,2	< 0,3	1,3

Table 16: Perfluorinated compounds in fish oil for feed

Sample code	Fish oil no.	Sample name	PFBS µg/kg	PFDA µg/kg	PFDS µg/kg	PFDoA µg/kg	PFHpA µg/kg	PFHxA µg/kg	PFHxS µg/kg	PFNA µg/kg	PFOA µg/kg	PFOSA µg/kg	PFOS µg/kg
R11-1335-2	1	Capelin oil	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50
R11-1335-4	2	Capelin oil	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50
R11-1335-6	3	Capelin oil	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50
R11-1335-8	4	Capelin oil	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50
R11-593-2	5	Capelin oil	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50	< 0,50

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

(b)(4) Manufacturing Information

(b)(4) Manufacturing Information

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(b)(4) M f t i	KERECIS MARIGEN WOUND	Page 1 of 12

(b)(4) Manufacturing Information

[redacted]

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(b)(4) Manufacturing Information

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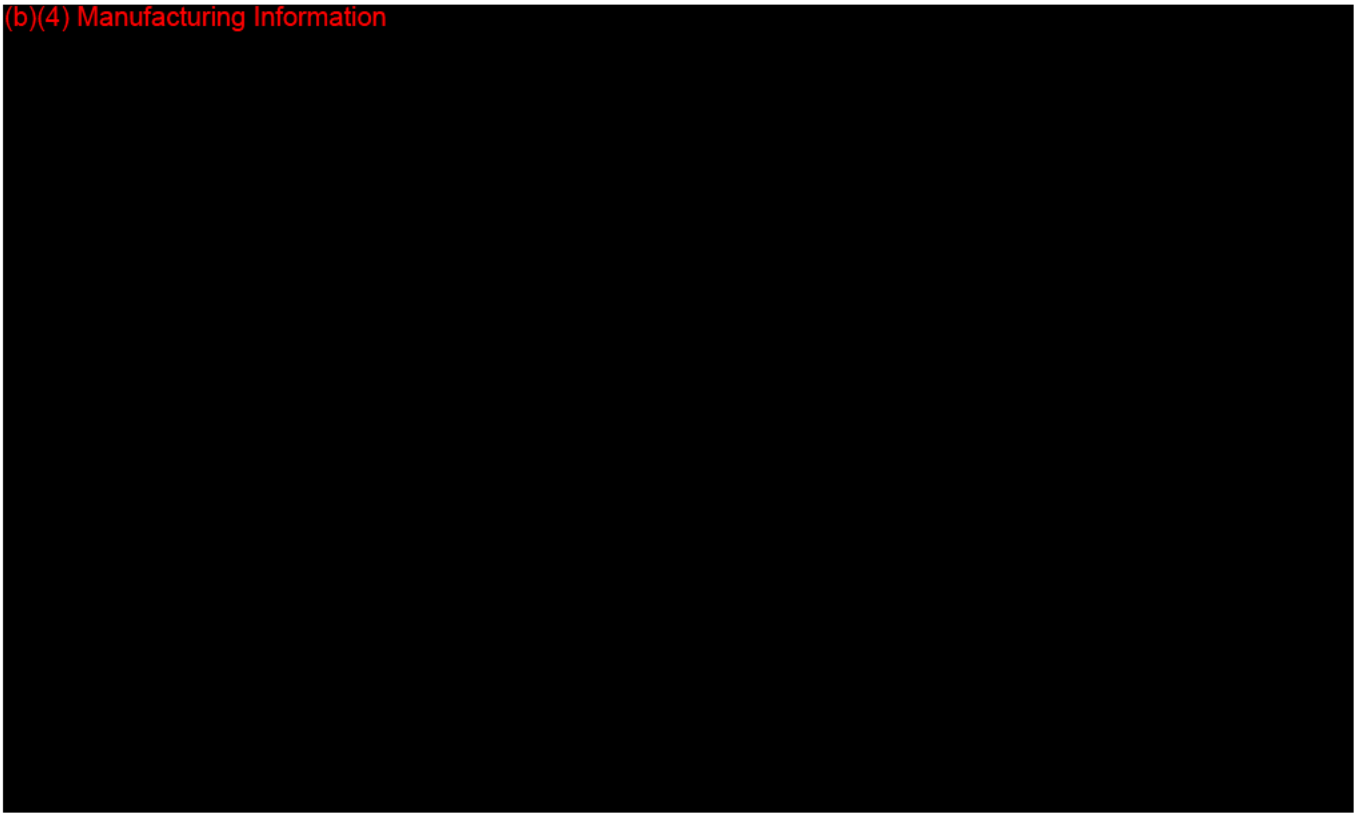
Part 2, translated:

2. Quality and product description

(b)(4) Manufacturing Information



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

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Appendix 11-19

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

(b)(4) Third Party Information

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Appendix 11-20

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(b)(4) Third Party Information

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KERECIS

Appendix 11-21

(b)(4)

Study

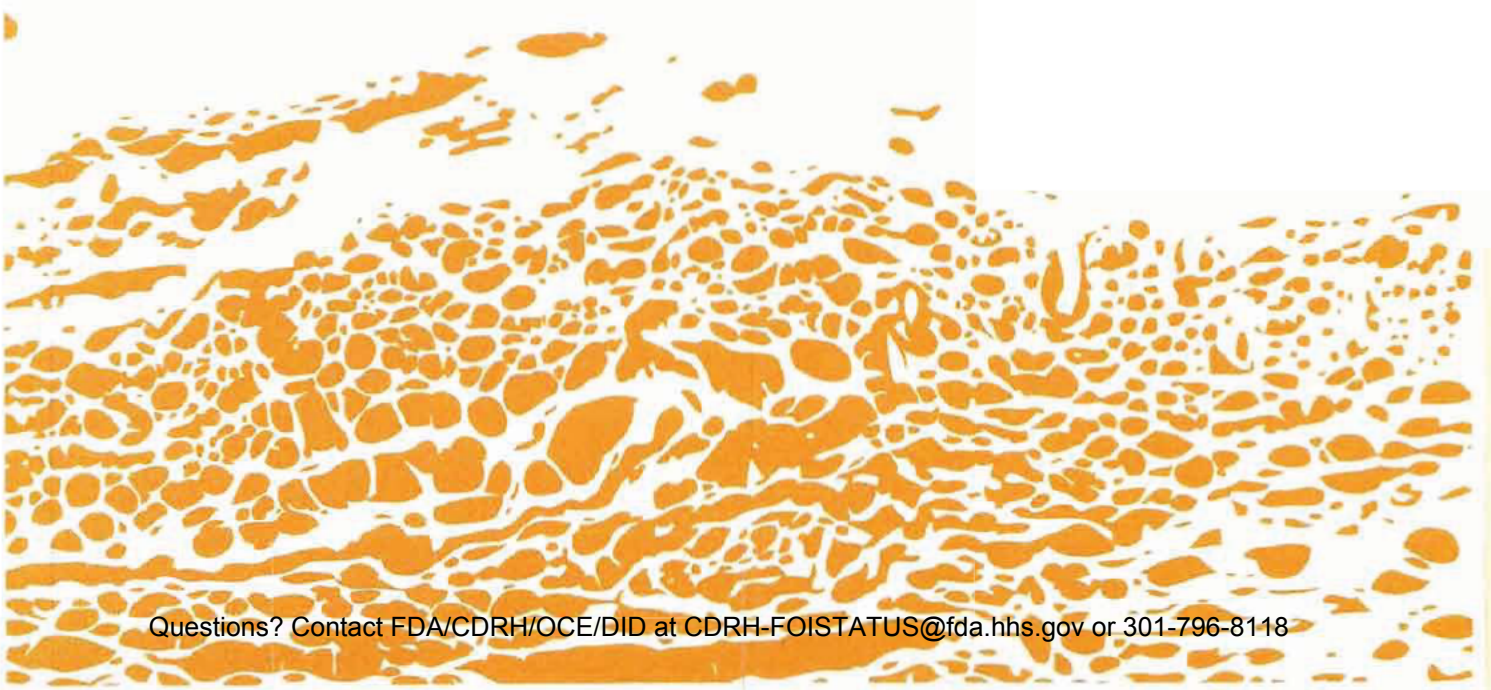
(b)(4)

MariGen Wound

R&D Manager
(b)(6)

(b)(6)

Date: 16. January 2012



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

(b)(4) Testing

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Section 12: Substantial Equivalence

12 SUBSTANTIAL EQUIVALENCE DISCUSSION

12.1 Substantial equivalence

The MariGen Wound Dressing is substantially equivalent in design function and intended use to the following predicate devices listed in the table below:

Name	510k number	Appendix
Mesynthes Endoform™ Dermal Template	K092096	12-1
ACell MatriStem™	K092976	12-2
Integra™ Wound Matrix (Integra Life Sciences)	K021792	12-3
LifeCell Corporation's LTM Wound Dressing	K082103	12-4
TEl Biosciences Inc. PriMatrix	K083440	12-5
Hemcon Chitoflex Surgical Dressing	K071519	12-6
Cook Biotech, Oasis	K061711	12-7

12.2 Intended Use/ Indications for Use

MariGen Wound is indicated for the management of wounds including:

- Partial and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second-degree burns, skin tears)
- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence)
- Draining wounds

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

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12.3 List of proposed predicates

	Kerecis	Mesynthes	Cook Biotech (New)	ACell, Inc
510K		K092096	K061711	K092926
Device name	MariGen Dressing	Endoform™ Dermal Template	Oasis Wound Matrix	MatriStem® Wound Sheet
Product Codes	KGN	KGN	KGN	KGN
Intend. use	Wound dressing	Wound dressing	Wound dressing	Wound dressing
Indications	(b)(4) Draft - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds	Partial and full-thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - tunneled/undermined wounds - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds	Partial and full thickness wounds: - Pressure ulcers; - Venous ulcers; - Diabetic ulcers; - Chronic vascular ulcers; -Tunneled/ undermined wounds; - Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence); - Trauma wounds (abrasions, lacerations, second-degree burns and skin tears); - Draining wounds	Partial and full-thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - tunneled/undermined wounds - surgical wounds - trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) - draining wounds
Animal origin	(b)(4)			
Tissue type				
Nominal sizes	3 x 3.5 cm (10.5 cm^2) 3 x 7 cm (21 cm^2) 7 x 20 cm (140 cm^2)	Sizes ranging from 9 cm^2 to 400 cm^2, fenestrated, meshed	3 x 3.5cm 7x20cm	3 x 3.5 cm (10.5 cm^2) 3 x 7 cm (21 cm^2)
Presentation	(b)(4)			
Components				

Table 12-1 Comparison to predicates

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

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	Integra Life Sciences	LifeCell Corporation's	HemCon, Inc (New)	TEI Biosciences Inc.
510K	K021792	K082103	K071519	K083440
Device name	Integra™ Wound Matrix	LTM Wound Dressing	Hemcon Chitoflex-Surgical Dressing	PriMatrix
Product Codes	FRO	KGN	FRO	KGN
Intend. use	Wound dressing	Wound dressing	Wound dressing	Wound dressing
Indications	Partial and full thickness wounds: - pressure ulcers - venous ulcers - diabetic ulcers - chronic vascular ulcers - surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence) - trauma wounds (abrasions, lacerations, second-degree bums, and skin tears) - draining wounds.	Partial and full thickness wounds: - Pressure ulcers; - Venous ulcers; - Diabetic ulcers; - Chronic vascular ulcers; - Tunneled/ undermined wounds; - Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence); - Trauma wounds (abrasions, lacerations, second-degree burns and skin tears); - Draining wounds - And other bleeding surface wounds. -supports wound healing and control of minor bleeding.	Intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations and abrasions. May also be used for temporary treatment of severely bleeding wounds such as surgical wounds (operative, postoperative, dermatological, etc.) and traumatic injuries.	Partial and full thickness wounds: · Pressure, diabetic, and venous ulcers · Second-degree burns * Surgical wounds-donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence * Trauma wounds-abrasions, lacerations, and skin tears · Tunneled/undermined wounds * Draining wounds
Animal origin	(b)(4)			
Tissue type				
Nominal sizes	5 x 5cm 10 x 12.5cm 10 x 25cm 20 x 25cm	8cm x 16cm 5cm x 16cm 20cm x 25cm 10cm x 16cm	1 x 3 in 3x 9 in 3x 28 in	4 x 4 cm 6 x 6cm 8 x 12 10 x 12 20 x 25cm
Presentation	(b)(4)			
Components				

Table 12-2 Comparison to predicates (continued)

12.4 Design

The design of the proposed predicate devices is very similar. Six of the predicates are made from mammalian decellularized collagen and one of the predicates is made from crustacean derived chitosan. All the predicates are intended to function as scaffolds for various wound types.

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The major difference between the proposed MariGen Wound Dressing and the mammalian sourced predicate devices is the source of the collagen. The collagen used in the proposed MariGen is sourced (b)(4) [redacted]

12.5 Operational Characteristics

The operational characteristics of the proposed MariGen are identical to the predicate devices in that they are intended to be placed in a wound environment for the management of partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, surgical wounds (donor sites/grafts, post-Moh's surgery post-laser surgery, podiatric, wound dehiscence) and trauma wounds (abrasions, lacerations, second-degree burns, and skin tears).

12.6 Technological Characteristics

In evaluating the impact of different technological characteristics, FDA historically has implemented the statutory definition of substantial equivalence with the following analysis:

- Could the new characteristics affect safety or effectiveness?
- Do the new characteristics raise new questions of safety or effectiveness?
- Are there accepted scientific methods for evaluation of whether safety or effectiveness has been adversely affected as a result of the use of new technological characteristics?
- Is there information to demonstrate that the new technological features have not diminished safety and effectiveness?

The proposed and predicate devices have technological differences. Although they are all (b)(4) [redacted]

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

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(b)(4)

[redacted]

12.7 Substantial Equivalence pathway

FDA's guideline document on the pathway to substantial equivalence is used in Figure 12-1 to demonstrate substantial equivalence.

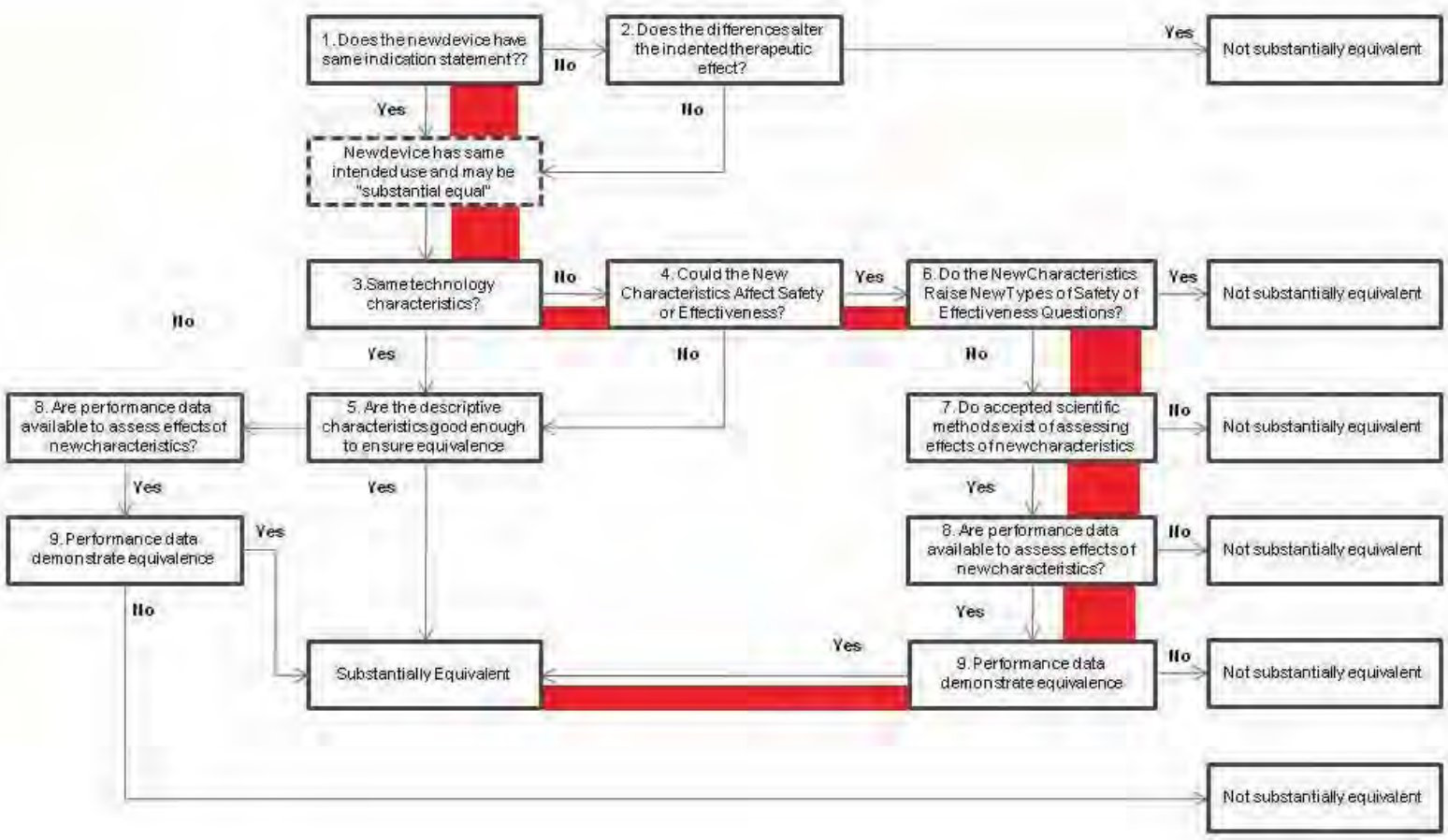

Figure 12-1 Substantial equivalence pathway

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

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Test	Notes
1. Does the new device have same indication statement?	(b)(4) [redacted]
3. Same technology characteristics?	
4. Could the New Characteristics Affect Safety or Effectiveness?	
6. Do the New Characteristics Raise New Types of Safety or Effectiveness Questions?	
7. Do accepted scientific methods exist that are able of assessing the effects of the new characteristics?	
8. Are performance data available to assess effects of new characteristics?	
9. Performance data demonstrate equivalence	

Figure 12-2 Rationale for the substantial equivalence pathway choose in figure 12-1

12.8 Conclusions

The MariGen Wound Dressing has the same intended use and indications for use as many 510k cleared wound dressings. (b)(4) [redacted]

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

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12.9 Selected comparative tests

(b)(4)

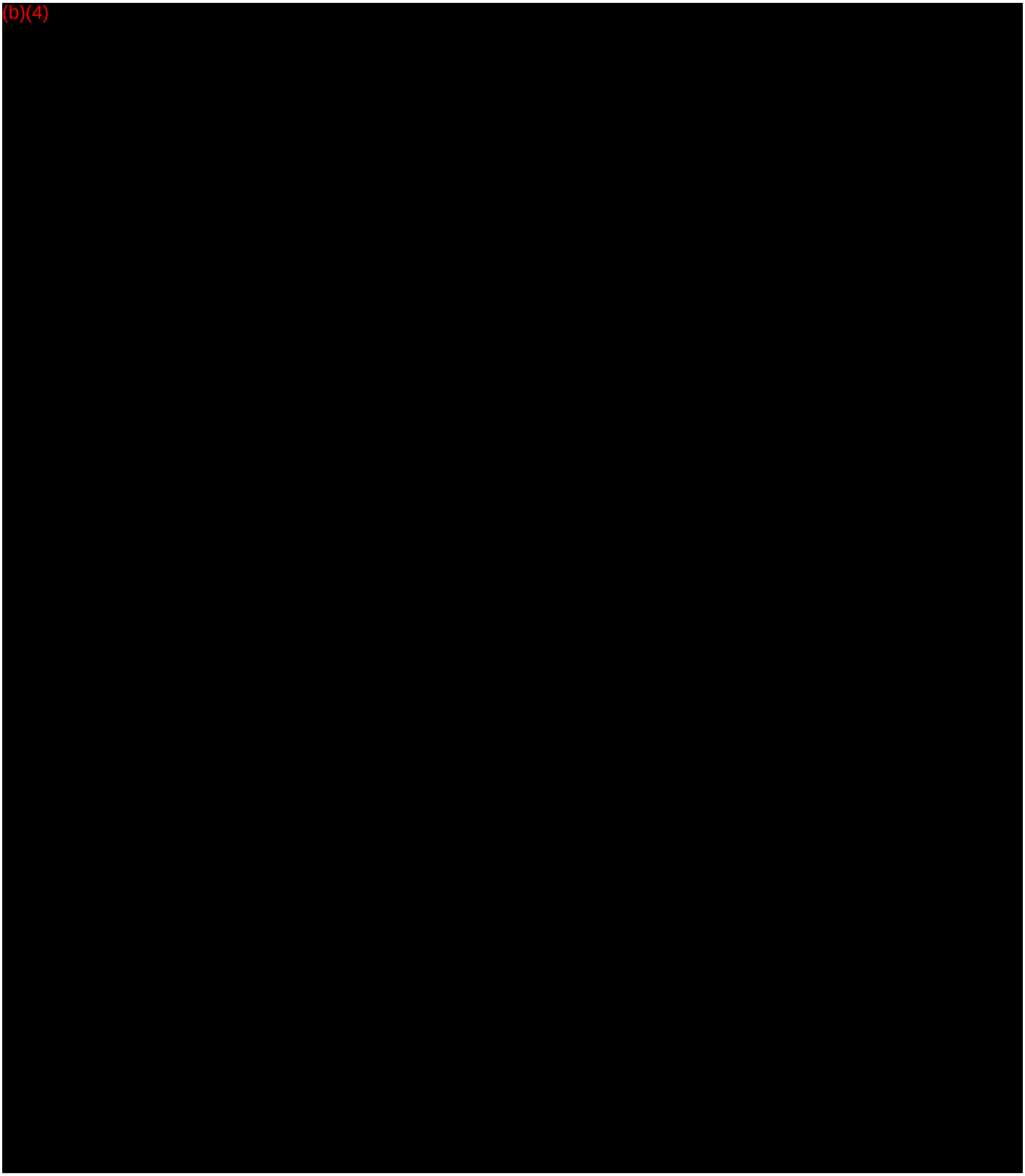

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Table 12-3 Design Release Criteria for MariGen Wound, compared with two of the predicates

The release criteria protocol and report for MariGen Wound is presented in APPENDIX 11-21.

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

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Appendix 12-1

510(k) Summary
for the
Mesynthes Limited, Endoform™ Dermal Template

1. SUBMITTER/510(K) HOLDER

Mesynthes Ltd
69 Gracefield Road
Lower Hutt
Wellington
New Zealand 5010

JAN 21 2010

Contact Person Brian Ward
Telephone: (+64 4) 931-3275

Date Prepared: July 10, 2009

2. DEVICE NAME

Proprietary Name: Endoform™ Dermal Template
Common/Usual Name: Endoform™
Classification Name: Collagen Wound Dressing

3. PREDICATE DEVICES

- OaSIS® Wound Matrix (Cook Biotech) (K061711, K973170, K993948)
- UBM Lyophilized Wound Dressing (MatriStem™) (ACell) (K021637)
- Unite Biomatrix™ (Pegasus Biologics) (K071425)
- Promogran® Matrix Wound Dressing (Johnson and Johnson) (K014129)
- Integra™ Wound Matrix (Integra Life Sciences) (K021792)

4. DEVICE DESCRIPTION

Endoform™ Dermal Template is a wound dressing primarily composed of ovine collagen and is supplied as a sterile intact, perforated or meshed sheet ranging in size from $9cm^2$ to $400cm^2$.

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5. INTENDED USE

Endoform™ is supplied sterile and is intended for single use in the treatment of the following wounds:

- partial and full-thickness wounds
- pressure ulcers
- venous ulcers
- diabetic ulcers
- chronic vascular ulcers
- tunneled/undermined wounds
- surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence)
- trauma wounds (abrasions, lacerations, second-degree burns, and skin tears)
- draining wounds

6. TECHNOLOGICAL CHARACTERISTICS AND SUBSTANTIAL EQUIVALENCE

The Endoform™ Dermal Template is substantially equivalent to the predicate devices with respect to material composition, device characteristics and intended use.

7. PERFORMANCE TESTING

The Endoform™ Dermal Template has been subjected to extensive non-clinical testing to assess the biocompatibility and the performance of the device. Endoform™ Dermal Template was shown to be safe and effective as a wound dressing.

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room W-O66-0609
Silver Spring, MD 20993-0002

JAN 21 2010

Mesynthes Limited
% Medical Device Consultants, Inc.
Ms. Mary McNamara-Cullinane, RAC
Senior Regulatory Consultant
49 Plain Street
North Attleboro, Massachusetts 02760

Re: K092096
Trade/Device Name: Endoform™ Dermal Template
Regulatory Class: Unclassified
Product Code: KGN
Dated: December 21, 2009
Received: December 22, 2009

Dear Ms. McNamara-Cullinane:

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

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

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

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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" (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/cdrh/mdr/ 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/cdrh/industry/support/index.html.

Sincerely yours,

Mark N. Melkerson
Director
Division of Surgical, Orthopedic
and Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Indications for Use

510(k) Number (if known):

Device Name: Endoform™ Dermal Template

Indications for Use:

The Endoform™ Dermal Template is supplied sterile and is intended for single use in the treatment of the following wounds:

- partial and full-thickness wounds
- pressure ulcers
- venous ulcers
- diabetic ulcers
- chronic vascular ulcers
- tunneled/undermined wounds
- surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence)
- trauma wounds (abrasions, lacerations, second-degree burns, and skin tears)
- draining wounds

Prescription Use X AND/OR Over-The-Counter Use___
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

David Krause for MXM

(Division Sign-Off)
Division of Surgical, Orthopedic,
and Restorative Devices

510(k) Number K092096

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

K092926
Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

ACell, Inc.
8671 Robert Fulton Drive, Ste. B
Columbia, MD 21046
Toll Free: 800-826-2926
Phone: 410-715-1700
Fax: 410-715-4511
Website: www.acell.com

510(k) Summary

OCT 2 8 2009

Submitted by: ACell, Inc.
8671 Robert Fulton Drive, Suite B
Columbia, MD 21046

Contact Person: Rodney W. Bosley, Sr. Vice President
Phone: (410) 715-1700
Fax: (410) 715-4511

Date Prepared: September 21, 2009

Device Trade Name: ACell® MatriStem® Wound Sheet
Common/Usual Name: Wound Dressing
Proposed Classification: Dressing, Wound, Collagen
Unclassified, 79 KGN – General & Plastic Surgery

Device Description:

ACell® MatriStem® Wound Sheets are sterile, porcine-derived, lyophilized single or multi-layer extracellular matrix sheets available in various sizes with or without fenestrations or meshed.

Indications For Use:

ACell® MatriStem® Wound Sheet is intended for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, skin tears) and draining wounds. The device is intended for one-time use.

Predicate Device:

510(k) #	Device	Manufacturer
K021637	ACell® UBM Lyophilized Wound Dressing	ACell, Inc.

Substantial Equivalence:

ACell® MatriStem® Wound Sheets are identical to the predicate device with respect to fundamental scientific technology, materials, processing and intended use. The addition of multiple layers and fenestrations/meshes do not raise new issues of safety and effectiveness. MatriStem® Wound Sheets are substantially equivalent to the legally marketed predicate device.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

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

ACell, Inc.
% Mr. Rodney W. Bosley
Sr. Vice President
8671 Robert Fulton Drive, Suite B
Columiba, Maryland 21046

OCT 2 6 2009

Re: K092926
Trade/Device Name: ACell® MatriStem® Wound Sheet
Regulatory Class: Unclassified
Product Code: KGN
Dated: September 21, 2009
Received: September 23, 2009

Dear Mr. Bosley:

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

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); 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.

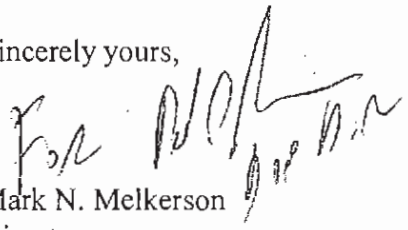
Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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" (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/cdrh/mdr/ 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/cdrh/industry/support/index.html.

Sincerely yours,



Mark N. Melkerson
Director
Division of Surgical, Orthopedic
and Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Indications For Use

510(k) Number (if known): K092926

Device Name: ACell® MatriStem® Wound Sheet

Indications for Use:

ACell® MatriStem® Wound Sheet is intended for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns and skin tears) and draining wounds. The device is intended for one-time use.

Prescription Use ✓ AND/OR Over-The-Counter-Use _____
(Part 21 CFR 801 Subpart D) (Part 21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Daniel Krause for MXH
(Division Sign-Off)
Division of Surgical, Orthopedic,
and Restorative Devices

510(k) Number K092926

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 12-3

K021792

Bilayer Matrix Wound Dressing
510(K) SUMMARY

AUG 1 4 2002

Submitter's name and address:

Integra LifeSciences Corporation
311 Enterprise Drive
Plainsboro, NJ 08536 USA

Contact person and telephone number:

Diana M. Bordon
Manager, Regulatory Affairs,
(609) 275-0500

Date: May 23, 2002

Name of the device:

Proprietary Name:	Bilayer Matrix Wound Dressing
Common Name:	Wound Dressing
Classification Name:	Dressing, Product Code 79FRO

Substantial Equivalence:

Bilayer Matrix Wound Dressing is substantially equivalent in function and intended use to the following products which have been cleared to market under Premarket Notifications 510(k): Oasis™ SIS Wound Dressing II (K993948), Fortaderm™ Wound Dressing (K014129), VitaChoice™ Wound Dressing (K896455) and Biobrane® II Temporary Wound Dressing (K896110).

Intended Use:

Bilayer Matrix Wound Dressing is indicated for the management of wounds including: partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) and draining wounds. The device is intended for one-time use.

Device Description:

Bilayer Matrix Wound Dressing is an advanced woundcare device comprised of a porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan and a semi-permeable polysiloxane (silicone) layer. The semi-permeable silicone membrane controls water vapor loss, provides a flexible adherent covering for the wound surface and adds increased tear strength to the device. The collagen-glycosaminoglycan biodegradable matrix provides a scaffold for cellular invasion and capillary growth.

Tests and Test Results

Biocompatibility studies have demonstrated Bilayer Matrix Wound Dressing to be non-cytotoxic, non-pyrogenic, non-irritating, non-sensitizing, non-hemolytic and non-toxic.

Conclusion

Valid scientific evidence through biocompatibility and physical property testing provide reasonable assurance that Bilayer Matrix Wound Dressing is safe and effective under the proposed conditions of use, and is, with respect to intended use and technological characteristics, substantially equivalent to the predicate devices.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG 1 4 2002

Integra LifeSciences Corporation
Diana M. Bordon
Manager, Regulatory Affairs
311 Enterprise Drive
Plainsboro, New Jersey 08536

Re: K021792
Trade/Device Name: Bilayer Matrix Wound Dressing
Regulation Name: Wound Dressing
Regulatory Class: Unclassified
Product Code: FRO
Dated: May 30, 2002
Received: May 31, 2002

Dear Ms. Bordon:

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

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

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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

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

Sincerely yours,

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

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

INDICATIONS FOR USE

510(k) Number: K021792

Device Name: Bilayer Matrix Wound Dressing

Indications for Use:

Bilayer Matrix Wound Dressing is indicated for the management of wounds including: partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) and draining wounds. The device is intended for one-time use.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

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

510(k) Number K021792

Prescription Use X
(Per 21 CFR 801.109)

OR

Over-the-Counter Use ____
(Optional Format 1-2-96)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Appendix 12-4

OCT 0 8 2008

III. 510(K) SUMMARY

LifeCell Corporation's LTM Wound Dressing

Submitter's Name, Address, Telephone Number, Contact Person and Date Prepared:

LifeCell Corporation
One Millennium Way
Branchburg, NJ 08876

Phone: (908) 947-1131
Facsimile: (908) 947-1095

Contact Person: Manal Morcos

Date Prepared: July 24, 2008

Names of Device and Name/Address of Sponsor:

LTM Wound Dressing
LifeCell Corporation
One Millennium Way
Branchburg, NJ 08876

Common or Usual Name

Collagen Wound Dressing

Classification Name

Dressing, Wound, Collagen

Classification:

Unclassified

Product Code:

KGN

Predicate Devices:

Pegasus Biologics, Inc. – Unite Biomatrix (K071425)
LifeCell Corporation – LTM Surgical Mesh (K070560)

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Intended Use / Indications for Use

The LTM Wound Dressing is intended for the management of wounds including:

- Partial and full thickness wounds;
- Pressure ulcers;
- Venous ulcers;
- Diabetic ulcers;
- Chronic vascular ulcers;
- Tunneled/undermined wounds;
- Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence);
- Trauma wounds (abrasions, lacerations, second-degree burns and skin tears);
- Draining wounds
- And other bleeding surface wounds.

The LTM Wound Dressing provides an environment that supports wound healing and control of minor bleeding.

The device is intended for single patient, one time use only.

Technological Characteristics

The LTM Wound Dressing device is identical in materials and construction to the Company's recently cleared LTM Surgical Mesh (K070560). Like the LTM Surgical Mesh, LTM Wound Dressing consists of a terminally sterilized sheet of the processed porcine dermal matrix provided in prescribed geometric configurations and thickness, and packaged in a double pouch configuration.

Performance Data

LifeCell's LTM Wound Dressing is technologically identical to the cleared LTM Surgical Mesh (K070560). The LTM Surgical Mesh has undergone extensive biocompatibility testing, animal testing, viral inactivation testing, and biomechanical testing. The data indicates that the device is biocompatible and that the manufacturing process is capable of inactivating any viral components that may come with the starting material. In all instances, the LTM Surgical Mesh functioned as intended and the performance observed was as expected. As LTM Wound Dressing is the exact same device technologically as the LTM Surgical Mesh, the Company submits that testing conducted on the LTM Surgical Mesh is equally applicable to the LTM Wound Dressing.

Substantial Equivalence

The LifeCell LTM Wound Dressing is as safe and as effective as the legally marketed predicate devices, Pegasus Biologics, Inc.'s Unite Biomatrix (K071425), and LifeCell Corporation's LTM Surgical Mesh (K070560). The LifeCell LTM Wound Dressing has the same intended uses and the same or similar indications, technological characteristics, and principles of operation as its predicate devices. Performance data demonstrates that LifeCell's LTM Wound

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

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Dressing is as safe and effective as the predicate device. Thus, LifeCell's LTM Wound Dressing is substantially equivalent to the predicate devices.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

OCT 0 8 2008

LifeCell Corporation
% Manal Morcos
Manager, Regulatory Affairs
One Millenium Way
Branchburg, New Jersey 08876

Re: K082103
Trade/Device Name: LTM Wound Dressing
Regulatory Class: Unclassified
Product Code: KGN
Dated: July 24, 2008
Received: July 25, 2008

Dear Manal Morcos:

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

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

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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. 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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

K082103 1/1

II. INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K082103

Device Name: LTM Wound Dressing

Indications for Use:

The LTM Wound Dressing is intended for the management of wounds including:

- Partial and full thickness wounds;
- Pressure ulcers;
- Venous ulcers;
- Diabetic ulcers;
- Chronic vascular ulcers;
- Tunneled/undermined wounds;
- Surgical wounds (donor sites/grafts, post-Moh's surgery, post laser surgery, podiatric, wound dehiscence);
- Trauma wounds (abrasions, lacerations, second-degree burns and skin tears);
- Draining wounds
- And other bleeding surface wounds.

The LTM Wound Dressing provides an environment that supports wound healing and control of minor bleeding.

The device is intended for single patient, one time use only.

Prescription Use __X__ AND/OR Over-The-Counter Use____
(Part 21 C.F.R. 801 Subpart D) (21 C.F.R. 807 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Mark A. Melkerson

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

510(k) Number K082103

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

Appendix 12-5
Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

K083440
1/2

510(k) Summary

This 510(k) summary for PriMatrix is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitted by
TEI Biosciences Inc.
7 Elkins Street
Boston, MA 02127
(617) 268-1616
(617) 268-3282 (fax)

DEC 12 2008

Contact Person
Kenneth James, Ph.D.
Vice President, Product Sciences and Regulatory Affairs

Date Prepared
November 14, 2008

Device Information

Proprietary name:	PriMatrix
Common name:	Animal-derived, extracellular matrix wound care product
Classification:	Unclassified

Device Description
PriMatrix is an acellular dermal tissue matrix. The device is supplied sterile and is provided in sheet form in a variety of sizes to be trimmed by the surgeon to meet the individual patient's needs.

Intended Use
PriMatrix is intended for the management of wounds that include:

- Partial and full thickness wounds
- Pressure, diabetic, and venous ulcers
- Second-degree burns
- Surgical wounds—donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence
- Trauma wounds—abrasions, lacerations, and skin tears
- Tunneled/undermined wounds
- Draining wounds

Legally Marketed Devices to which Equivalence is Being Claimed
PriMatrix is substantially equivalent in function and intended use to:

Predicate Devices	Manufacturer	510(k) Number
PriMatrix	TEI Biosciences	K061407
Oasis	Cook Biotech	K061711

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

K083440
2/2

Summary of Technological Characteristics and Biocompatibility

PriMatrix is substantially equivalent to other wound care products with respect to its design and application.

A rigorous biocompatibility assessment performed by an independent certified laboratory demonstrated the biocompatibility of PriMatrix. The tests performed included: cytotoxicity, sensitization, intracutaneous reactivity, acute systemic toxicity, genotoxicity, hemolysis, and pyrogenicity. The manufacturing methods for PriMatrix were also tested by an independent laboratory to assure safe levels of viral inactivation.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

TEI Biosciences, Inc.
% Kenneth James, Ph.D.
VP, Product Sciences and
Regulatory Affairs
7 Elkins Street
Boston, Massachusetts 02127

DEC 12 2008

Re: K083440
Trade/Device Name: PriMatrix Dermal Repair Scaffold
Regulatory Class: Unclassified
Product Code: KGN
Dated: November 14, 2008
Received: November 20, 2008

Dear Dr. James:

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

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

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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. 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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Mark N. Melkerson

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

K083440

Indications for Use

510(k) Number (if known):

Device Name: PriMatrix Dermal Repair Scaffold

Indications For Use:

PriMatrix is intended for the management of wounds that include:

- Partial and full thickness wounds
- Pressure, diabetic, and venous ulcers
- Second-degree burns
- Surgical wounds—donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence
- Trauma wounds—abrasions, lacerations, and skin tears
- Tunneled/undermined wounds
- Draining wounds

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Neil R Ogden for mkm

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

510(k) Number K083440

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

Appendix 12-6 Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

HemCon ChitoFlex™-Surgical 510(k) Notification

AUG - 6 2007

5. SECTION 5 - 510(K) SUMMARY

Name and Address of Sponsor:

HemCon Medical Technologies, Inc.
10575 SW Cascade Avenue, Suite 103
Portland, OR 97223

Device Name:

Proprietary Name: HemCon ChitoFlexTM-Surgical Dressing

Common Name: Traumatic Wound Dressing
Classification Name: Dressing
Product Code: FRO

Establishment Registration Number:

9053189

General Description:

The HemCon ChitoFlex™-Surgical Dressing is a sterile chitosan based dressing intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations and abrasions.

It may also be used for temporary treatment of severely bleeding wounds such as surgical wounds (operative, postoperative, donor sites, dermatalogical, etc.) and traumatic injuries.

The HemCon ChitoFlex™-Surgical Dressing is nearly identical to the legally marketed HemCon® Bandage (K043050, cleared June 3, 2005) in composition, design and processing; the only major difference is the size and the modification of the intended use for temporary treatment of severely bleeding wounds such as surgical wounds. In this respect, the indications for use are identical to the Bloxx Rapid Clotting Agent (K061722, cleared August 2, 2006).

Indication for Use:

HemCon ChitoFlex™-Surgical is intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations and abrasions.

It may also be used for temporary treatment of severely bleeding wounds such as surgical wounds (operative, postoperative, donor sites, dermatalogical, etc.) and traumatic injuries.

Contact Person(s) and Phone Number:

Kevin Hawkins
Director – Quality & Regulatory
Phone (503)245.0459 x114 Fax (503)245.1326

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

HemCon Medical Technologies, Inc.
% Mr. Kevin Hawkins
Director, Quality & Regulatory
10575 SW Cascade Avenue, Suite 130
Portland, Oregon 97223-4363

AUG - 6 2007

Re: K071519
Trade/Device Name: HemCon ChitoFlex™ -Surgical Dressing
Regulatory Class: Unclassified
Product Code: FRO
Dated: May 31, 2007
Received: June 5, 2007

Dear Mr. Hawkins:

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

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

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

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0115 Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

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4. SECTION 4- INDICATIONS FOR USE STATEMENT

Applicant: HemCon, Inc.
510(k) Number (if known): Not Yet Assigned
Device Name: HemCon ChitoFlex™-Surgical Dressing

Indications for Use:

HemCon ChitoFlex™-Surgical is intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations and abrasions.

It may also be used for temporary treatment of severely bleeding wounds such as surgical wounds (operative, postoperative, dermatalogical, etc.) and traumatic injuries.

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 If Needed)

Concurrence of CDRH, Office of Device Evaluation (ODE)

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

510(k) Number K071519

Page of

(Posted November 13, 2003)

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

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K061711

1/1

Attachment 4 (Modified 18 July 2006)

SPECIAL 510(K) SUMMARY

JUL 19 2006

Submitted By: Cook Biotech Incorporated
1425 Innovation Place
West Lafayette, IN 47906
Perry Guinn,
VP Quality Assurance & Regulatory Affairs
Tel: (765) 497-3355
Fax: (765) 497-2361
July 18, 2006

Names of Device:
Trade Name: OASIS® Wound Matrix
Common/Usual Name: Animal-derived, extracellular matrix wound care product
Classification:

Unclassified

Performance Standards: No performance standards have been established under Section 514 of the Food, Drug and Cosmetic Act applicable to this device.

Intended Use:
The OASIS® Wound Matrix device's intended use is for the management of wounds including:

- **partial and full-thickness wounds,**
- **pressure ulcers,**
- **venous ulcers,**
- **diabetic ulcers,**
- **chronic vascular ulcers,**
- **tunneled/undermined wounds,**
- **surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence),**
- **trauma wounds (abrasions, lacerations, second-degree burns, and skin tears),**
- **draining wounds.**

The device is supplied sterile and is intended for one-time use.

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 19 2006

Cook Biotech, Inc.
% Mr. Perry W. Guinn
Vice President, Quality Assurance
and Regulatory Affairs
1425 Innovation Place
West Lafayette, Indiana 47906

Re: K061711
Trade/Device Name: Oasis Wound Matrix
Regulatory Class: Unclassified
Product Code: KGN
Dated: June 16, 2006
Received: June 19, 2006

Dear Mr. Guinn:

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

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

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

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Barbara Buch MD
for

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

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K061711

Indications for Use

510(k) Number (if known): K061711

Device Name: Oasis Wound Matrix

Indications For Use:
The Oasis Wound Matrix is intended for the management of wounds including:

- Partial and full thickness wounds;
- Pressure ulcers;
- Venous ulcers;
- Diabetic ulcers;
- Chronic vascular ulcers;
- Tunneled, undermined wounds;
- Surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence);
- Trauma wounds (abrasions, lacerations, second-degree burns, and skin tears);
- Draining wounds.

The device is intended for one-time use.

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Barbara Buchlin for MKM

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

510(k) Number K061711

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

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Section 13: Proposed Labeling

13 PROPOSED LABELING

The label of MariGen Wound, medical device and the Instructions for Use [IFU] was designed to fulfill the requirements outlined in FDA 21 CFR 801, Subpart A "General Labeling Provisions" and the standard EN 1041 "Information supplied by the manufacturer with medical devices". All symbols used in the IFU and label are in accordance with ISO 15223 "Medical devices Symbols to be used with medical device labels, labeling and information to be supplied". Appendix 13-1 contains the label for MariGen Wound and Appendix 13-2 the IFU.

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

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Pouch Label

(b)(4)

MariGen Wound

Business Development Manager
(b)(6)

Clinical Lead
(b)(6)

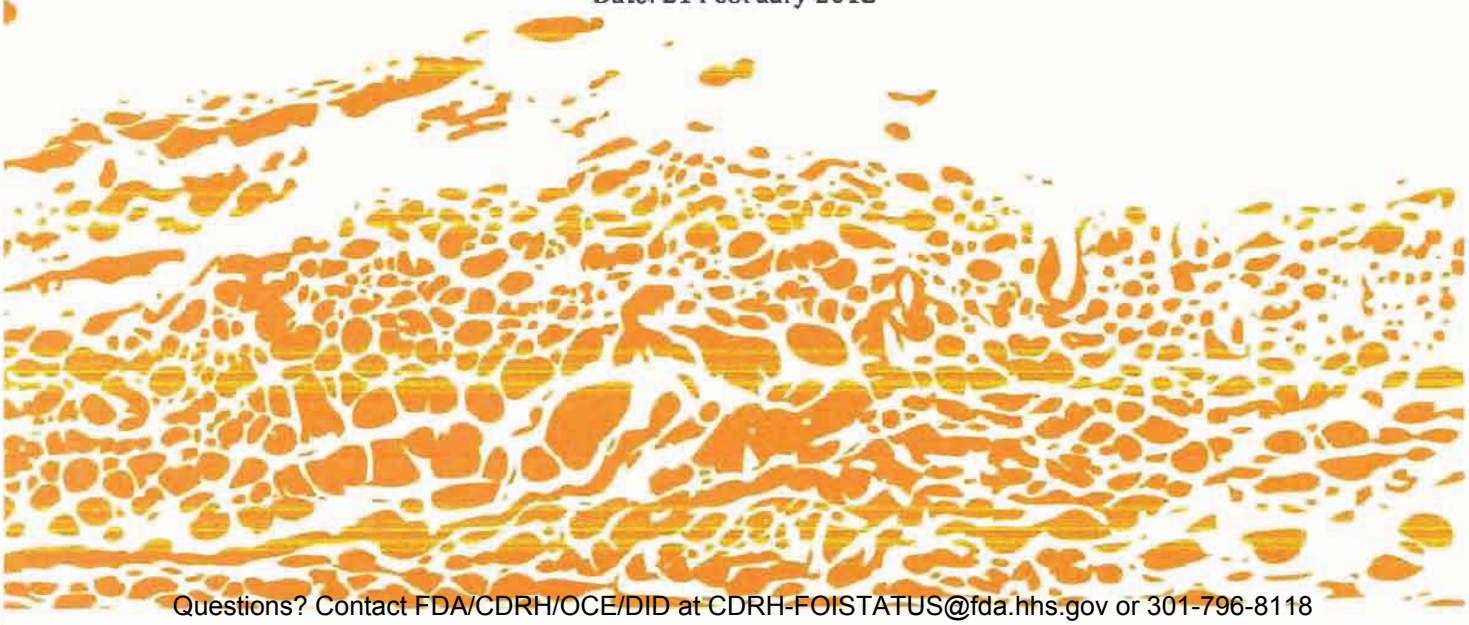
Project Manager
(b)(6)

(b)(6)

Signature (b)(6)

(b)(6)

Date: 21 February 2012



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

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

Appendix 13-2
Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

MariGen™ Wound

INSTRUCTIONS FOR USE

Fish derived, naturally occurring lyophilized extracellular matrix (ECM) wound dressing

INTENDED USE

MariGen Wound is indicated for the management of wounds including:

- Partial and full thickness wounds
- Pressure ulcers
- Venous ulcers
- Chronic vascular ulcers
- Diabetic ulcers
- Trauma wounds (abrasions, lacerations, second degree burns, skin tears)
- Surgical sounds (donor sites/grafts, post Mohs surgery, post laser surgery, podiatric, wound dehiscence)
- Drainage Wounds

CAUTION

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

CONTRAINDICATIONS

This device is derived from a fish source and should not be used in patients with a known allergy or other sensitivity to fish material.

MariGen Wound - PRECAUTIONS

• Remove most of necrotic tissue prior to device application.
• Remove exudate and control bleeding prior to device application.
• Do not reuse or re sterilize.
• Discard unused portions of device.
• Sterile if package is unopened and undamaged.
• Do not use device if package seal has been broken or if handling has caused damage or contamination.
• Do not use in case of known fish allergies.

MariGen Wound - POTENTIAL COMPLICATIONS

The following complications are possible. If any of these conditions occur, the device should be removed.
• Infection
• Chronic inflammation (Initial application of wound dressings may be associated with transient, mild, localized inflammation)
• Allergic reaction
• Excessive redness, pain, swelling, or blistering

STORAGE

This device should be stored in a clean, dry location at room temperature.

STERILIZATION

This device has been sterilized using gamma irradiation.

SUGGESTED INSTRUCTIONS FOR USING MariGen Wound

The following recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgment concerning patient care. Always handle MariGen Wound in an aseptic manner.

Initial application

1. When applying MariGen Wound for the first time, clean the wound bed by removing necrotic tissue to obtain a fresh tissue surface. Irrigate excessive exudate. Control bleeding.
2. Remove the MariGen Wound sheet from the pouch in an aseptic manner.
3. Cut the sheet roughly to the size of the area to be covered and pre hydrate in NaCl solution.
4. Apply sheet directly to wound.
5. In large wounds, more than one sheet may be necessary for complete coverage. Overlap sheet edges slightly to assure coverage of the entire wound.
6. The amount of MariGen Wound needed on a daily basis varies with the proteolytic activity in the wound which, again, is often the cause of the chronicity. The quantity of MariGen Wound necessary can vary between 1 cm^2 per same area of wound, every other day to once a week.
7. Apply a secondary non adherent absorptive wound dressing to maintain a moist wound environment.

Follow-up application

1. Inspect wound every 2 7 days.
2. Insert a new MariGen Wound sheet if the previously applied sheet has been absorbed and is no longer visible.
3. Change the secondary dressing as needed to maintain a moist, clean wound area.

As wound healing occurs, redness and swelling of wound edges will decrease and the level of exudate will be reduced. These are signs of wound healing and are often seen before epithelization is obvious. Make sure to use an appropriate type of secondary wound dressing at all times to maintain a moist, clean wound area.

Should you suspect any adverse reaction from this product please report it to the e mail adversereactions@kerecis.com leaving a phone number and e mail address. Adverse reactions might also be subject to mandatory reporting to the authorities. Please submit the data on the package or pouch i.e. "batch number" and "use before" date.

MANUFACTURED

by Kerecis Limited, Eyrargata 2, 400 Isafjordur, Iceland.
tel +354 562 2601, email: info@kerecis.com, www.kerecis.com
Patent Pending. Kerecis and MariGen are trademarks or registered trademarks of Kerecis Limited.

KM XX XXX

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

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Section 14: Sterilization and Shelf Life

14 STERILIZATION AND SHELF LIFE

14.1 Sterilization Information

(b)(4)

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

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(b)(4) Sterilization

[redacted]

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

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14.3 Product Shelf Life

Kerecis has undertaken an extensive study (b)(4) Testing

(b)(4) Testing

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

(b)(4) Manufacturing Information

(b)(4) Manufacturing Information

(b)(4) Manufacturing Information

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

KERECIS

MariGen Wound – (b)(4) Sterilization (b)(4) (b)(4)

MariGen Wound

Author
(b)(6)

(b)(6)

Quality Manager
(b)(6)

Signa (b)(6)

Date: 10 April 2013

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

(b)(4) Sterilization Testing

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KERECIS

(b)(4)

Test Report

(b)(4)

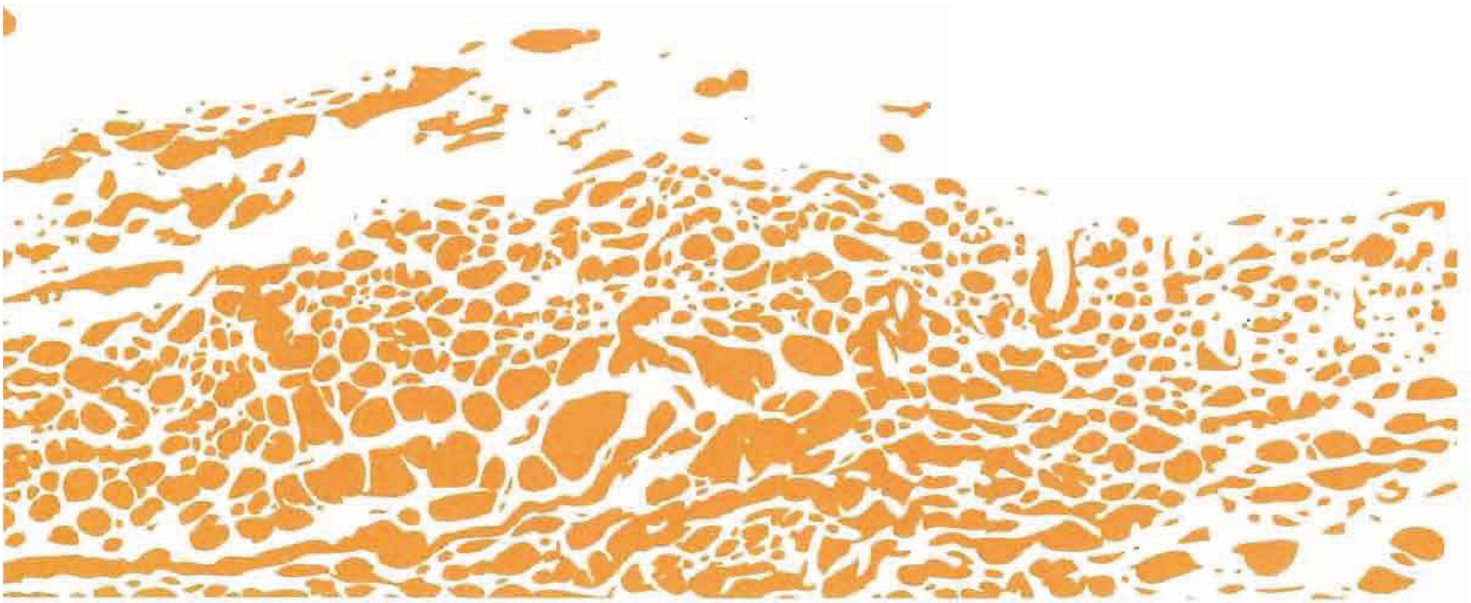
MariGen™ Wound

R&D Manager
(b)(6)

Quality Manager
(b)(6)

(b)(6)

Date: 16 January 2012



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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

MARIGEN™ Wound (b)(4) Test Report

(b)(4)

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

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Section 15: Biocompatibility Testing

15 BIOCOMPATIBILITY TESTING

(b)(4) Testing

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

(b)(4) Testing

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Appendix 15-11 (b)(4)

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MARIGEN WOUND (b)(4) Testing

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KERECIS

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MariGen Wound

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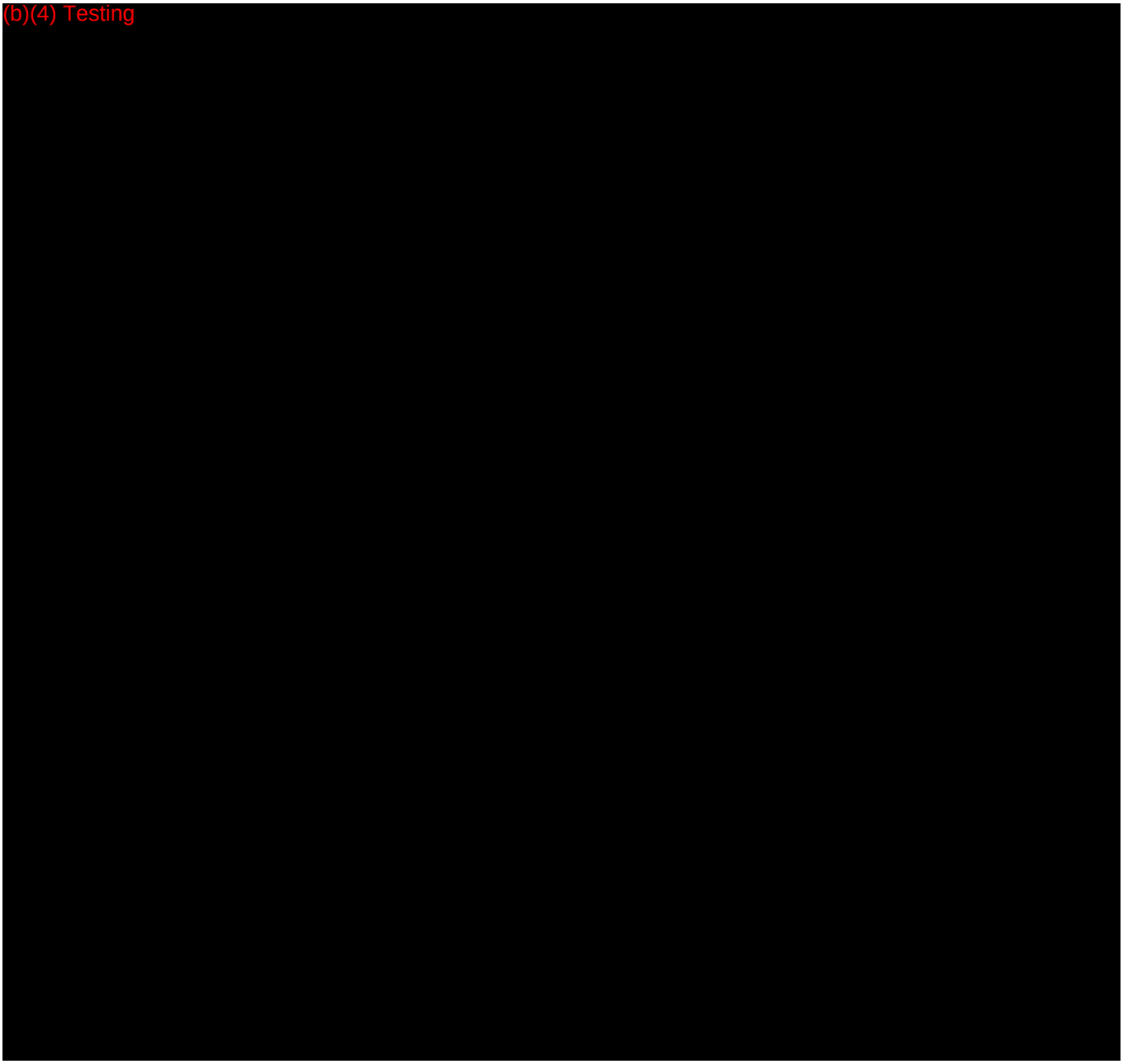

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Section 16: Software Information

16 SOFTWARE

This Section is not applicable

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Section 17: Electromagnetic Compatibility/Electrical Safety

17 ELECTROMAGNETIC COMPATIBILITY / ELECTRICAL SAFETY

This Section is not applicable.

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

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Section 18: Performance Testing - Bench

18 PERFORMANCE TESTING – BENCH

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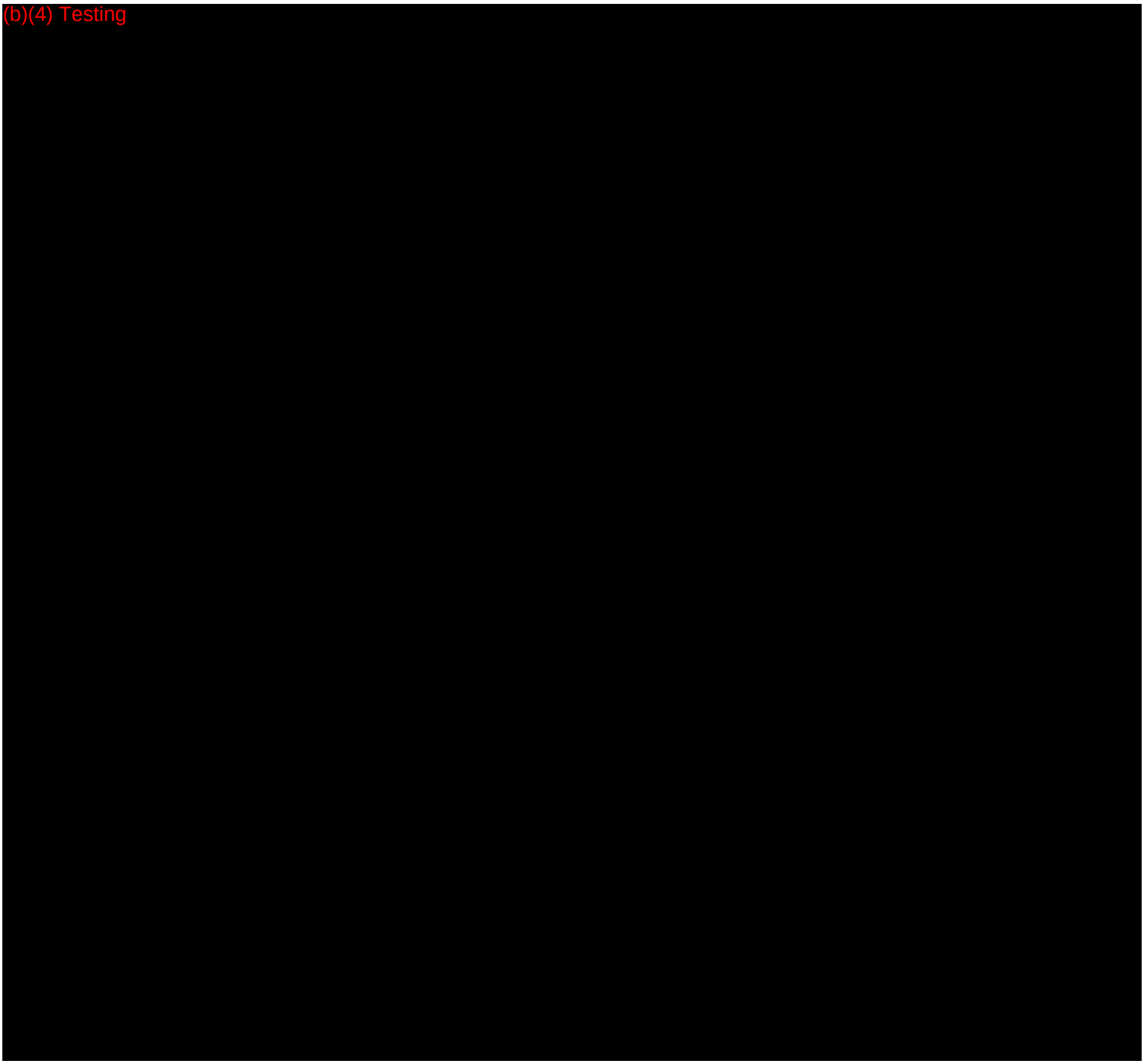

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 18-1

(b)(4) test

(b)(4) MariGen Wound (b)(4)

(b)(4)

MariGen Wound

R&D Manager
(b)(6)

(b)(6)

Date: 23 February 2012

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

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Appendix 18-2

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Test

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MariGen Wound,

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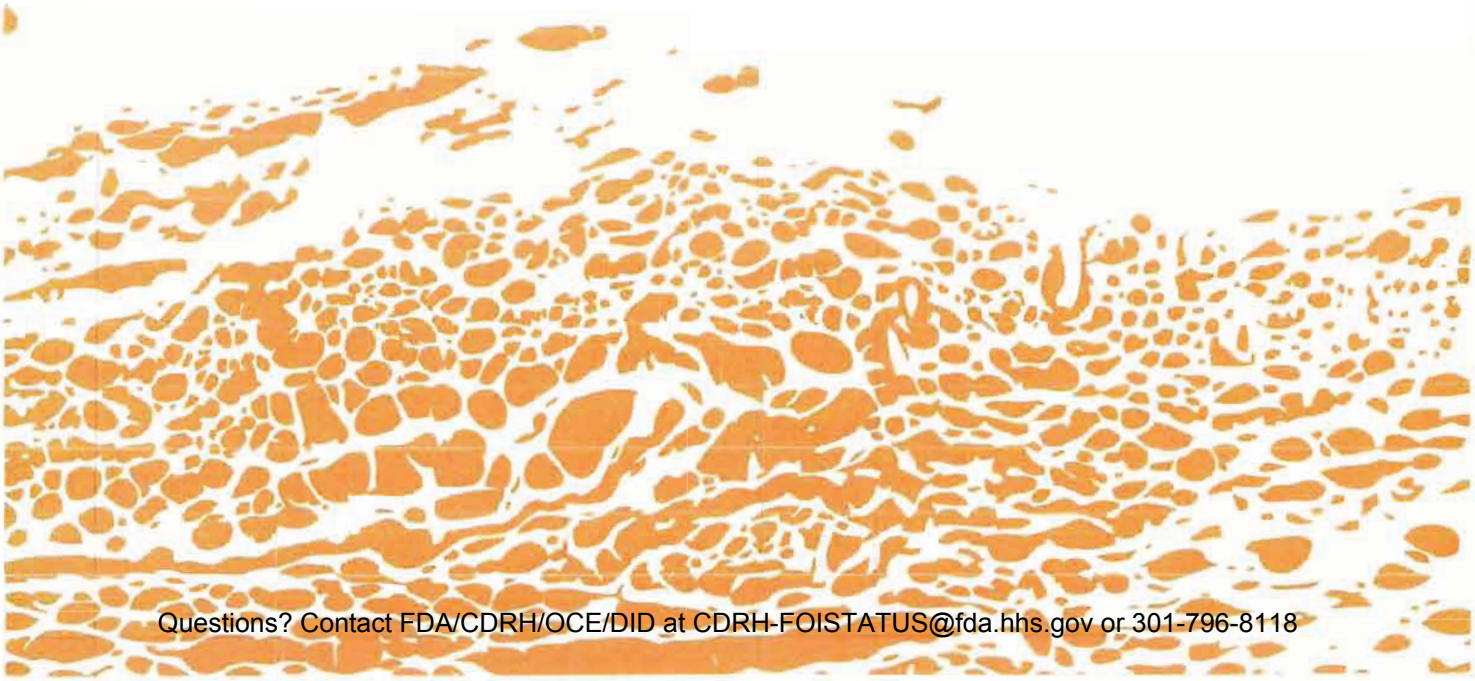
MariGen Wound

R&D Manager

(b)(6)

(b)(6)

Date: 23 February 2012



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Appendix 18-3

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MariGen Wound

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Clinical Lead
(b)(6)
Medical Director

Date: 23 February 2012

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

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Appendix 18-4

KERECIS

(b)(4) Testing

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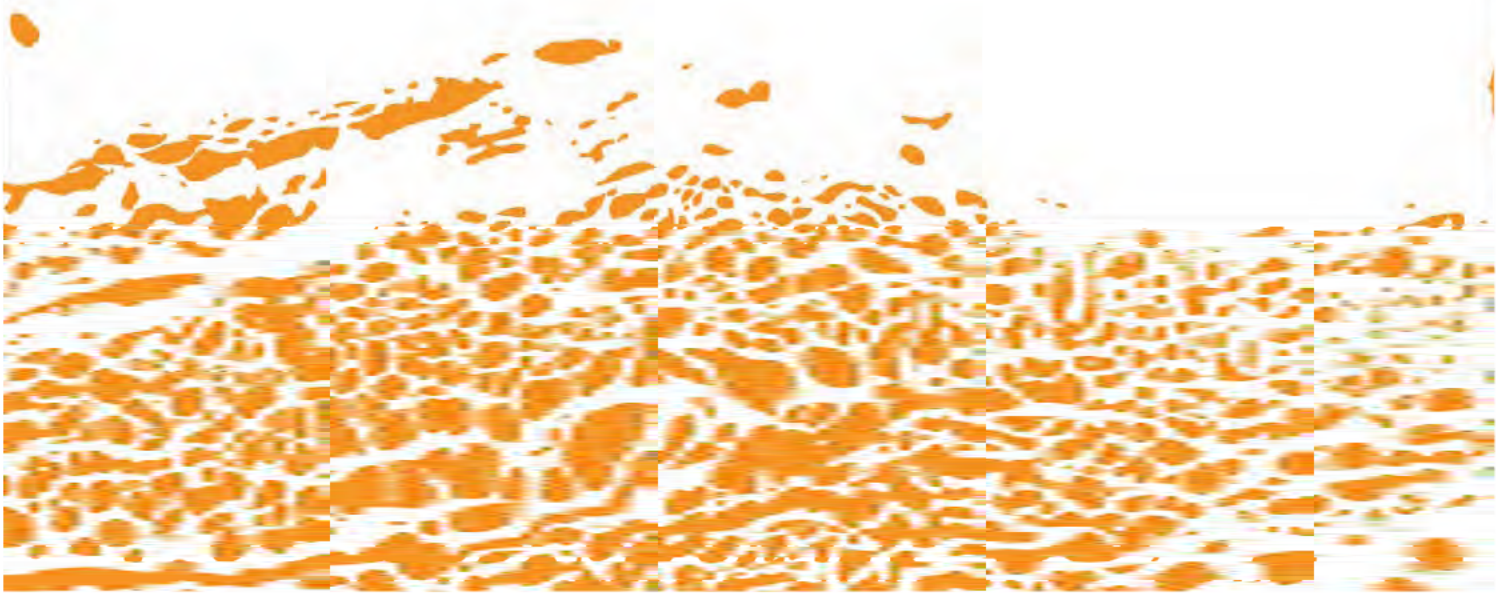
MariGen Wound

Author
(b)(6)
VP Science & Technology

(b)(6)

Date: 27 October 2010



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

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Appendix 18-5

(b)(4) Manufacturing Information [redacted]

(b)(4) [redacted]

MariGen Wound

R&D Manager
(b)(6) [redacted]

(b)(6) [redacted]

Date: 12 January 2012

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

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Section 19: Performance Testing - Animal

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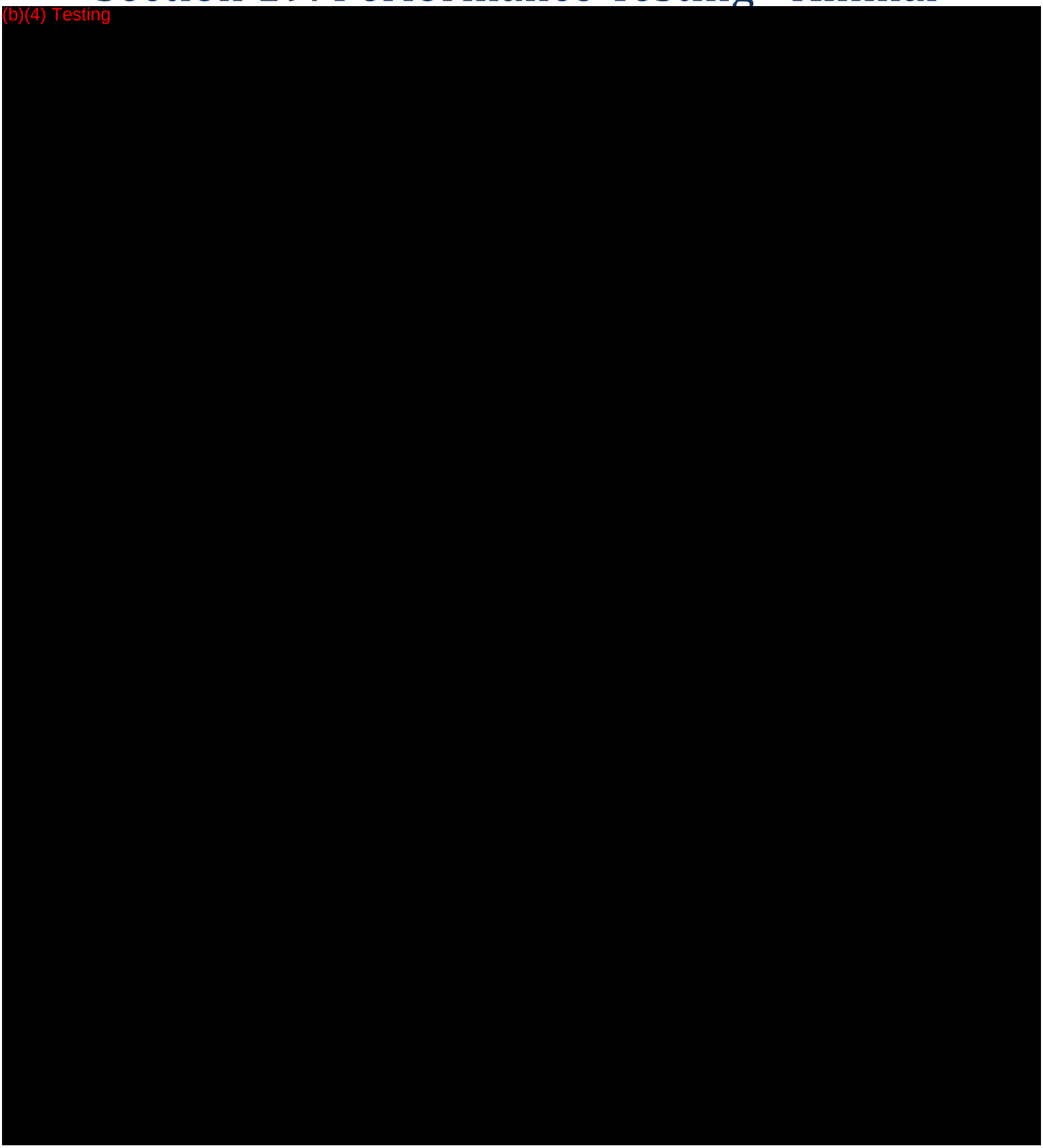

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Appendix 19-1-7
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Evaluation of NovoSorb™ novel biodegradable polymer for the generation of a dermal matrix
Part 2: In-vivo Studies

Greenwood JE, Li A, Dearman BL & Moore TG

Abstract

In previous work, the biocompatibility, safety and potential of three variants of NovoSorb™ (a family of novel biodegradable polyurethanes) as dermal scaffolds were determined *in-vitro*. This paper documents the subsequent *in-vivo* work. Subcutaneous implantation of the three candidate NovoSorb™ polymers in rats demonstrated no systemic toxic effects of the materials or their degradation products. The anticipated local foreign body reaction compared favourably with commercially-available medical sutures. Assessment of a three-dimensional polymer matrix followed. When engrafted onto a surgically-created full-thickness sheep wound, the non-cellular matrix integrated, healed with an epidermis supported by a basement membrane and was capable of withstanding wound contraction. The resistance to contraction compared favourably to a commercially-available collagen-based dermal matrix (Integra™). These results suggest that the NovoSorb™ matrix could form the basis of an elegant 2-stage burn treatment strategy with an initial non-cellular Biodegradable Temporising Matrix to stabilise the wound bed followed by the application of cultured composite skin.

Key words: Dermal matrix; Polymer; Wound healing; Burn injury; Biodegradable polyurethane

Abbreviations: BTM, Biodegradable Temporising Matrix; GAG, glycosaminoglycan; CEA, cultured epithelial Autograft; PAS, Periodic Acid Schiff.

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Introduction

Although the split-skin graft remains the workhorse of the burn surgeon, it has limitations. As burn surface area increases, available donor site decreases. Eventually the point is reached when, even with maximal (reasonable) mechanical expansion, sufficient skin cannot be harvested to cover all debrided burn wounds and still achieve an acceptable functional result and cosmetic appearance. The number of re-harvests from a donor area is finite because each harvest (no matter how thin) includes a variable thickness of dermis which will not be replaced when donor site re-epithelialisation occurs. The surgeon must gauge correctly when a further re-harvest will result in a donor wound which will not heal spontaneously and promptly [1]. How frequently these limited re-harvests can occur is dependent on robust re-epithelialisation, itself a factor of the thickness of the harvested graft as well as the thickness of the remaining dermis at the site. It is seldom, if ever, that re-harvesting can be contemplated within 10 days. With the patient already susceptible to infection due to loss of mechanical restriction to

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pathogen ingress and generalised immunocompromisation, the donor site extends the area of skin loss and inflicts further physiological insult.

The use of the split skin graft does not replace 'like with like'. Grafts are taken so that the donor site will re-epithelialise rapidly by proliferation, differentiation and migration of keratinocytes from both the wound edge and retained adenexal epidermal cell nests. Adenexal structures are not transported with a split-skin graft to the recipient site. Grafts thus have no means of auto-hydration and can dry and crack, causing itch. The thermoregulatory and sensory functions of grafted areas are also reduced. Thin grafts used to replace deep or full thickness skin loss cannot confer the same degree of robustness to mechanical, thermal or chemical insult, such that further injury requires less insult. Nor does providing a reduced thickness of elastic dermis often allow complete restitution of the supple envelope that uninjured skin provides to facilitate joint mobility and range. Without underlying dermal support, the junction between pieces of skin graft is often visible as a 'seam' and the sharp demarcation where graft meets normal skin is sometimes very obvious. Because the skin graft contains dermis, a donor site scar (however good) is always created since the dermis is not capable of regaining its pre-injury architecture. Finally, it is seldom possible to choose the donor site for its colour match to the recipient site, potentially creating mildly hypo- or hyper-pigmented skin grafts scars.

The property of split-skin graft which is most desirable (and thus far impossible to emulate in 'skin substitutes' is the speed of re-vascularisation and when one considers the speed with which split skin grafts "pink up" compared to the relative latency of neovascularisation; it becomes obvious that inosculation is occurring as the mechanism for the reestablishment of blood flow within grafts [2]. Neovascularisation should be expected to (and does) take much longer than inosculation since the angiogenetic process alone is responsible for a neovasculature to invade and supply a relatively thick structure. The vascularisation of Integra™ dermal matrix, for example, takes ~20 days in the acute (hot) burn setting but can take 4 to 5 weeks in reconstructive (cold) cases. This vascularisation can occur only from the wound bed since no vascular elements exist in Integra™. In developing a composite skin, either possessing cultured vessels or a means to rapidly establish a vasculature within the composite, must form part of the structural design.

Materials and methods

Production of polymer fibres and mats

Polymer fibres were produced by curing the polymers prior to extrusion (using a twin screw reactive extrusion process) into polymer fibrils ranging from 60-100µm in diameter. 10cm lengths of each polymer fibre were wound around two parallel rods spaced 1 cm apart in a 'figure of 8' conformation and tied in the centre. This configuration provided a 'dumb-bell' of length 10mm and width 5mm (at the two widest points). Two commercially available sutures, Prolene™ (polypropylene, non-resorbable, Ethicon Inc., Piscataway, NJ, USA) and Monocryl™ (polyglecaprone; resorbable, Ethicon Inc., Piscataway, NJ, USA) were used as controls. These were used in the cytotoxicity and rat safety studies.

After the initial biocompatibility testing, the most suitable candidate polymer (BTM-2) was spun into 3-dimensional porous mats. These matrices comprised of 6 layers of fibres at 90° orientation and of 0.65mm in thickness with intervening pores of 200-500µm in diameter. The fibres were orientated in such a way that the matrix resisted compression in one direction but not the other.

All materials were again sterilised with 25KGy γ-irradiation prior to use in experiments.

For the animal studies, the tissues collected were fixed in 10% neutral-buffered formalin then processed for paraffin embedding. 2µm sections were stained with haematoxylin and eosin (H&E) for histological analysis. Sections were also stained for a basement membrane with Periodic Acid Schiff (PAS). All animal tissue sections were examined by a veterinary pathologist who had no prior knowledge of the trial protocol or the nature of the implants.

Rat implantation procedure and analysis

Twelve male and 12 female Sprague Dawley rats, >12 weeks old and weighing 200-300g each were randomly assigned to groups by a weight-ordered distribution. A small incision was made in the flank. The subcutaneous fascia was blunt-dissected anteriorly and dorsally to approximately 2cm and the implant, a figure 8 BTM or control polymer, was inserted until completely covered by skin. The wound was closed with one or two stainless steel clips. All surgical procedures were performed under aseptic conditions using isoflurane in oxygen anaesthesia.

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Body weights were recorded prior to implantation, daily for the week post-implantation, then weekly for the duration of the experiment. Clinical records were taken daily throughout the study. Six animals (3 male/3 female) from each study group were humanely killed at weeks 3, 6, 12 and 24. Terminal (fasting) blood samples were taken from anaesthetised animals via cardiac puncture, and analysed for haematological and biochemical parameters prior to the administration of 2-4mL of 4M potassium chloride into the heart. Results of these parameters were analysed using unpaired t-test and two-way ANOVA.

All animals were subjected to a comprehensive necropsy (defined as examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities, and their contents) by the Veterinary Pathologist. All implants were collected for histology at the above time points. When the actual implant could not be located, large sections of skin and subcutaneous tissue were collected from the area deep and anterodorsal to the implantation scar. The collected samples were processed for histological analysis.

Sheep implantation procedure and analysis

A total of 6 male (wethers) Merino sheep weighing 50-55kg each were used. The animals were housed individually in pens, in a controlled environment and exposed to a 12h/12h light/dark cycle for the first two weeks after implantation, after which they were kept in groups of three in sheltered outside pens exposed to ambient temperature and natural light.

Surgery was performed in two groups of three animals approximately three weeks apart under isoflurane in oxygen anaesthesia. The left and right flanks of each animal were shaved. Two test sites (5cm by 5cm) at least 5cm apart were created per flank along lines parallel to and equidistant (18cm) from the spine. The sites were infiltrated with 0.25% bupivacaine (Marcaine™) and 1:400,000 adrenaline (to facilitate haemostasis and afford post-operative analgesia) before full thickness skin squares were removed leaving the underlying panniculus carnosus intact, creating a strong model of wound contraction. The implants were applied and secured with 3/0 Prolene™ sutures. The wounds were dressed with Mepitel™ (Mölnlycke Health Care AB, Göteborg, Sweden), Cutilin™ (Defries Industries Pty Ltd, Keysborough, Aust) and held in place with Tubular-Net™ (Sutherland Medical Pty Ltd, Oakley, Aust). All animals were administered prophylactic penicillin for four days post-operatively.

Each animal received two test articles, BTM at 0° (transverse) and 90° (axial), as well as Integra™ dermal regeneration template (Life Sciences, New Jersey, USA). One of the test sites on the animals received no graft and was allowed to heal by secondary intention (granulation and contraction). The orientation of the BTM polymer refers to the orientation of the dominant fibre pattern. Materials were randomly allocated to ensure that each was used at least once in the four treatment sites. The silicone layer of the Integra™ was maintained in the first three animals but removed under aseptic conditions prior to placement on the wounds of the second group.

Measurement of the four vertices of each test site was taken using micrometer callipers on alternate days for the first two weeks, then every 3-4 days. The area of each test site was measured using a wound measurement system, Visitrak Digital and grid (Smith & Nephew Ltd). Photographic capture of the progress of the test sites accompanied these measurements with a scale appended. Prior to necropsy, the animals were humanely killed with a captive bolt to the skull. Wound/scar tissue samples were harvested under the supervision of the pathologist. Samples of skin (implant and 2cm surrounding tissue) were collected and processed for histological analysis. All results were examined by an independent veterinary pathologist.

The sheep study data was analysed as individual values by animal (clinical observations and physical examinations). Two-way ANOVA (where possible) was performed to ascertain if there were differences between the groups over time.

Results

BTM polymers caused no adverse local or systemic reactions in vivo

The possible local and systemic cytotoxic effect of the candidate BTM polymers and their degradation products *in-vivo* was investigated by implantation of 'figure of 8' polymer fibres subcutaneously in rats for 24 weeks. Throughout the experimental period the animals thrived and gained weight with no significant difference in weight between the groups. The rats displayed no behavioural change and there were no unscheduled deaths or cases of morbidity.

Analyses of blood samples collected at 3, 6, 12 and 24 weeks post-implantation showed all haematological parameters

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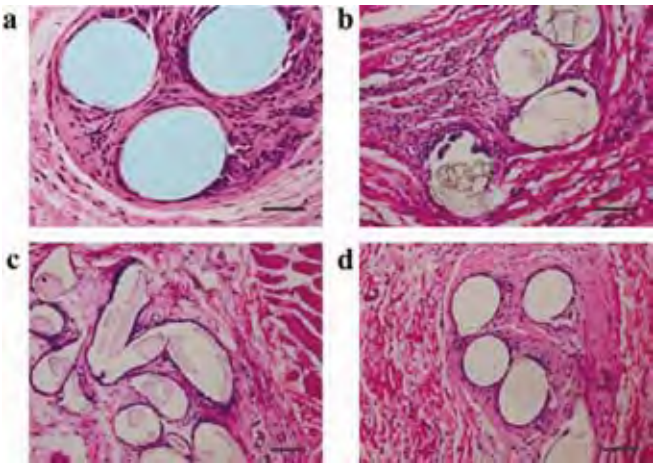

Figure 1. Histological analysis of polymer fibre implants in rats at week 3 post-implantation.

(a) Prolene™ 'spheroids' with blue-green hue seen for all inert control sections. (b) Tissue section containing BTM-1 polymers showing eosinophilic fragments within the spheroids. (c) Monocryl™ reactive control showing fragmented 'spheroid/ovoid' content. (d) Tissue section containing BTM-2 polymers showing non-staining spheroids with definite limiting membrane. Scale bar = 50µm.

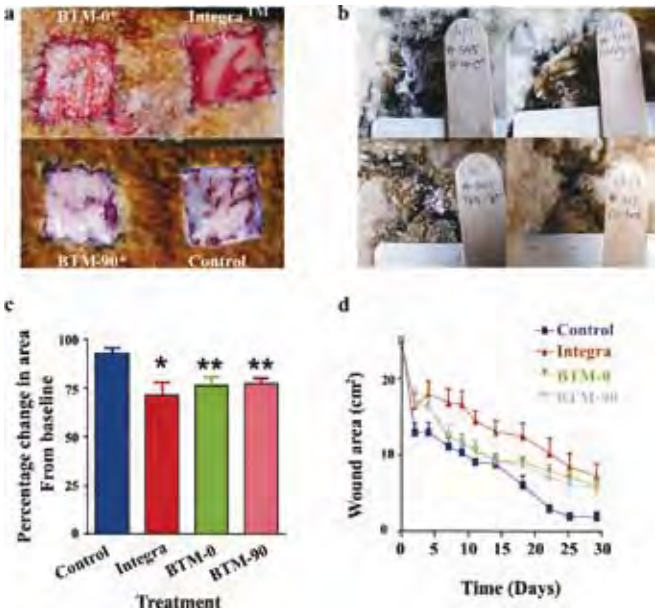

Figure 2. Contraction of full thickness wounds in sheep treated with BTM-2 matrices.

*(a) Full thickness wounds were surgically created on the back of sheep and grafted with either BTM-2 matrices or Integra™ or left un-grafted. (b) The wound sites as seen at day 29 when all sites had healed. (c) Mean+SEM change in wound/scar area (n=6 for days 7-28, n=2-5 for days 2-7). (d) Percentage change in wound/scar area at day 29 compared to baseline (n=6 for all data points), showing significant differences from the control wounds (*p<0.05).*

were within normal range. There were no clinically significant differences in blood biochemical parameters. Macroscopic analysis of all organs examined at necropsy showed that all were normal except for a degree of lung redness. There were no significant differences between the groups in any organ weights.

There was no evidence of infection or inflammation at the implantation wound site in any animal at any of the collection time points. By week 24, all wounds had healed, with only the faintest scarring detectable at the site. The histopathological appearance was remarkably similar in all 5 implant types. The BTM and control polymers were surrounded by a granulomatous reaction composed of epithelioid macrophages and multinucleated giant cells with variable fibrosis (Figure 1). Interestingly, Prolene™, appeared to elicit a more robust granulomatous reaction than the BTM polymers or Monocryl™ (Figure 1a).

The degradation rate of each polymer was faithfully reflected in the appearance of the material post-implantation. At week three, BTM-1 implants could not be detected macroscopically but eosinophilic comma-shaped fibre fragments surrounded by a non-staining (artefact) halo (Figure 1b). The time of BTM-1 fragmentation was similar to that of Monocryl™ which also began to degrade by 3 weeks (Figure 1c). BTM-2 implants showed no signs of degradation at week 3 and resisted the ingress of the stains, thus were seen as rows of spheroidal to oval, non-staining 'spaces', many with a definite limiting 'membrane' which is the outer surface of the polymer strand (Figure 1d). By the 12 and 24 week time-points, the BTM-2 implants were becoming difficult to discern macroscopically. All BTM-3 implants were located at weeks 3 and 6, most at week 12 and one at week 24.

Assessment of 3-D BTM as a dermal scaffold in a full-thickness wound model

The potential of a BTM-2 matrix to resist wound contraction and the quality of scaffold invasion by fibroblasts and blood vessels *in-vivo* was assessed in a sheep wound model.

By day 29, the two BTM and one Integra™ grafted sites as well as the ungrafted control site on all sheep had healed (Figure 2a and 2b). A graph of the change in wound area over this time illustrated that in the initial days following grafting,

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all four sites showed a considerable decrease in area which then levelled out; with the exception of the untreated control which showed a further rapid wound contraction between day 15 and 20 (Figure 2c). This resulted in ~75% decrease in area in the treated sites which was significantly less compared to the ungrafted control at 92 ± 3% (Figure 2d). BTM-2 mats placed with the dominant fibre either transversely (BTM-0°) or axially (BTM-90°) showed no increased resistance in wound contraction in the dorsal-ventral and rostral-caudal axes.

The potential importance of a 'sealing' silicone layer in preventing wound contraction was also investigated by leaving the silicone layer on the Integra™ in the first group of sheep but removed in the second group. 2 out of 3 sheep grafted with intact Integra™ had infections which caused premature separation of the silicone layers. The silicone sheets were not removed and the infections were not treated. There were no significant differences in wound contraction between the two groups at the conclusion of the experiment, suggesting that the advantage of the silicone layer was limited and may inadvertently facilitate an increased incidence of wound infection.

Re-epithelialisation was observed in all wounds. The neo-epidermis appeared acanthotic and hyperkeratotic compared to adjacent normal epidermis (Figure 3a) and was intact in both the untreated control (Figure 3c) and the BTM-2 treated sites (Figure 3e) in spite of some superficial erosion in the latter. In contrast, the Integra™ treated sites showed extensive epidermal erosion with sometimes severe epidermal ulceration and secondary acute dermatitis. In these cases, there was an abundant accumulation of necrotic cellular debris heavily admixed with polymorphonuclear cells over the denuded epidermis. More importantly, Periodic Acid Schiff (PAS) staining revealed a well developed basement membrane at the dermal-epidermal junction of the BTM-2 grafted sites (Figure 3g).

The dermal tissue of the un-grafted control sites showed extensive reparative fibrosis (Figure 3c & 3d) compared with normal dermal tissue (Figure 3a & 3b) with an increased prominence of small blood vessels due to endothelial hyperplasia, perivascular oedema and lymphocytic cuffing.

In sections containing BTM-2, a large number of polymer fibres were observed in the subcutis, but fewer in the dermis and epidermis (Figure 3e). These polymers were surrounded by a granulomatous (foreign body) reaction of epithelioid macrophages (often attenuated) and multinucleated giant cells (Figure 3h). There was effacement of much of the dermis and subcutis by reparative collagenous connective tissue with elongated fibroblastic/fibrocytic nuclei embedded in

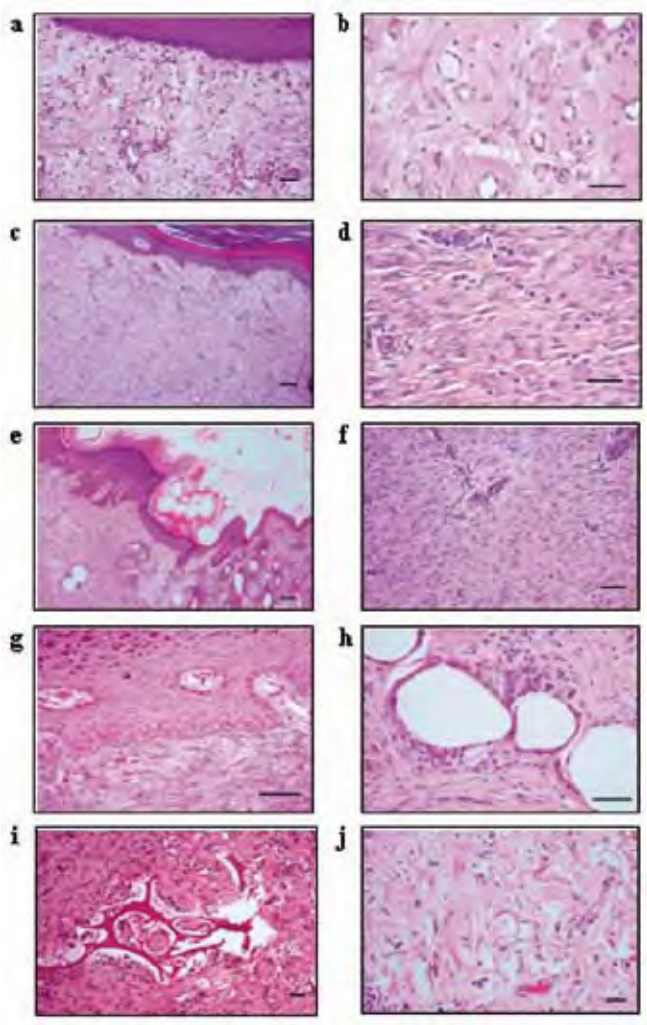

Figure 3. Histological analysis of wounds in sheep grafted with BTM-2 matrix.

Tissue collected from sheep engrafted with BTM-2 matrix was stained with H&E. (a) A section of normal sheep skin. (b) higher magnification of normal dermal tissue. (c) Section of the full-thickness wound left to heal by secondary intention showing a hyperkeratotic epidermis with dense fibrotic dermis. (d) Fibrosis of the ungrafted site. (e) Regenerated epidermis over fibrotic; normal epidermis is depicted to right of the picture. (f) Effacement of the dermis and subcutis by reparative collagenous connective tissue with elongated fibroblastic/fibrocytic nuclei embedded in collagen in polymer-containing sections. (g) Normal basement membrane between epidermis and polymer 'dermis'. (h) Granulomatous (foreign body) reaction of epithelioid macrophages and multinucleated giant cells around BTM-2 fibres. (i) Integra™ in skin sections showing eosinophilic, branching core distinguishing it from surrounding tissue. (j) Integra containing skin with loose fibrovascular penetration and collagen deposition. Scale bar = 50μm.

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collagen (Figure 3f). Scattered throughout this fibrous tissue were capillaries and arterioles. The endothelial cells in the dermal tissue were frequently hypertrophied and hyperplastic. Inflammatory cells were often loosely distributed in replacement connective tissue, especially sub-epidermally where fibrosis was sometimes less dense; with actively proliferating fibroblasts and neovascularisation. Some fibrous tissue in this region appeared uniformly homogeneous and more hyalinised as indicated by high eosinophilic staining.

The Integra™ in the dermis and subcutis was clearly distinguishable from surrounding tissue as the branching, deeply eosinophilic core (Figure 3i). The lattice was often loosely invaded by fibroblasts and capillaries with variable and often loose collagen deposition compared to BTM-2 matrix (Figure 3j). It was also mildly infiltrated by a few inflammatory cells, principally lymphocytes and eosinophils. The Integra™ was occasionally attended by a few epithelioid macrophages and multinucleated giant cells, but this foreign body granuloma reaction was minimal. The dense collagenous connective tissue surrounding Integra™ was similar to that observed around BTM-2, extending from beneath the epidermis to the panniculus carnosus.

Taken together, these results demonstrated that BTM-2 matrix engrafted at the site of full-thickness wounds, exhibited mechanical robustness to wound contraction and allowed controlled development of dermal granulation tissue, the mechanism by which all dermal scaffolds work.

Discussion

In this study we investigated the biocompatibility of three NovoSorb™ variants for use as biodegradable temporising matrix in full thickness wounds as well as a scaffold for the generation of a skin composite.

The prior success of culturing keratinocytes, fibroblasts and MVECs to confluence in the presence of the polymer fibres was extremely suggestive that subsequent *in-vivo* work would be uneventful from a biocompatibility perspective. Indeed subcutaneous implantation of the BTM polymers in rats to assessment the foreign-body reaction showed that

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it was no greater than a commonly used absorbable suture Monocryl™ and less than that generated by Prolene™, a suture frequently used to create permanent meshes for hernia repair, as well as skin suturing. The implantation of the very rapidly degrading BTM-1 ensured that one group of rats would sustain an early bolus of polymer degradation products within the first three weeks. This group showed no clinically significant differences to the other groups of rats. Ideally a dermal scaffold should maintain its structural integrity for the first three months for guided infiltration of host cells and regeneration of the dermis, but completely degrade and resorbed within 6 months, thus allowing further tissue remodelling. The degradation rate of BTM-2 (in-vitro and in-vivo in the rat model) fulfilled these criteria and was thus ideal for development into a 3-dimensional scaffold for the large animal wound study.

The sequential production of a covering epidermal tissue over the dermal composite with existing microvasculature will generate a material capable of replacing skin autografts. The use of such a composite skin mandates the consideration of protecting and preparing the excised burn wound whilst the composite is in culture (potentially 21 days). Given that the BTM-2 matrix integrated into the full thickness animal wounds in a manner comparable to Integra™ and was able also to restrain wound contraction to a similar degree, this material can also be used as an immediate non-cellular implant to temporise the wound. The observation that the BTM-granulation tissue supported the migration of keratinocytes from the wound edge to form a more robust epithelium and produced the appropriate signals to ensure the development of a normal basement membrane, provided further evidence that the BTM therapeutic model would work. Since it can be produced at a fraction of the cost of the Integra™, it could already represent an attractive treatment option.

The necessity of the silicone layer on Integra™ to further limit wound contraction was not firmly established in this study due to delamination of the silicone layer by pus when it was left on. Despite an increased incidence in wound infection observed in this study, it may still play an important role in sealing and protecting the debrided wound against moisture loss and should still be considered in the design of optimised BTM.

Conclusion

In this study, we demonstrated that the series of biodegradable polyurethanes created as candidates for generation of a dermal scaffold are biocompatible with no observable cytotoxic effect *in-vivo*. Implantation studies in both rat and sheep demonstrated that the inflammatory response and granulomatous reaction to the polymers were comparable to clinically used materials including sutures and the dermal regeneration template Integra™. Of the three biodegradable polyurethanes tested, BTM-2 displayed the desired degradation profile for a dermal scaffold and was developed into a 3-dimensional porous matrix for further study. We demonstrated that this (as yet un-optimised) matrix performed as well as Integra™ as a dermal scaffold in preventing wound contraction but allowing re-epithelialisation over the resultant dermal granulation tissue with normal basement membrane formation. We also demonstrated that the BTM-2 matrix can be used to create a rudimentary bi-layered composite skin which may eliminate our reliance on skin autografts. Our previous study suggested that a vascular structure can be generated by culturing MVECs in the BTM-2 matrix, having potential in the generation of a 'pre-vascularised' composite skin and other tissue engineered organs.

Conflict of interest

NovoSkin is a joint venture established to investigate the role of NovoSorb in wound management applications between PolyNovo Pty Ltd (who own 80%) and Skin Pty Ltd (20%). A/Prof John Greenwood is a 50% stakeholder of Skin Pty Ltd.

Acknowledgements

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Both the rat safety and sheep implantation studies were approved by the Animal Ethics Committee of IMVS and conducted in accordance with the IMVS standard operating procedures (SOP), and the OECD Principles of Good Laboratory Practice.

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Purpose

(b)(4) Testing

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Tissue reactions to collagen scaffolds in the oral mucosa and skin of rats: Environmental and mechanical factors

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ABSTRACT

Objective: To compare the tissue reactions to implanted collagen scaffolds in the palate and the skin of rats.

Design: Crosslinked collagen scaffolds were implanted submucoperiosteally in the palate, and subcutaneously on the skull and on the back of 25 rats and evaluated after up to 16 weeks. On H&E stained sections, the cell density and the number of giant cells within the scaffolds were determined. Blood vessels, inflammatory cells, and myofibroblasts were detected by immunohistochemistry.

Results: A faster ingrowth of myofibroblasts and blood vessels in the palate was found during the first week compared with the skin. A more severe inflammatory response was initially found in the back skin. Furthermore, about twice as much giant cells were present in these scaffolds.

Conclusion: The oral environment seems to promote the ingrowth of myofibroblasts and blood vessels into the scaffolds. Mechanical stimuli seem to enhance the initial inflammatory response. Overall, the scaffolds were gradually integrated within the host tissue, eliciting only a transient inflammatory response. The scaffolds were biocompatible and are promising for future applications in oral surgery.

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1. Introduction

Collagen scaffolds, either or not with additional extracellular matrix (ECM) components and/or growth factors, are widely studied for the treatment of skin burns or other skin defects.[1] Scar formation in exposed areas of the body causes esthetical problems, while around the joints it may impair function. Similar problems may occur after cleft palate surgery.[2] A promising approach to reduce these problems might be the implantation of a scaffold loaded with growth factors to reduce scar formation. In the last decade, tissue engineered scaffolds have already been developed for the treatment of skin wounds. These scaffolds, loaded with growth factors, enhanced wound healing and reduced scar formation after implantation in the skin.[3,4] Particularly collagen is widely used to prepare these substrates, due to its good biocompatibility and biodegradability in the skin.[5] Crosslinking of these scaffolds reduces the inflammatory response and collagen degradation, thereby prolonging their survival.[6] Subgingivally implanted collagen for periodontal regeneration therapy showed similar results in rats and humans.[7] The implantation of collagen scaffolds alone was already found to reduce wound

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contraction and scar formation in skin wounds in animal[8] and human wound models.[9]

Collagen scaffolds might also be suitable for tissue engineering in the palate and elsewhere in the oral cavity. However, the oral environment is quite different from that of the skin. In addition, differences between oral and dermal fibroblasts in vitro have been reported.[10,11] Indeed, it has been shown that wound healing in the skin and in the oral cavity is quite different. Oral wound healing is generally considered to proceed without scar formation. However, most studies on intra oral wound healing and the implantation of substrates were performed in buccal mucosa.[12–15] In contrast to buccal mucosa, the palatal mucosa is a mucoperiosteum; hence, mucosa and periosteum are merged and attached to the palatal bone, providing a stable mechanical environment. The palatal mucoperiosteum is also much stiffer than buccal mucosa, due to the higher collagen content and the lower number of elastin fibres.[16] Studies focussed on palatal wound healing show the formation of rigid scar tissue tightly attached to the bone.[17,18] This is generally accepted as the cause of the growth disturbances after cleft palate repair.[2] Also in skin wounds, the location and mechanical conditions seem to influence healing.[19]

The primary aim of this study is to evaluate the tissue reaction to collagen scaffolds implanted in the palates of rats. These results are compared with scaffolds implanted in the skin. Secondly, a comparison is made between collagen scaffolds implanted in the skin on the skull and on the back. We have chosen the skin on the skull since, as in the palate, underlying bone is present. Comparison with the loose skin on the back might indicate the influence of mechanical factors. We hypothesize that the tissue reaction to collagen scaffolds implanted in the palatal mucoperiosteum is different from that of scaffolds in the skin since the environment is different. We further hypothesize that the reactions in the skull skin are more comparable to the palatal mucoperiosteum than to the back skin, since the mechanical conditions are similar.

2. Materials and methods

2.1. Animals

Thirty one five week old male Wistar rats (Harlan, Zeist, the Netherlands), weighing between 106 and 166 g, were used. All animals were kept under normal laboratory conditions and were fed standard rat chow and water ad libitum. The rats had been acclimatized to the animal housing facility for 1 week before the start of the experiment. The experiment was approved by the Board for Animal Experiments of Radboud University Nijmegen.

2.2. Collagen scaffolds

Type I collagen was purified from bovine Achilles tendon; and a chemically crosslinked scaffold was prepared.[20] Briefly, a 0.8% (w/v) type I collagen suspension in 0.5 M acetic acid was shaken overnight at 4 °C and homogenised on ice using a Potter Elvehjem homogeniser. Air bubbles were removed by centrifugation at 250 × *g* for 10 min at 4 °C. The suspension was then slowly poured into a plastic mould (10 ml per 25 cm^2), frozen in a bath of ethanol and solid CO_2 (80 °C), and lyophilised in a lyophiliser (Zirbus, Bad Grund, Germany). Scaffolds were crosslinked using 33 mM 1 ethyl 3 (3 dimethyl aminopropyl) carbodiimide (EDC) and 6 mM *N* hydroxysuccinimide (NHS) in 50 mM 2 morpholinoethane sulphonic acid

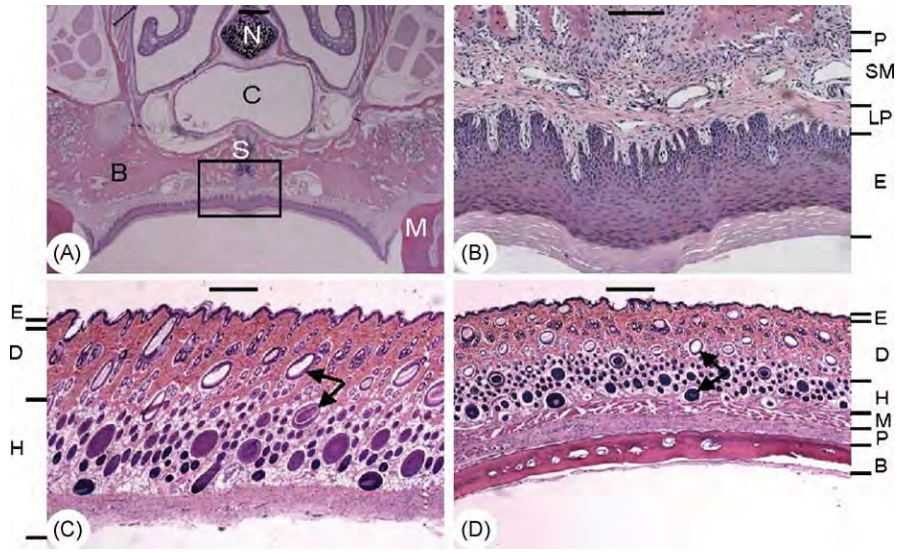

Fig. 1 – General histology of the implant locations. H&E staining of tissue sections of the palate, the back skin and the skull skin. (A) The palate. Indicated are the nasal septum (N), the nasal cavity (C), the mid-palatal suture (S), the palatal bone (B) and the second molars (M) (bar = 625 μm). (B) Higher magnification of the palate. Indicated are the periosteum (P), the submucosa (SM), the lamina propria (LP) and the epithelium (E) (bar = 200 μm). (C) The back skin. Indicated are the epithelium (E), the dermis (D) and the hypodermis (H). Hair follicles are indicated by the arrows (bar = 200 μm). (D) The skull skin. Indicated are the epithelium (E), the dermis (D), the hypodermis (H), the muscle (M), the periosteum (P) and the skull bone (B). Hair follicles are indicated by the arrows (bar = 200 μm).

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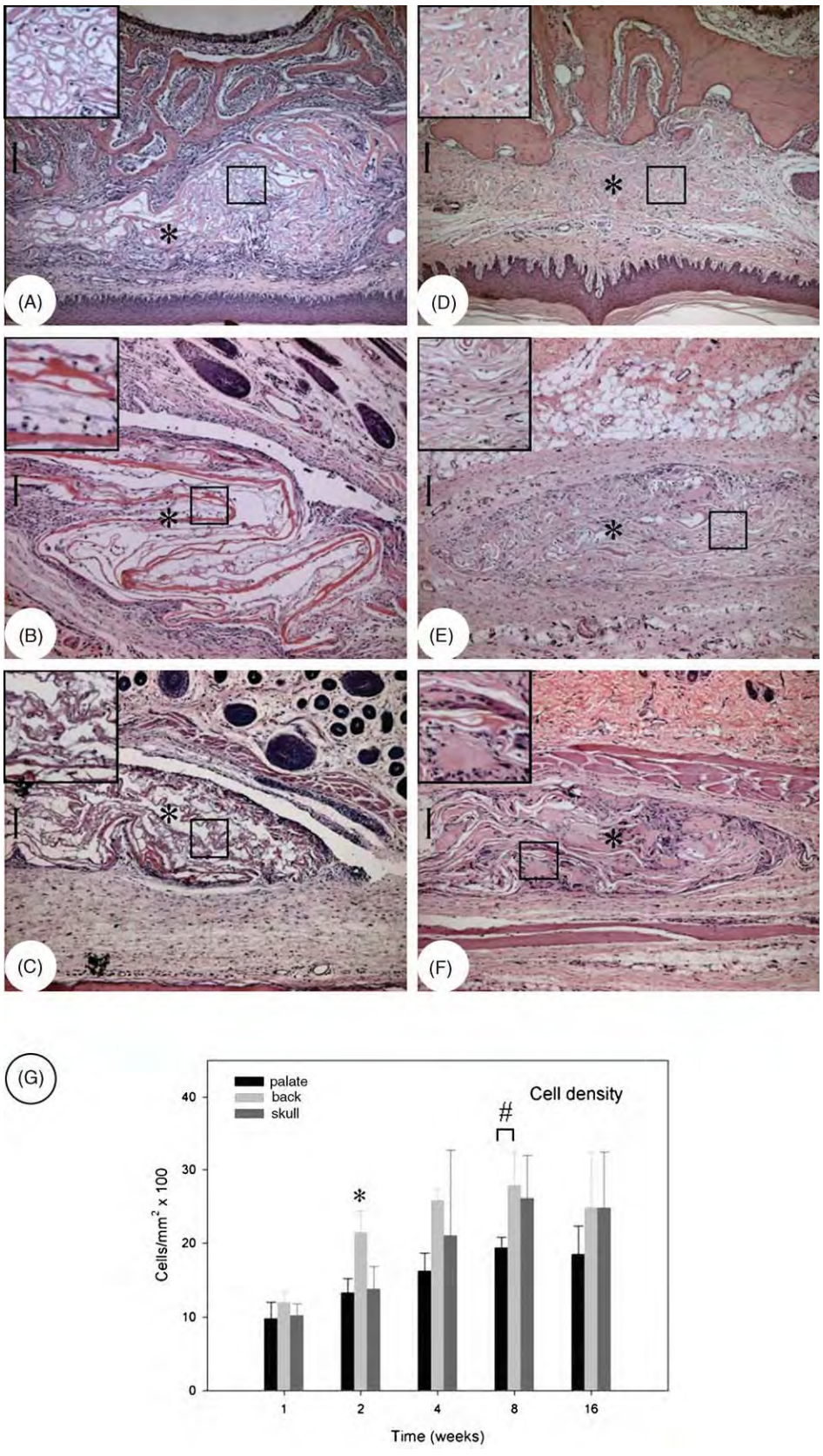

Fig. 2 – Cell density within the scaffolds. Representative H&E-stained sections of 1 and 16-week samples are shown. A gradual increase in cell density is shown. In the left upper corner of the images insets are placed with a higher magnification. (A) Palatal sample 1 week after implantation. (B) Back sample 1 week after implantation. (C) Skull sample 1 week after implantation. (D) Palatal sample 16 weeks after implantation. (E) Back sample 16 weeks after implantation. (F)

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(MES) pH 5.0 containing 40% ethanol (20 ml per 25 cm^2) for 4 h at 22 °C. Scaffolds were then washed with 0.1 M Na_2HPO_4, 1 M NaCl, 2 M NaCl, and MilliQ water, frozen in ethanol/CO_2 again and lyophilised.

2.3. Surgical procedures

The rats were anaesthetized with an intraperitoneal injection of 1 ml per kg body weight of ketamine (Nimatek, Eurovet, Bladel, the Netherlands) combined with an intraperitoneal injection of 0.25 ml per kg body weight of xylazine (Sedamun, Eurovet, Bladel, the Netherlands). A standardized transversal incision of 3 mm was made in the palatal mucoperiosteum at the level of the contact points between the first and second molar. The mucoperiosteum was then elevated caudally for 3 mm with a periodontal probe to create a submucoperiosteal envelope. A circular collagen scaffold with a diameter of 3 mm was placed in the envelope and a 10 × 0 vicryl suture was used to close it. On the skull between the ears and on the back between the shoulders of the rats, the skin (4 cm^2) was shaved and disinfected with iodine. An envelope was created under the skin, and the scaffold was implanted. A 1 mm long platinum wire (∅ 0.1 mm) was inserted into the scaffolds to detect them on a radiograph after sacrifice. The envelope was closed with a 5 × 0 vicryl suture. The rats were medicated post operatively with 0.02 mg per kg body weight buprenorfine (Temgesic®; Schering Plough, Brussels, Belgium) subcutaneously as an analgesic. The same procedure without placement of the scaffold was performed in the sham groups.

2.4. Study design

Groups of five rats were sacrificed at 1, 2, 4, 8 and 16 weeks post implantation and processed for histological analyses of the wound tissue. Groups of three rats without scaffolds were sacrificed at 1 and 2 weeks post surgery, serving as sham groups.

2.5. Histology

The rats were perfused using freshly prepared 4% paraformaldehyde in phosphate buffered saline (PBS). Four cm^2 of the skin between the shoulders and 4 cm^2 of skull bone with overlying skin containing the implants was cut out and a radiograph was taken to determine the position of the scaffolds. The samples were trimmed accordingly. The rats were then decapitated and the palate was dissected from the skull. The palate samples and the skin samples were fixed in 4% paraformaldehyde solution for 24 h. Hereafter, the skull and palate samples were decalcified in 10% EDTA in PBS at 4 °C. Decalcifation was checked with radiographs. All samples were embedded in paraffin. Hereafter, the platinum wire was carefully removed from each skin sample. Serial paraffin sections of 6 μm were cut in the transversal plane for the palate and cross sectional for the two skin samples and stained with hematoxylin and eosin (H&E, according to Delafield). Histomorphometric analyses were performed using an ocular micrometer with the time points blinded. The total number of giant cells and the cell density in the scaffolds were determined on three sections (150 μm apart) for every sample. The cell density in the scaffolds was determined with a microscopic grid, and expressed as the number of cells per mm^2. On every section, the cell count was performed in the middle of the scaffolds on a row of 10 adjacent squares of 0.01 mm^2. At 1 and 16 weeks, the cell density in the tissue surrounding the scaffolds was also determined.

2.6. Immunohistochemistry

Paraffin sections were collected on Superfrost Plus slides (Menzel Gläser, Braunschweig, Germany), deparaffinated and rehydrated. Before staining, the slides were rinsed in PBS for 10 min. α Smooth muscle actin staining was performed to detect myofibroblasts, ED 1 staining to detect inflammatory cells and collagen type IV staining to detect blood vessels.

2.7. α-Smooth muscle actin staining

Sections were treated with 3% H_2O_2 in methanol for 10 min to block endogenous peroxidase and rinsed in PBS. Then, the sections were pre incubated in 10% normal donkey serum (NDS) (Chemicon Europe, Hampshire, United Kingdom) in PBS. After pre incubation, the sections were incubated with monoclonal mouse anti α smooth muscle actin (Sigma Chemical Co, St. Louis, MO, USA) 1:6400 for 60 min. After washing with PBS, detection was carried out using biotinylated donkey anti mouse IgG (Jackson Labs, West Grove, PA, USA) 1:100 for 60 min, and the avidin biotin complex (ABC) method (Vectastain ABC Elite kit, Vector Laboratories, Burlingame, CA, USA). The presence of myofibroblasts was scored on a scale from 0 to 3 on three sections (150 μm apart) for every sample.

0	No, or only a few myofibroblasts present
1	Groups of myofibroblasts around the scaffold; no or only a few myofibroblasts inside the scaffold
2	Groups of myofibroblasts around and inside the scaffold
3	Myofibroblasts throughout the scaffolds and the surrounding tissue

2.8. ED-1 staining

The ED 1 staining was performed similar to the α smooth muscle actin staining, but the sections were incubated with monoclonal mouse anti rat ED 1 (Serotec, DPC, Breda, the Netherlands) 1:400 for 60 min. This antibody recognizes a single chain glycoprotein of 90 110 kDa that is expressed predominantly on the lysosomal membrane of myeloid cells.[21] It mainly stains macrophages and monocytes. The inflammatory response was scored on a scale from 0 to 3 on three sections (150 μm apart) for every sample.

Skull sample 16 weeks after implantation (bar = 100 μm). The scaffolds (*) are indicated. (G) Quantification of the cell density within the scaffolds (mean ± S.D.). (*) denotes a significant higher cell density in the back samples than in the palate and skull samples at 2 weeks. (#) denotes a significant higher cell density in the back samples than in the palate samples at 8 weeks.

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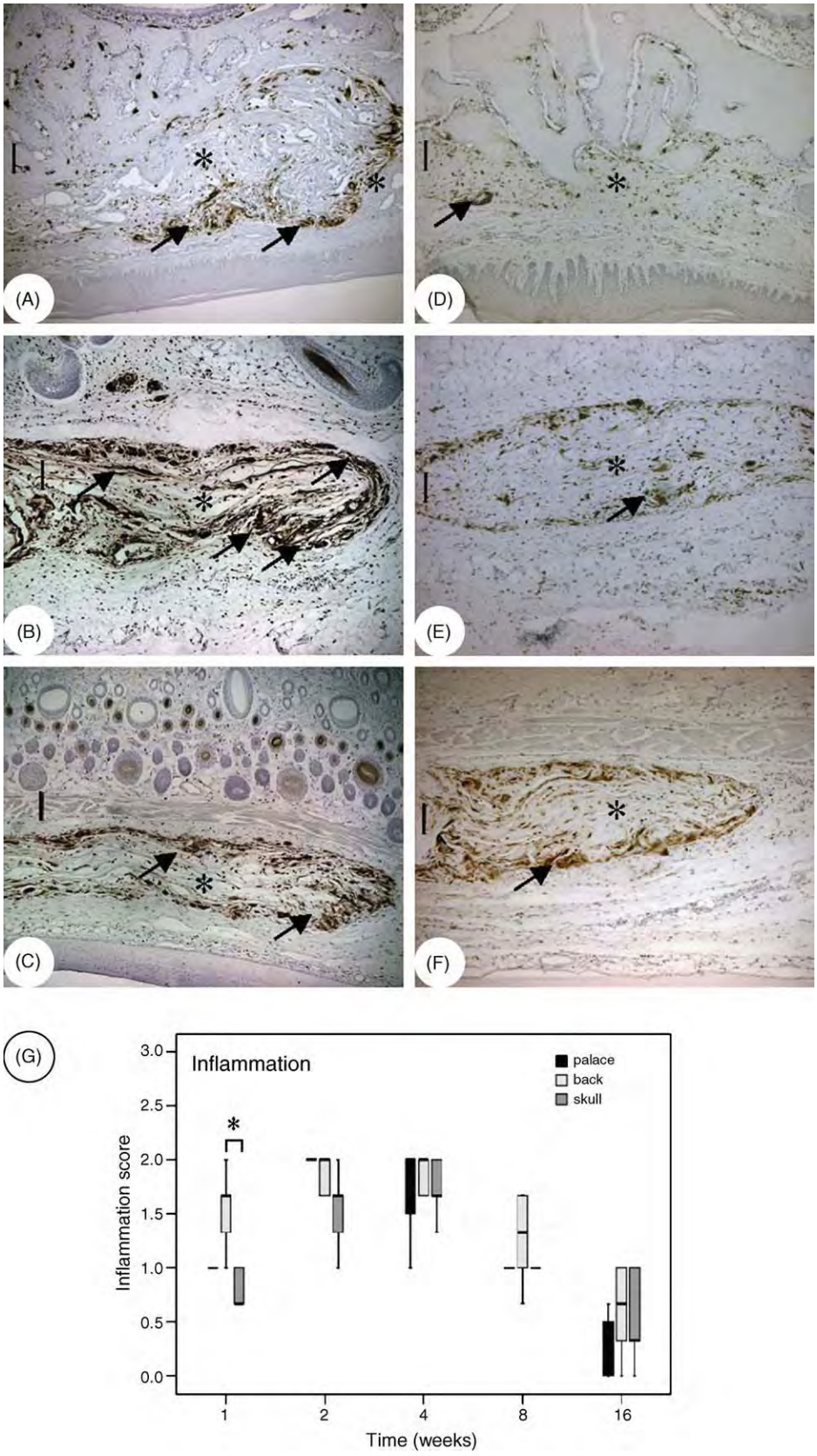

Fig. 3 – Inflammatory response. Inflammatory cells were detected with ED-1 staining. Representative ED-1-stained sections of 1 and 16-week samples are shown. The number of inflammatory cells increased from 1 week to 4 weeks, and diminished afterwards. More inflammatory cells were found in the back samples at 1 week. (A) Palatal sample 1 week after implantation. (B) Back sample 1 week after implantation. (C) Skull sample 1 week after implantation. (D) Palatal sample 16 weeks after implantation. (E) Back sample 16 weeks after implantation. (F) Skull sample 16 weeks after implantation

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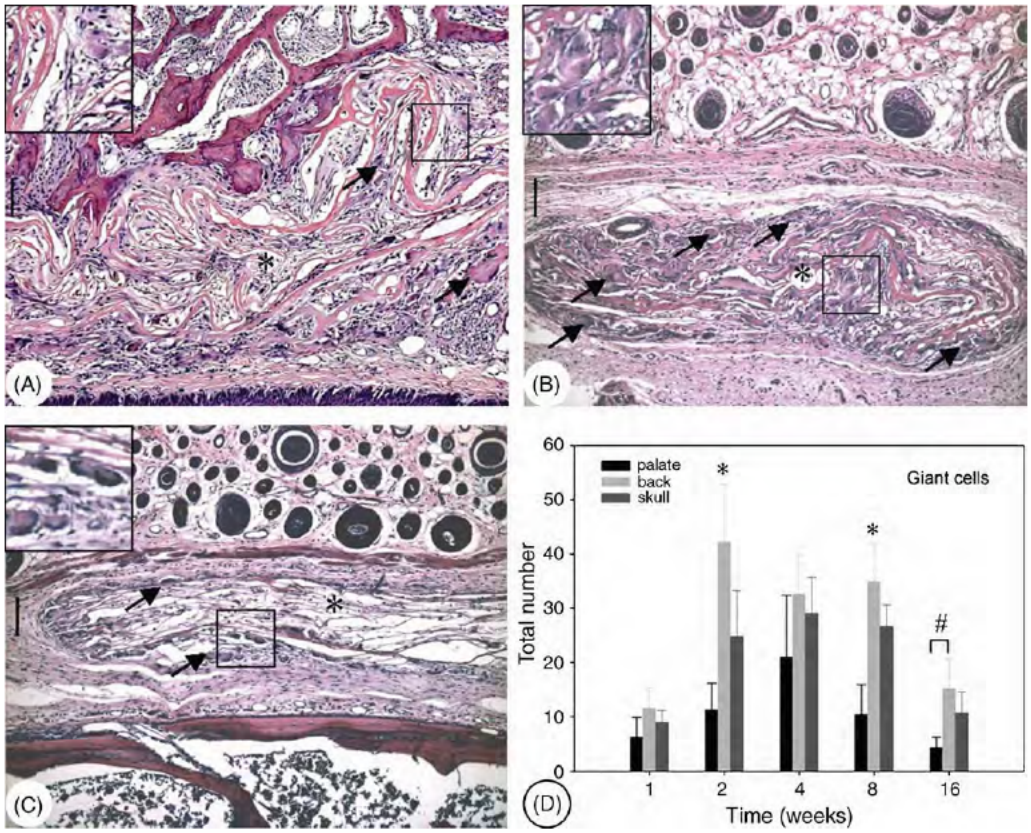

Fig. 4 – Giant cells. The total number of giant cells in the scaffolds was determined on H&E-stained sections. Two-week samples are shown. In the left upper corner of the images insets are placed with a higher magnification. An increase in the number of giant cells generally occurred between 1 week and 8 weeks, while at 16 weeks the numbers were reduced again. (A) Palatal sample 2 weeks after implantation. (B) Back sample 2 weeks after implantation. (C) Skull sample 2 weeks after implantation (bar = 100 μm). Scaffolds (*) and giant cells (arrows) are indicated. (D) Number of giant cells within the scaffolds (mean ± S.D.). (*) Denotes significant differences between the back samples compared with the palate and the skull samples. (#) denotes a significant difference between the skull samples and the palate samples.

0	No, or only a few inflammatory cells present
1	Groups of inflammatory cells around the scaffold; no or only a few cells inside the scaffold
2	Groups of inflammatory cells around and inside the scaffold
3	Inflammatory cells throughout the scaffold and the surrounding tissue

2.9. *Type IV collagen staining*

The type IV collagen staining was performed similar to the α smooth muscle actin staining, but the sections were incubated with rabbit anti collagen type IV (Euro diagnostica B.V., Arnhem, The Netherlands) 1:200 for 60 min. The total number of blood vessels present in the scaffolds was counted on three sections (150 μm apart) for every sample.

2.10. *Statistics*

All measurements were performed on triplicate sections from each sample. The data for cell density, the number of blood vessels and the number of giant in the three different locations were compared at each time point with a one way ANOVA. Significant differences were further analyzed by the Holm Sidak method.

Differences in the scores for the number of myofibroblasts and the degree of inflammation for the three locations were compared at each time point by a Kruskal Wallis one way ANOVA on ranks. Significant differences were further ana lyzed by the Tukey test. In all tests, a p value of less than 0.05 was considered significant.

3. Results

3.1. *General histology*

3.1.1. *Normal palatal mucoperiosteum and skin*

The palatal bone is divided in half by the mid palatal suture, which is a cartilaginous tissue (Fig. 1A). It is covered by the palatal mucoperiosteum at the oral side. A molar is visible at

(bar = 100 μm). The scaffolds (*) and inflammatory cells (arrows) are indicated. (G) Inflammation scores. The box plots display the 25th, 50th, and 75th percentiles, if available. (*) denotes a significant difference.

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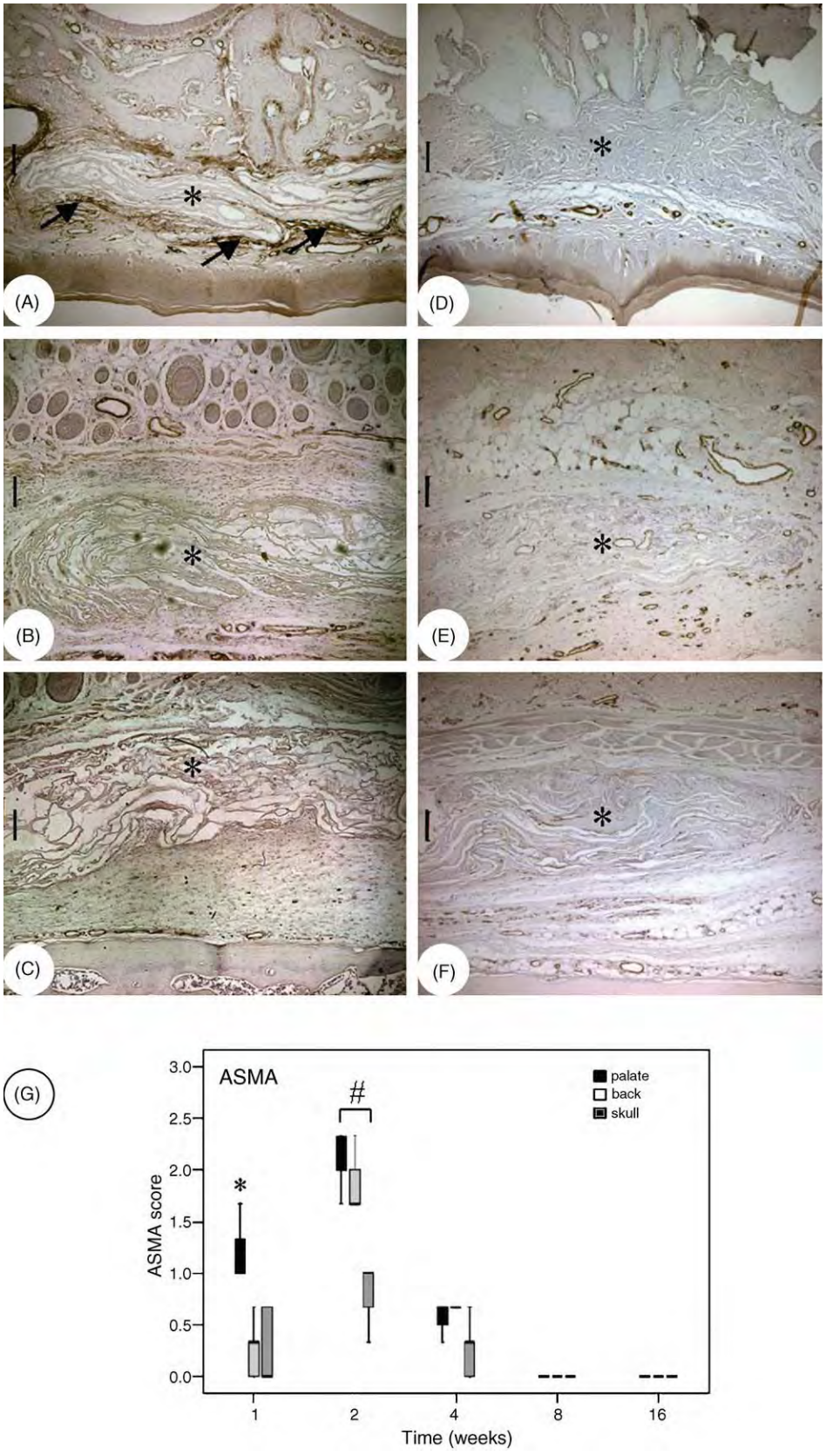

Fig. 5 – Myofibroblasts. Myofibroblasts are stained with an antibody against α-smooth muscle actin (ASMA), which also stains the blood vessel walls. Representative ASMA-stained sections of 1 and 16-week samples are shown. The number of myofibroblasts increased between 1 and 2 weeks and had decreased again after 4 weeks. At 8 and 16 weeks, myofibroblasts were no longer present. (A) Palatal sample 1 week after implantation. (B) Back sample 1 week after

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each side of the section. The palatal mucoperiosteum consists of four layers: the epithelium, the lamina propria and the merged submucosa and periosteum (Fig. 1B). The epithelium is of the orthokeratotic stratified squamous type and about 15 cell layers thick. The lamina propria consists of two sub layers: a papillary layer containing a relatively loose network of collageneous fibres and a deeper layer with more densely packed collageneous fibres. The submucosa contains the major arteries, veins and nerves of the palate. The periosteum consists of two sub layers, a fibrous layer and an osteogenic layer.

The back skin consists of two layers (Fig. 1C): the epidermis and the dermis, which are connected to the underlying tissue through the hypodermis. The epidermis is also an orthoker atotic stratified squamous epithelium, but contains only two to four cell layers, in contrast with the palatal epithelium. The dermis is divided into a papillary layer and a reticular layer. It contains mainly blood vessels, lymph vessels, nerves, hair follicles and a dense extracellulair matrix. The hypodermis contains mainly adipose tissue, a loose extracellulair matrix and hair follicles. The skin on the skull is largely comparable to that on the back. The hypodermis connects the skin with the underlying muscle, which is lying over the periosteum and the skull bone (Fig. 1D).

3.1.2. *Palatal mucoperiosteum and skin after implantation*

At 1 week after implantation, the collagen scaffolds were easily detected, due to their specific fibrous structure (Fig. 2A C). Some inflammatory cells were present around the scaffolds, but only a few cells had invaded them. Some giant cells were present at the edges of the scaffolds. Later, more inflammatory cells were present around the scaffolds, which had been invaded by cells. Also, the number of giant cells in and around the scaffolds increased in time (see below). The first blood vessels also appeared in the scaffolds at 1 and 2 weeks. After 8 and 16 weeks, there were virtually no inflammatory cells or giant cells present in and around the scaffolds (Fig. 2D F). The collagen bundles of the scaffolds had become thinner, and the scaffolds themselves seem to have decreased in size. In the next sections, some histological aspects have been quantified and additional (immuno) histochemical staining performed.

3.1.3. *Cell density*

The cell density within the scaffolds was determined on H&E stained sections (Fig. 2). At one week, cells had already infiltrated the scaffolds (Fig. 2A C) while full ingrowth was visible after 16 weeks (Fig. 2D F). There was a gradual increase in cell density from 1 week (Fig. 2G; mean $\pm$ S.D.: 9.8 ± 2.2, 12.0 ± 1.4 and 10.2 ± 1.6, respectively, for palate, back, and skull), until 8 weeks (mean $\pm$ S.D.: 19.4 ± 1.4, 27.8 ± 4.7, and 26.1 ± 6.0). After 2 weeks, a significantly higher density was observed in the back samples, compared with the other two locations (mean $\pm$ S.D.: 21.4 ± 3.0 vs. 13.3 ± 1.9 (palate) and 13.8 ± 3.1 (skull)). After 8 weeks, this difference remained between the back and the palate samples (mean $\pm$ S.D.: 27.8 ± 4.7 vs. 19.4 ± 1.4). At 16 weeks, no more statistical differences were found among the different locations (Fig. 2G). The cell density in the palate samples seemed to be consistently lower than in the skin samples, but this was mostly not significant at the separate time points. At 1 and 16 weeks, the cell density outside the scaffolds was also determined for comparison. Among the three locations, no differences were found at 1 week (mean $\pm$ S.D.: of 22.2 ± 2.7 (palate), 19.9 ± 2.1 (back) and 20.1 ± 1.8 (skull)) or at 16 weeks (mean of 20.7 ± 1.9 (palate), 19.3 ± 1.7 (back) and 20.2 ± 1.6 (skull)). At 1 week, the cell density in the scaffolds was significantly lower than outside the scaffolds, while at 16 weeks no significant differences remained.

3.1.4. *Inflammation*

Inflammation was scored on a scale from zero to three on ED 1 stained sections (Fig. 3). ED 1 also stains giant cells, but these were counted separately on the H&E stained sections (see below). At 1 week, inflammatory cells were mainly found at the edges of the scaffolds in the palate (Fig. 3A) and the skull samples (Fig. 3C). However, in the back samples (Fig. 3B), inflammatory cells were already observed inside the scaffolds. The inflammatory response was significantly higher than in the skull samples (Fig. 3G; median of 1.7 vs. 0.7). At 2 and 4 weeks, inflammatory cells were observed both in and around all scaffolds. The median of the scores ranged from 1.7 to 2.0 (Fig. 3G). At 8 weeks, less inflammatory cells were visible; at 16 weeks almost all inflammatory cells had disappeared (Fig. 3D F). In the sham samples, groups of inflammatory cells present after 1 week had largely disappeared 1 week later (not shown).

The number of giant cells in the scaffolds was counted on the H&E stained sections (Fig. 4). There was a general increase in the number of giant cells from 1 week (see Fig. 2A C) to about 2 weeks (Fig. 4A C). After 8 weeks, their numbers decreased. At 2 and 8 weeks, there were signifi cantly more giant cells present in the back samples, compared with the other two locations (Fig. 4D; 2 weeks: 42.1 vs. 11.2 (palate) and 24.8 (skull); 8 weeks: 34.9 vs. 10.4 (palate) and 26.7 (skull)). At 16 weeks, the palate samples contained significantly fewer giant cells than the back samples (mean 4.3 vs. 15.1).

3.1.5. *Myofibroblasts*

α Smooth muscle actin was detected in blood vessels and in myofibroblasts (Fig. 5). There were marked differences in myofibroblast scores related to time and location. At 1 week, myofibroblasts were abundantly present at the borders of the scaffolds in the palate; but only a few myofibroblasts were present in the skin samples (Fig. 5A C). This resulted in a significant difference between the myofibroblast score after 1

implantation. (C) Skull sample 1 week after implantation. (D) Palatal sample 16 weeks after implantation. (E) Back sample 16 weeks after implantation. (F) Skull sample 16 weeks after implantation (bar = 100 μm). Scaffolds (*) and myofibroblasts (arrows) are indicated. (G) Myofibroblast scores. Box plots display the 25th, 50th, and 75th percentiles, if available. (*) denotes a significant difference between the palate samples and the skin samples. (#) denotes a significant difference between the palate samples and the skull samples.

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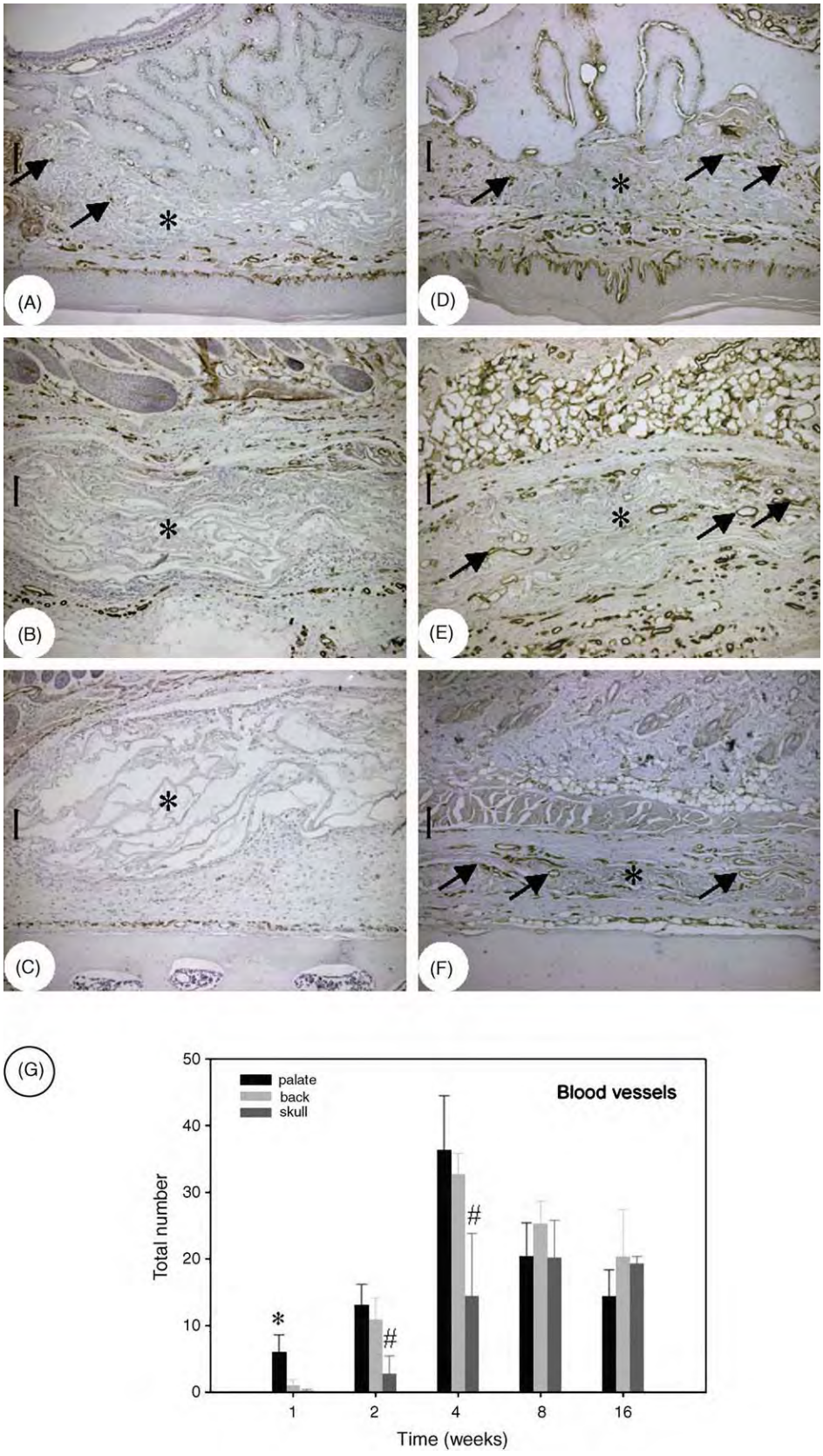

Fig. 6 – Blood vessels. Blood vessels are stained with an antibody against collagen type IV, which stains all basement membranes. Representative collagen type IV-stained sections of 1 and 16-week samples are shown. The number of blood vessels increased up to 4–8 weeks after implantation. (A) Palatal sample 1 week after implantation. (B) Back sample 1 week after implantation. (C) Skull sample 1 week after implantation. (D) Palatal sample 16 weeks after implantation. (E) Back

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week in the palate samples and the skin samples (Fig. 5G; median of 1.0 vs. 0.3 and 0.0). One week later, the number of myofibroblasts in the scaffolds reached its maximum and they were found throughout the scaffolds. A significant difference remained between the palate and the skull samples (Fig. 5G; median of 2.0 vs. 1.0). At 4 weeks, only a few myofibroblasts remained. At 8 and 16 weeks, myofibroblasts were no longer present (Fig. 5D G). In the sham groups, myofibroblasts were also present in the palatal samples after 1 and 2 weeks, but there were fewer in the skin samples (not shown).

3.1.6. *Vascularisation*

The number of newly formed blood vessels within the scaffolds was counted on sections stained for type IV collagen, which is present in all basement membranes (Fig. 6). A gradual increase in the number of blood vessels was found from 1 week (Fig. 6A C) to 4 weeks (Fig. 6G). At 1 week, a significantly higher number of blood vessels was found in the palate samples, compared with the skin samples (mean of 5.9 (palate) vs. 0.9 (back) and 0.1 (skull)). At 2 weeks, significantly fewer blood vessels were counted in the skull samples, compared with the other two groups (mean of 2.7 (skull) vs. 13.0 (palate) and 10.8 (back)). These differences remained at 4 weeks (mean of 14.4 (skull) vs. 36.2 (palate) and 32.6 (back)). At 8 and 16 weeks, the number of blood vessels seemed to stabilize (Fig. 6G) and there were no longer any significant differences at the different locations (Fig. 6D F).

4. Discussion

The tissue reactions to collagen scaffolds implanted in the skin have been described extensively. In general, a mild transitional inflammatory response occurs and new tissue ingrowth is observed, indicating the biocompatibility of these scaffolds.[22,23] In the field of cleft palate repair, but also in periodontal regeneration therapy, collagen scaffolds might be of clinical value. However, the tissue reactions to collagen implanted in the oral mucosa are largely unknown. The aim of this study was to analyze the tissue reactions to collagen scaffolds implanted in the palatal mucoperiosteum and to compare these with the reactions to scaffolds implanted subcutaneously on the skull and on the back of rats.

Both in the palate and in the skin, the scaffolds proved biocompatible, as no severe tissue reactions were observed. These findings are in agreement with studies on collagen scaffolds implanted in the skin and in the gingival mucosa.[23,7] However, marked differences in tissue reactions occurred among the three locations in the first 4 weeks after implantation. The back samples showed a stronger initial inflammatory response, a higher number of giant cells and faster ingrowth of cells than the other samples. The stronger inflammatory response might be caused by the higher mobility of this tissue. The skull skin and the mucoperiosteum both possess an underlying bony structure. Therefore, we assume that the mechanical conditions in the tissue are similar. The mechanical conditions in the back skin are different as it is more mobile, and not supported by bone. Repeated mechanical irritations are known to induce local inflammations, for example, around percutaneous devices.[24,25] Inflammatory cells are known to produce chemotactic factors, which might stimulate faster ingrowth of cells and the generation of giant cells.[26]

Distinct differences were also found in myofibroblast numbers during the first 2 weeks. Myofibroblasts are essential for wound contraction and scar formation during wound healing.[27,28] The palate samples initially showed a larger number of myofibroblasts than both the skin samples, but after 4 weeks these differences had disappeared. Studies on oral wound healing models show similar results. Myofibroblast numbers in palatal wounds in rats and dogs showed a maximum around 8 days,[29–32] while in skin wounds the maximum generally occurred later.[31,33] This indicates that myofibroblast differentiation and migration into the wounds is slower in skin than in the palate. This also correlates with the general observation that wounds in the oral mucosa heal faster than dermal wounds.[12,34] The oral environment is clearly different; and a specific fibroblast phenotype has been described in vitro.[35,10] The oral environment is characterized by the presence of saliva, which contains many active proteins such as growth factors and antimicrobial factors.[39] The healing of incisional and open wounds in the oral mucosa is generally reported to occur faster and to be more fetal like [12,10,36] with less scarring than skin wounds.[12,34] Desalivated oral wounds also contain fewer myofibroblasts than control oral wounds, which also appear later.[37] This shows the crucial role of saliva in the oral wound healing process. On the palate, wound healing was reported to be delayed, compared to skin.[14] That study, however, used an open wound model and only followed the healing process for 2 weeks.

Marked differences were also found in the vascularization of the scaffolds in the first 4 weeks. Initially, vascularization progressed faster in the palate samples than in both the skin samples. Vascular endothelial growth factor (VEGF) is considered to play a critical role in angiogenesis[38] and is also present in saliva.[39] Furthermore, fibroblast growth factor 2 (FGF 2) in saliva acts synergistically with VEGF.[40] The growth factors in saliva might therefore cause the faster vascularization. Comparing the two skin locations, vascularization of the scaffolds was faster in the back than in the skull samples. In the back skin, vascular ingrowth can occur from all sides, while in the skull skin the scaffolds are directly situated on the bone. This probably reduces access for new blood vessels.

In summary, we conclude that, especially in the first few weeks after implantation, both environmental factors and

sample 16 weeks after implantation. (F) Skull sample 16 weeks after implantation (bar = 100 μm). Scaffolds (*) and blood vessels within the scaffolds (arrows) are indicated. (G) Numbers of blood vessels within the scaffolds (mean ± S.D.). (*) denotes a significant higher number of blood vessels in the palate samples compared with the skin samples at 1 week. (#) denotes a significant lower number in the skull samples compared with the back and palate samples.

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local mechanical factors play an important role in the tissue reactions to implanted collagen scaffolds. A sustained inflammatory response or extensive foreign body reaction did not occur at any of the locations, indicating that the collagens scaffolds are biocompatible in all three locations, including the palate. Collagen scaffolds, either or not with additional growth factors, might therefore be suitable for improving cleft palate repair.

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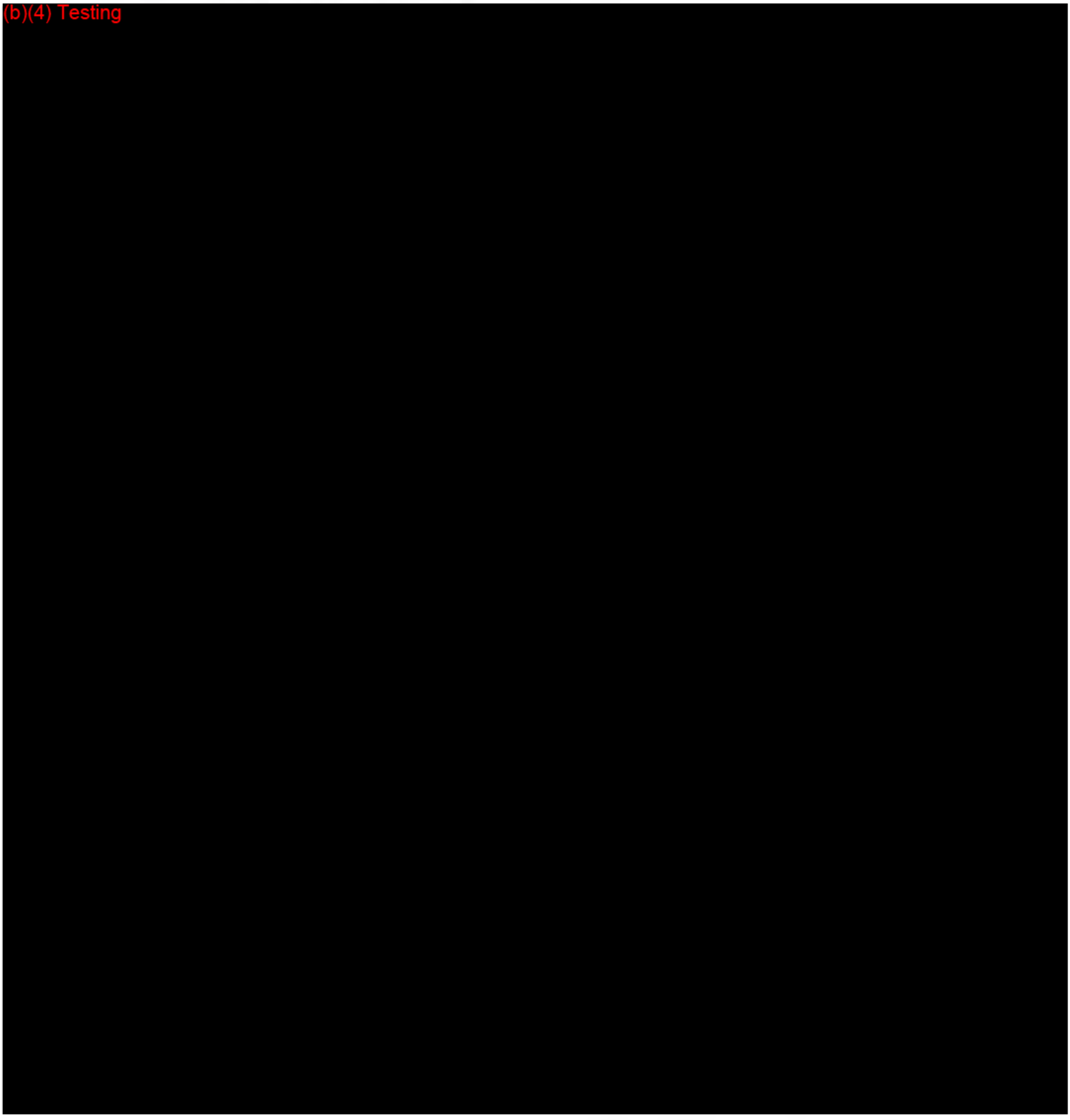

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Section 20: Performance Testing – Clinical

20 PERFORMANCE TESTING – CLINICAL

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Appendix 20-4 ((b)(4) Testing)

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Appendix 6 – Human Elisa

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An improved enzyme-linked immunosorbent assay of anti-collagen antibodies in human serum

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An improved enzyme-linked immunosorbent assay (ELISA) for the determination of anti-collagen antibodies in human serum has been developed. The method is based on the use of serum samples diluted to 1/50 with heat-inactivated normal rabbit serum adjusted to pH 8.0 with solid Tris (0.05 M), NaCl (0.15 M) and 2 M HCl. The use of normal rabbit serum minimizes non-specific adsorption of immunoglobulin G onto the plastic surface of microtiter plate. The applicability of the method for the quantitation of anti-collagen antibodies in human serum is demonstrated with 290 specimens of sera from normal controls (194) and patients with rheumatoid arthritis (96).

Key words: Anti-collagen antibody; ELISA; Serum, human; Serum, normal rabbit; Rheumatoid arthritis

Introduction

Enzyme-linked immunosorbent assay (ELISA) system is an extremely useful technique for detecting antibodies to a variety of antigens. The ELISA system has proven to be very sensitive for quantitative and qualitative analysis of antibodies experimentally produced in animals against different types of collagen (Gosslau and Barrach, 1979; Terato et al., 1985; Minamoto et al., 1988). However, it is obvious that an improved assay method is needed for an accurate analysis of human antibodies against collagens, because of their low serum titers and the problems of non-specific reactions (Beard et al., 1979, 1980; Claque et al., 1983). This need is most evident in the study of anti-collagen autoantibodies often found in the sera of patients with connective tissue diseases, such as rheumatoid arthritis (RA) (Andriopoulos et al., 1976; Stuart et al., 1983; Wooley et al., 1984; Jasin, 1985; Watson et al., 1986) and relapsing polychondritis (RP) (Ebringer et al., 1981), where hypergamma-globulinemia is a frequent problem.

During the course of assaying sera from RA patients and normal healthy controls by a conventional ELISA (Gosslau and Barrach, 1979; Mackel et al., 1982), we observed wide variations of anti-

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Abbreviations: BSA, bovine serum albumin; CII, chick type II collagen; ELISA, enzyme-linked immunosorbent assay; HI, human type I collagen; HII, human type II collagen; HIII, human type III collagen; IgG, immunoglobulin G; NRS, normal rabbit serum; OD, optical density; RA, rheumatoid arthritis; RF, rheumatoid factor; RP, relapsing polychondritis.

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body titers from lot to lot of commercially available microtiter plates. Even control sera which are negative for anti-collagen antibodies show certain levels of reactivity regardless of collagen types coated on microtiter plate, suggesting a non-specific interaction of some serum components with plastic. Therefore, our efforts were aimed at understanding these interactions and developing a method which would minimize the non-specific reactivity and provide an assay with increased sensitivity.

Materials and methods

Serum specimens

Serum specimens from 96 patients with RA were stored at −20°C until use. Diagnosis of the disease were established according to the American Rheumatism Association criteria (Medsger and Masi, 1985). Another 194 specimens of sera from normal volunteers were used as controls.

Serum from a patient with classical RA who gave a high antibody titer was employed as positive control for the assay of anti-type II collagen antibodies. Serum obtained from a cynomolgus monkey with arthritis, induced by immunization with 1 mg of chick type II collagen (CII) in complete Freund's adjuvant, was also used for comparison (Terato et al., 1989).

Microtiter plates

Five different types of microtiter plate, Nunc UII (polystyrene, Roskilde, Denmark), Falcon 3910 (polystyrene, Becton Dickinson and Co., Lincoln Park, NJ), Costar Serocluster U (polyvinylchloride, Cambridge, MA), Eisai U plate (polystyrene) and gamma ray-irradiated Eisai U plate (Tsukuba, Ibaraki), were used to compare the binding capacity of human immunoglobulin G (IgG) and the sensitivity for anti-collagen antibody assay.

Preparation of collagens

Human type I (HI, from skin) (Epstein, 1974) and type III collagen (HIII, from placenta) (Fujii et al., 1986) were prepared by solubilization with limited pepsin digestion and by differential salt precipitation. Type II collagen was prepared from human articular cartilage (HII) and chick sternal cartilage (CII) respectively as reported (Miller, 1973).

Assay of anti-collagen antibodies

Antibodies against collagen were detected by ELISA. In this assay system, normal rabbit serum (NRS) was used as a blocking agent to diminish non-specific reactions which were conspicuously observed in ELISA for human sera. NRS was heat-inactivated for 20 min at 62°C and adjusted to pH 8.0 by adding solid Tris (0.05 M), NaCl (0.15 M) and 2 M HCl (buffered NRS). The tests were performed in commercially available microtiter plates which were coated with various types of collagen as antigens. Each collagen was dissolved in 0.05 M acetic acid at a concentration of 3 mg/ml, diluted with phosphate buffer ($\mu = 0.4$), pH 7.6, to the final concentration of 5 μg/ml and added to microtiter plates in 100 μl aliquots. The plates were sealed with adhesive plastic covers and kept overnight at 4°C. Prior to incubation with serum samples, the collagen-coated plates were washed with saline containing 0.05% Tween 20 (saline-Tween) three times, then coated with 100 μl of buffered NRS for 30 min at room temperature and finally washed with saline-Tween three times. Sera to be examined were diluted to 1/50 with buffered NRS and transferred to the wells in 100 μl aliquots. The plates were incubated for 2 h at room temperature and washed with saline-Tween three times. Peroxidase-conjugated rabbit anti-human IgG (Fc-specific) antibody (Cooper Biomedical Laboratories, Cochraville, PA) was diluted to 1/2000 with 0.1 M Tris-buffered saline, pH 8.0, containing 25% NRS and 100 μl was added to each well. After a 2 h incubation at room temperature, the plates were washed and developed using 100 μl of 0.05% *o*-phenylenediamine and 0.017% H_2O_2 dissolved in citrate-phosphate buffer, pH 5.0, as described previously (Terato et al., 1985). After incubation at room temperature (24–27°C) for 60 min, the reaction was stopped by adding 50 μl of 1.25 M H_2SO_4, and the optical density (OD) at 492 nm was measured using a microplate photometer (Type MTP-22, Corona Electric Co., Saitama, Japan). As a blank for each serum specimen, uncoated wells were run in parallel and the OD value (OD_{NON}) was subtracted

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from that of HII-coated (OD_{HII}) or HI-coated wells (OD_{HI}).

Inhibition assays

The specificity of the anti-collagen antibodies was monitored by inhibition tests with native or heat-denatured collagens by using the ELISA system described above with the exception that the sera were incubated for 1 h at 4°C before assay with 50 μl of each inhibiting antigen diluted with buffered NRS.

Results

Prevention of non-specific adsorption of human IgG on the plastic surface of microtiter plate by normal rabbit serum

To minimize the non-specific adsorption of human IgG on the plastic surface of microtiter plates, the effects of varying concentrations of NRS on the adsorption of human IgG onto a plastic surface were examined by using five different microtiter plates. As shown in Fig. 1*a*, the amount of IgG adsorbed was decreased with an increasing concentration of NRS. The presence of 50% or higher concentration of NRS in the serum sample was shown to minimize the adsorption of IgG, although the level of adsorption varied from plate to plate. The blocking effect of NRS seems to be due to competitive binding of rabbit IgG on the plastic surface, since rabbit IgG also showed high adsorption capacity to the microtiter plate (data not shown).

When adsorption of normal and RA sera on the plastic surface was compared by taking serially diluted sera with buffered NRS, RA sera at low dilutions gave much higher OD values than normal sera, suggesting a higher content of IgG in RA serum (Fig. 1*b*). Therefore, serum samples diluted to 1/50 with buffered NRS were used in the following experiments to prevent non-specific binding of IgG.

Selection of microtiter plate with high sensitivity and low background

In order to select an ELISA plate with high sensitivity and low background, standard sera from

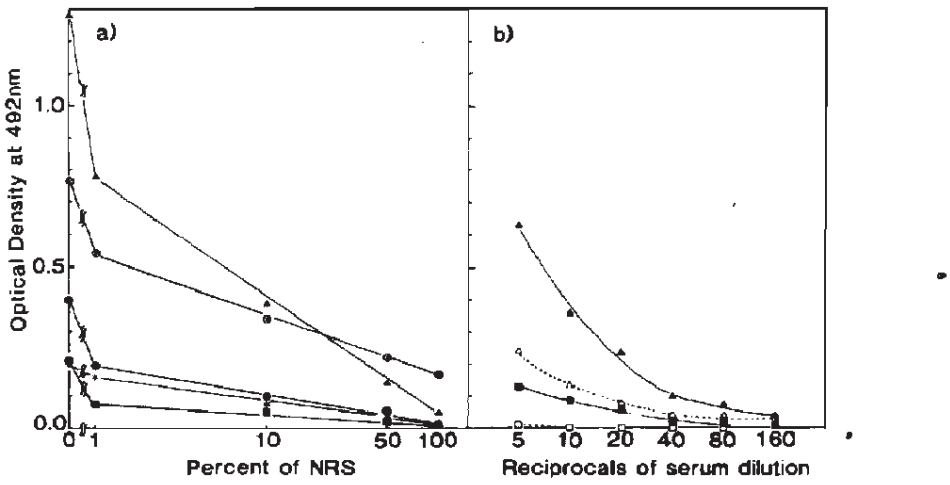

Fig. 1. Inhibitory effect of NRS on the hydrophobic adsorption of human IgG onto plastic surface of microtiter plates. *a*: serum from a patient with RA was diluted to 1/10 with 0.1 M Tris-HCl buffer, pH 7.5, containing 0.15 M NaCl and varying concentrations of NRS. Aliquots (100 μl each) of the diluted serum were added to microtiter plates and reacted for 2 h at room temperature. The amount of IgG adsorbed on the plates was determined by ELISA using peroxidase-conjugated rabbit anti-human IgG (Fc) as described in the text. ▲, Nunc UII (polystyrene); ●, Costar Serocluster U (polyvinyl chloride); ■, Falcon 3910 (polystyrene); *, Eisai (polystyrene); *, γ ray-irradiated Eisai plate. *b*: hydrophobic adsorption on microtiter plates of normal and RA sera serially diluted with buffered NRS. ▲, Nunc UII/RA serum; △, Nunc UII/normal serum; ■, Falcon 3910/ RA serum; □, Falcon 3910/normal serum.

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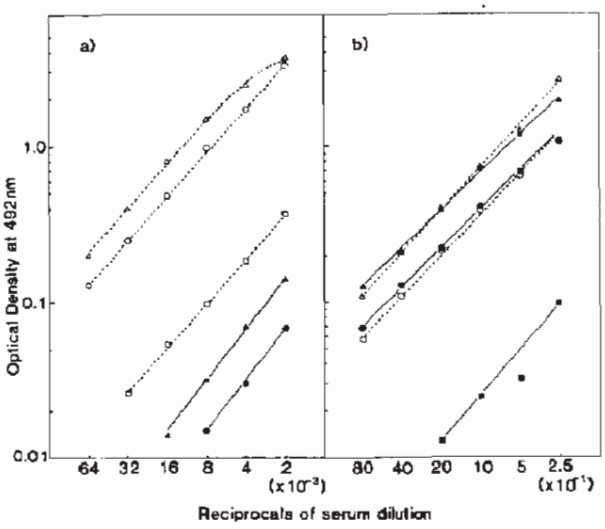

Fig. 2. Comparison of the sensitivity of ELISA for anti-type II collagen antibodies on three different microtiter plates. Sera from a collagen-induced arthritic monkey (*a*) and from a patient with RA (*b*) were assayed for the antibody titers using CII (open symbols) or HII (closed symbols) coated plates. Nunc UII (triangle), Costar (circle) and Falcon (square) plates were used. The data on monkey serum with HII-coated Falcon plate and RA serum with CII-coated Falcon plate are not shown because of their low OD values.

a monkey and a RA patient were tested on three different plates coated with CII or HII. As shown in Fig. 2*a*, Nunc and Costar plates gave high OD values in the assay for anti-CII antibodies in monkey serum. On the other hand, the Falcon plates only gave 1/10 of the OD values in comparison to the Nunc and Costar plates. Similar results were obtained with RA serum using HII- or CII-coated plates (Fig. 2*b*), indicating a poor adsorption of type II collagen on the Falcon plate. From the results described above, microtiter plates made of polyvinylchloride seem to be better for assaying anti-collagen antibodies among the plates tested.

Evaluation of the present method by using control and RA sera

To further confirm the applicability of the present ELISA system and to examine the variation of non-specific reactions in Costar plates, 100 specimens of sera from normal controls were assayed using uncoated, HI-coated and HII-coated wells. The OD values (mean ± SD) on these respective wells were as low as 0.02 ± 0.03, 0.03 ± 0.04 and 0.04 ± 0.04. The OD values on HI- and HII-coated wells (OD_{HI}, OD_{HII}) correlated with those on uncoated wells (OD_{NON}) (correlation coefficient: $r = 0.97$, $P < 0.001$ and $r = 0.82$, $P < 0.001$, respectively) as shown in Figs. 3*a* and 3*b*, again indicating that non-specific reactions observed in the present ELISA are due to the adsorption of IgG on plastic surface. OD values obtained with HI- and HII-coated plates were not statistically different from those seen with uncoated plates. Therefore, uncoated wells assayed with each serum specimen were employed as a blank. Based on this approach, antibodies against HI and HII were not detected in 194 sera from normal controls. The maximum OD values for corrected OD_{HI} and OD_{HII} in normal sera were 0.109 and 0.090, respectively.

Similar results were obtained when 96 unselected RA sera were examined, giving OD_{HI} values of 0.15 ± 0.13 and OD_{NON} of 0.13 ± 0.09, and the correlation coefficient between OD_{HI} and OD_{NON} was 0.82 ($P < 0.001$). Moreover, 7 (7.3%) and 20 (20.8%) of RA sera gave corrected OD_{HI} and OD_{HII} values greater than 0.1, whereas none of the normal individuals exceeded the value (Fig. 4). To exclude false positive reactions, inhibition tests using each collagen were performed to confirm the specificity of the antibody. When the

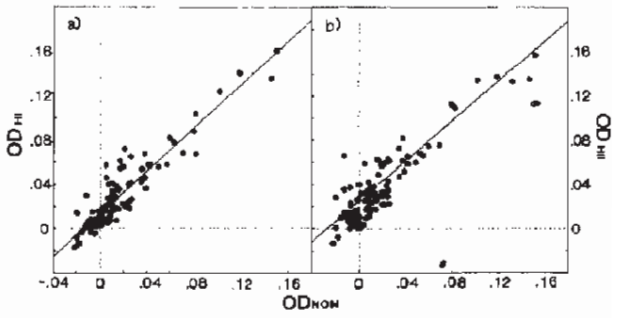

Fig. 3. Regression analysis of OD values against uncoated, HI- or HII-coated microtiter plates in ELISA for normal sera. 100 specimens of normal sera diluted to 1/50 with buffered NRS were reacted with uncoated, HI- or HII-coated wells of Costar plates as described in Fig. 1. Relationships between OD values of uncoated (OD_{NON}) and HI-coated (OD_{HI}) plates (*a*) and between OD_{NON} and OD values of HII-coated plate (OD_{HII}) (*b*) were shown by regression lines. *a*: $Y = 0.99X + 0.01$ ($r = 0.97$, $P < 0.001$). *b*: $Y = 0.91X + 0.02$ ($r = 0.82$, $P < 0.001$).

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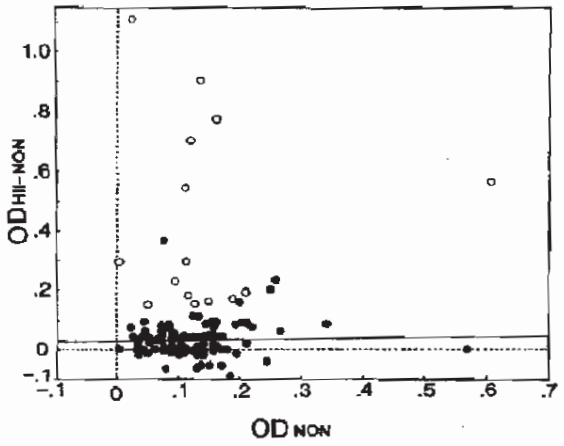

Fig. 4. Distribution patterns of corrected OD_{HII} ($OD_{HII} - OD_{NON}$) against OD_{NON} in RA sera. 96 specimens of RA sera diluted to 1/50 with buffered NRS were reacted with uncoated and HII-coated wells as described in Fig. 3. The OD values for OD_{NON} (blank value for each serum) were subtracted from OD_{HII} and were plotted against corresponding OD_{NON}. Open circle indicates anti-type II collagen antibody positive sera. An equation for regression line shown by a solid line; $Y = 0.024X + 0.03$ ($r = 0.032$, $P < 0.01$) was obtained from 81 specimens of antibody negative sera.

serum sample was inhibited more than 50% by a collagen, the result was regarded as positive confirmation. According to inhibition studies, 15 (15.6%) sera shown by open circles in Fig. 4 were confirmed to be positive for anti-HII antibodies. However, all of the sera were negative for anti-HI antibodies (data not shown).

To clarify the effect of serum rheumatoid factor (RF) on this ELISA system, we compared the OD_{NON} and OD_{HII} values of IgM-RF positive and negative sera from RA patients. IgM-RF levels were determined by hemagglutination test (Fujirebio, Tokyo). There were no significant differences in either OD_{NON} or OD_{HII} values between both groups (Figs. 5*a* and 5*b*), indicating that serum rheumatoid factor does not affect this assay system.

Comparison of the present method with conventional ELISA system

To further evaluate the applicability of the present method for the assay of anti-collagen antibodies, 30 specimens of sera showing relatively high reactivity with native HII by the conventional ELISA system (Gosslau and Barrach, 1979; Mackel et al., 1982) were selected from 510 RA patients as well as 20 specimens of control sera. The samples were assayed for their reactivity against native HI, HII and HIII by comparing the two methods. In the case of the conventional method, serum samples were diluted to 1/50 with 5% bovine serum albumin (BSA)/0.05 M Tris-HCl buffer, pH 7.5, containing 0.15 M NaCl (Gosslau and Barrach, 1979; Mackel et al., 1982) instead of buffered NRS. All of the other procedures in ELISA were the same as those described in the materials and methods section.

As shown in Fig. 6*a*, by conventional methodology, RA sera gave high OD values not only against HII, but also against HI and HIII. Even control sera showed high values ranging from 0.3 to 0.6 against all collagen types employed. On the other hand, assays by the present method using buffered NRS as a blocking agent showed high values only against HII with RA sera. In these assays, the level of OD values for control sera was less than 0.125 (Fig. 6*b*). The comparison of the two assays indicates that non-specific adsorption of human IgG on collagen-coated plates is a problem in the evaluation of anti-collagen antibody titers in human serum, and that the use of buffered

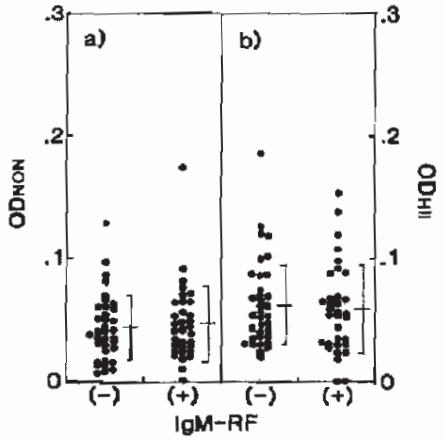

Fig. 5. Effect of serum rheumatoid factor on OD_{NON} and OD_{HII} values in ELISA. Serum IgM-RF negative (−, 35 specimens) and positive (+, 33 specimens) sera from RA patients were compared for the OD_{NON} and OD_{HII} values. IgM-RF was detected by hemagglutination test and defined as positive when hemagglutination occurred at 1/40 or higher dilution. Anti-HII antibody positive sera were not included in this assay.

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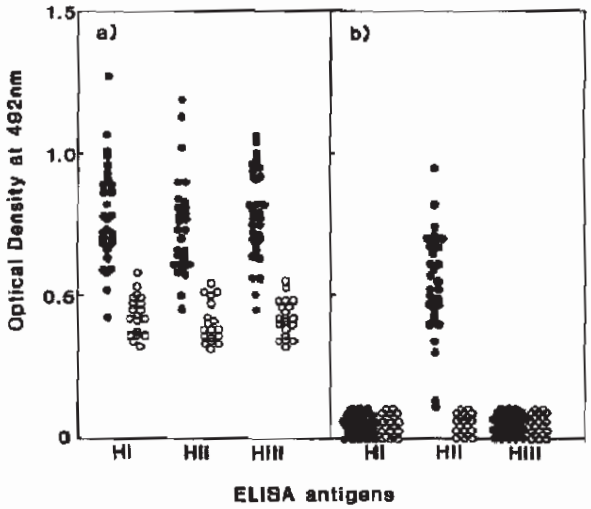

Fig. 6. Comparison of the assay of anti-collagen antibodies in control (20 specimens) and RA (30 specimens) sera by conventional and present ELISA systems. Serum samples diluted to 1/50 with 5% bovine serum albumin (*a*) or with buffered NRS (*b*) were assayed for the reactivity against HI, HII and HIII. ●, RA sera; ○, control sera.

NRS as a blocking agent minimizes the unfavorable interaction of IgG with the microtiter plate. Repeated assays using pooled sera showed reproducible results with a standard deviation of ±3%.

Finally, specific reactions of anti-HII antibodies in RA sera with HII in ELISA were confirmed by inhibition tests using native HI, HII, HIII and denatured HII as inhibitors. All positive reactions with HII in RA sera shown in Fig. 6*b* were inhibited by preincubation with HII (mean ± SD, 95.9 ± 4.5%), while neither HI nor HIII inhibited the reaction against HII (8.6 ± 9.0% and 3.9 ± 6.4%, respectively). A slight, but insignificant inhibition (16.2 ± 15.8%) was observed with denatured HII (Fig. 7*a*), indicating that the predominant reactions with HII are specific for anti-HII antibodies which recognize conformation-dependent epitope(s) rather than its primary structure. However, RA sera also contain a minor population of antibodies which recognize denatured HII since reaction of RA sera with denatured HII and inhibition by denatured HII were not insignificant (Fig. 7*b*).

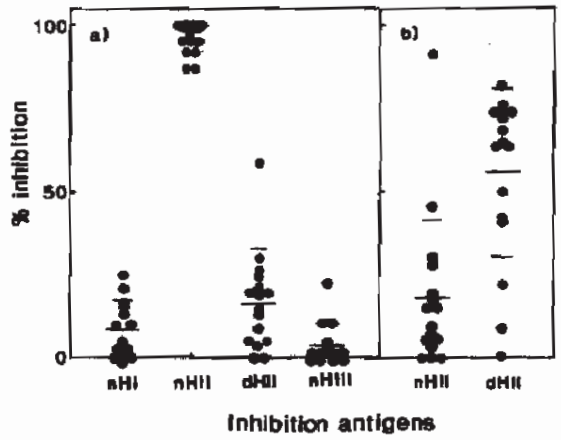

Fig. 7. Inhibition tests for the antibodies against native (*a*) and denatured (*b*) HII. 16 RA sera were diluted to 1/50 with buffered NRS containing each inhibition antigen (50 μg/ml). n, native; d, denatured.

Discussion

A major advantage of the present method is the use of heterologous serum as a blocking agent to minimize non-specific color development under the assay conditions employed. We studied the effect of Tween 20, BSA and different species of animal sera, such as rabbit, chick, bovine, horse and goat, on the diminution of non-specific binding of human IgG on plastic surfaces. It was determined that Tween 20 has no effect in preventing binding of human IgG onto the plastic surface. Also, BSA was found not to be effective, as shown in Fig. 6, since BSA has a poor binding capability to plastic. Although, all of the animal sera were shown to be effective in reducing the non-specific binding of human IgG to plastic, some degree of cross-reactivity with rabbit anti-human IgG antibodies was observed. Thus, we used normal rabbit serum as the blocking agent of the non-specific reaction. Normal goat serum can be used in place of normal rabbit serum, however, goat anti-human IgG antibodies should then be used as the second antibody. This is especially important when the ELISA system is utilized for the detection of anti-collagen antibodies in patient sera, which generally contain little or low levels of the antibodies.

The blocking mechanism by NRS was not fully studied in this experiment, however, IgG components in NRS seem to bind to plastic surfaces by

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competing with human IgG. This was supported by observations that the IgG fraction of NRS eluted from DEAE-cellulose columns reduced the non-specific reactions as effective as NRS, and gave the same OD values for RA sera as those obtained by ELISA using NRS. When this was incorporated into the present ELISA system, false positive reactions with plastic and collagen in both normal and RA sera were effectively minimized, allowing the detection of specific antibodies against type II collagen in RA sera. This finding is consistent with a previous report by Beard et al. (1980), who employed 0.4% NRS as a blocking agent in hemagglutination and solid fluorometric assays.

Subsequent inhibition tests for positive sera to type II collagen confirmed that the antibodies in RA sera were specific for native type II collagen. The antibodies in RA sera were also reactive with denatured type II collagen. This reactivity, however, was much less than that seen with native type II collagen.

It has been reported that antibodies against denatured collagen are more frequent and present in higher levels in RA sera than antibodies against native collagen (Clague et al., 1983; Rowley et al., 1986). It seems possible that some of these phenomena may reflect direct binding of human IgG to collagen (Eeckhout et al., 1979), or indirect binding of IgG to non-antibody proteins such as fibronectin, which are capable of reacting with denatured collagen (Beard et al., 1979). RF is another factor to be considered to affect the assay of antibodies in human sera. However, in this ELISA system, serum RF did not affect both OD_{NON} and OD_{HII} values. The same was true even with RA sera showing IgM-RF values positive at 1/2560 dilutions (data not shown). Unfortunately, we did not detect IgG-RF levels in this experiment. However, abnormal OD values were hardly noticed in more than 1000 RA and non-RA sera, and antigen-specific inhibition was observed. These results indicate that RF shows no significant effect on this assay system. This seems to be due to the adsorption of RF in human sera by excess amount of NRS. However, the most important factor which results in non-specific reactions in radioimmunoassay and ELISA is hydrophobic adsorption of IgG on plastic surfaces. The inclusion of heterologous sera in the assay circumvents this problem, and allows precise identification of specific antibody recognition.

Thus, this method is applicable for detecting anti-collagen antibodies of different isotypes such as IgG, IgM and IgA using the avidin-biotin method. The assay sensitivity of avidin-biotin method is several times higher than the conventional ELISA and is useful for more precise studies on the etiology of RA.

Acknowledgements

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Appendix 7 - Specificity of antibodies to type II collagen in rheumatoid arthritis

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SPECIFICITY OF ANTIBODIES TO TYPE II COLLAGEN IN RHEUMATOID ARTHRITIS

KUNIAKI TERATO, YASUNORI SHIMOZURU, KOU KATAYAMA, YOSHIHARU TAKEMITSU, IZUMI YAMASHITA, MAKOTO MIYATSU, KATSUYUKI FUJII, MITSUSADA SAGARA, SHIEGETO KOBAYASHI, MAKOTO GOTO, KUSUKI NISHIOKA, NOBUYUKI MIYASAKA, and YUTAKA NAGAI

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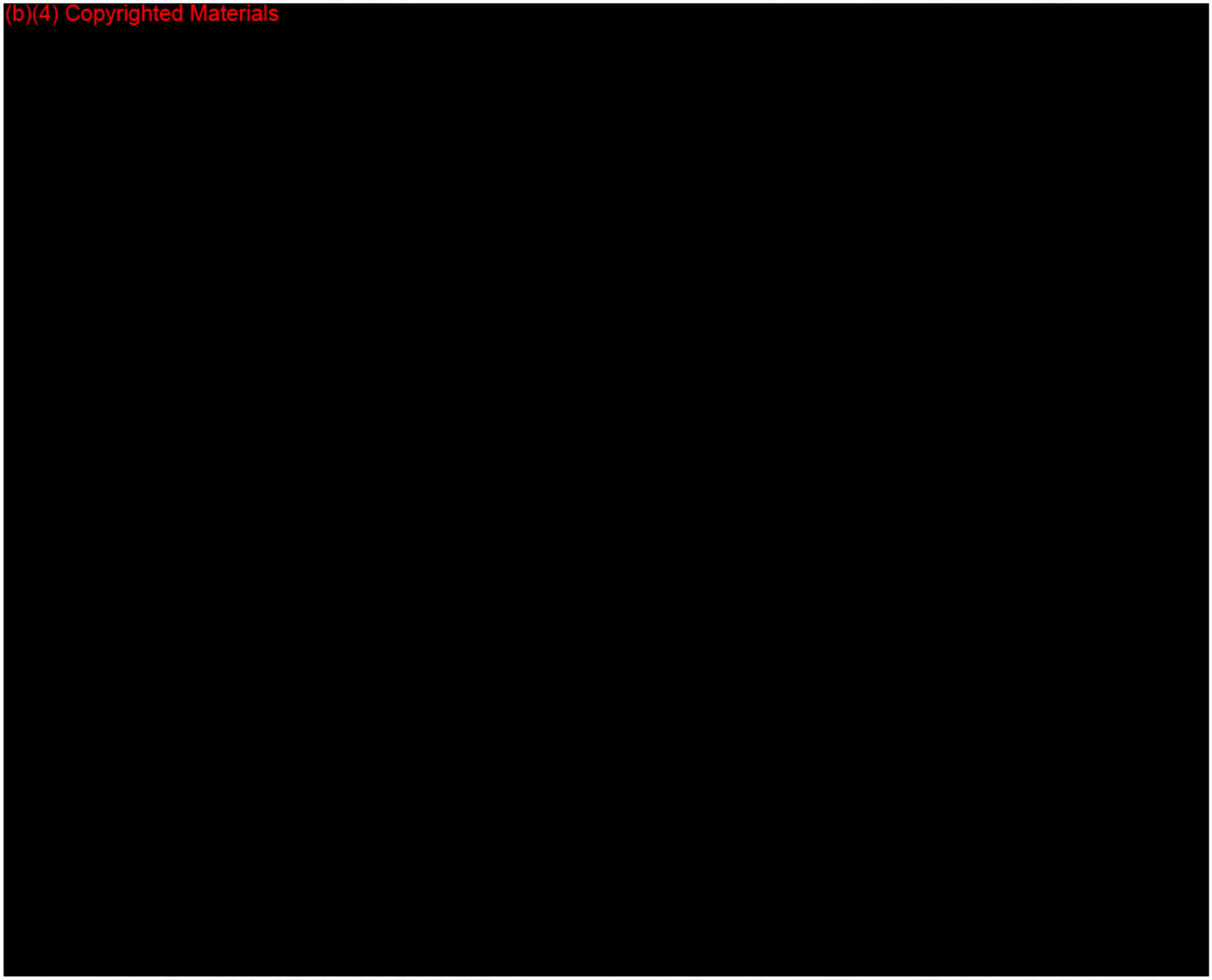

Arthritis and Rheumatism, Vol. 33, No. 10 (October 1990)

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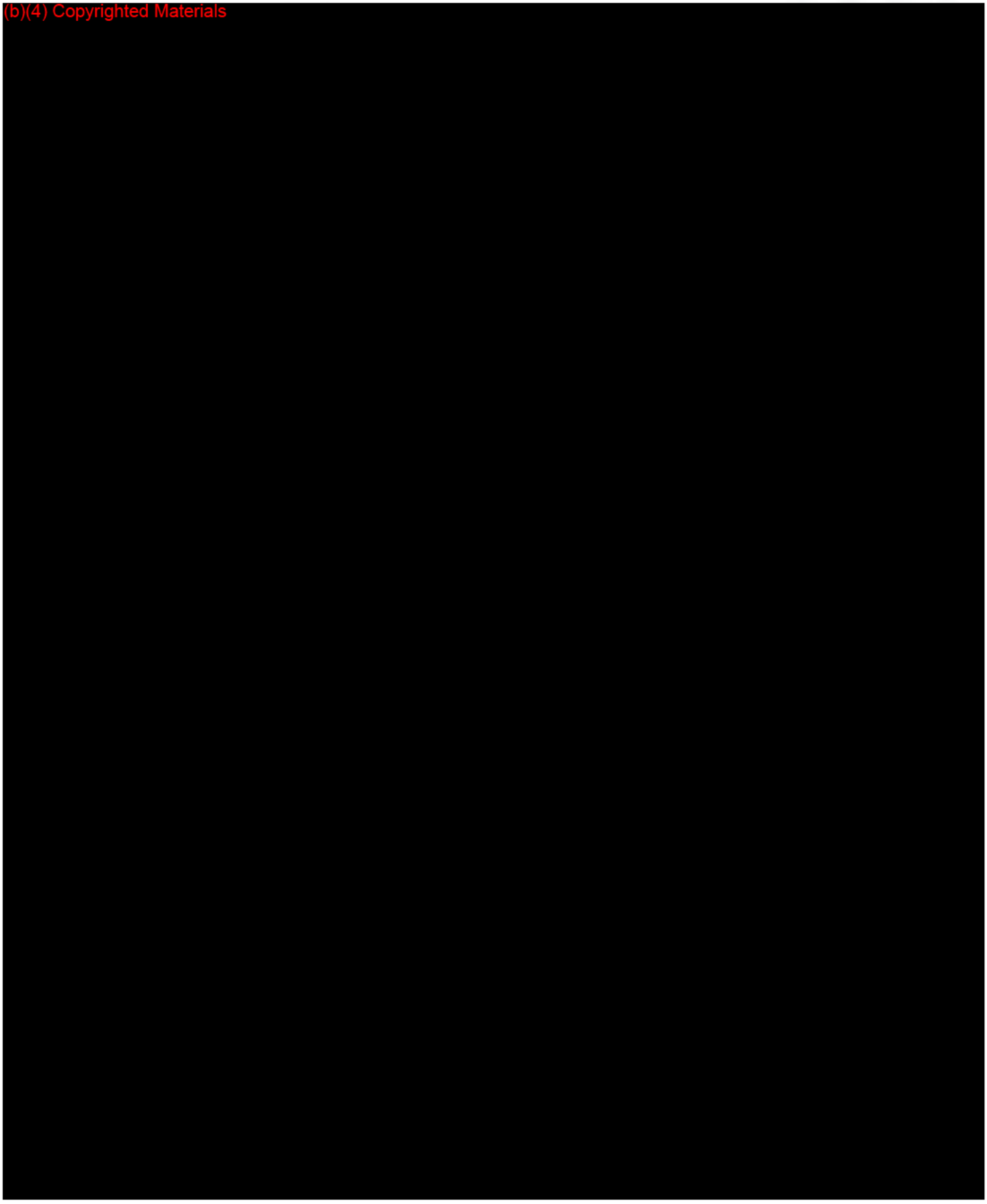

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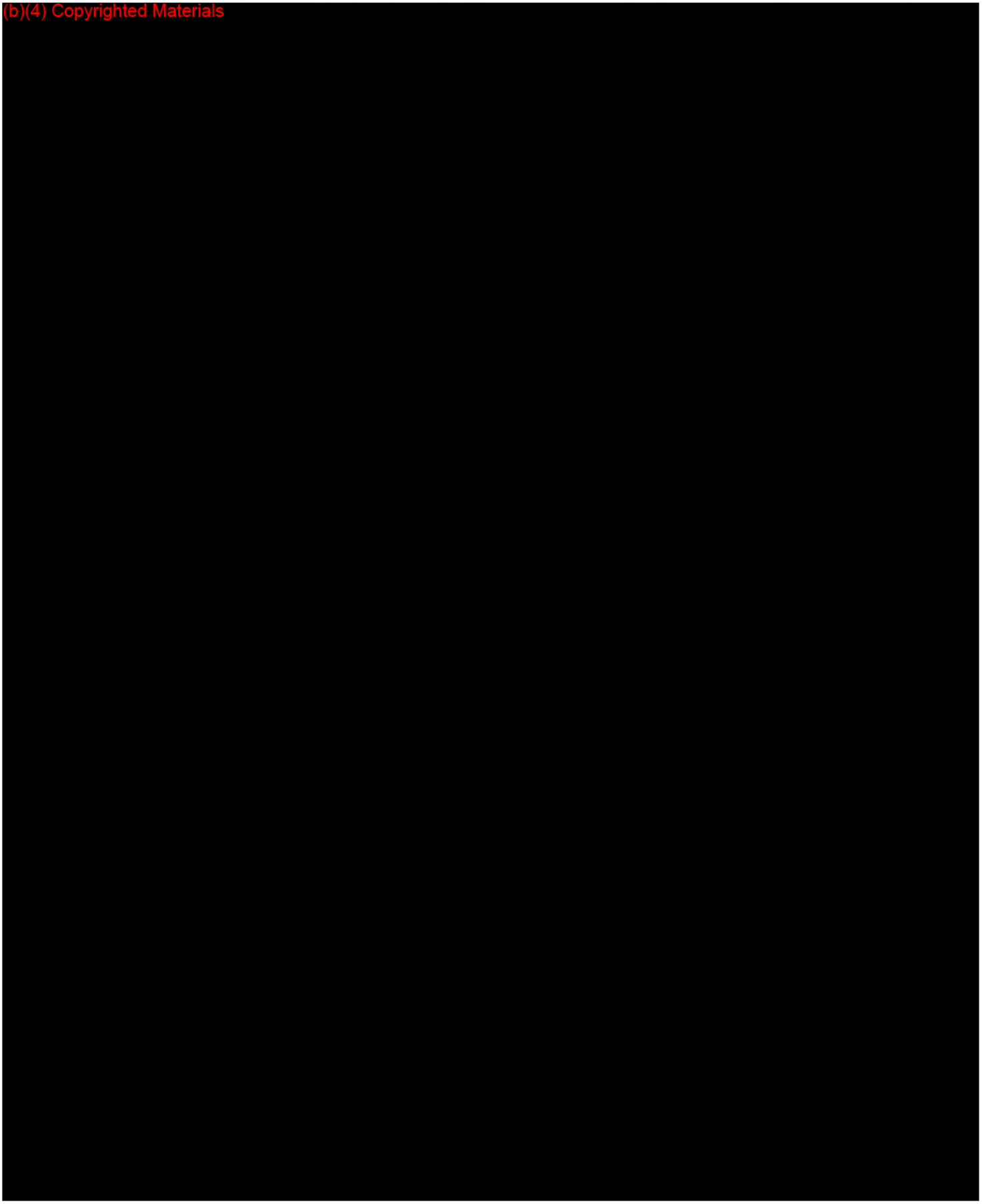

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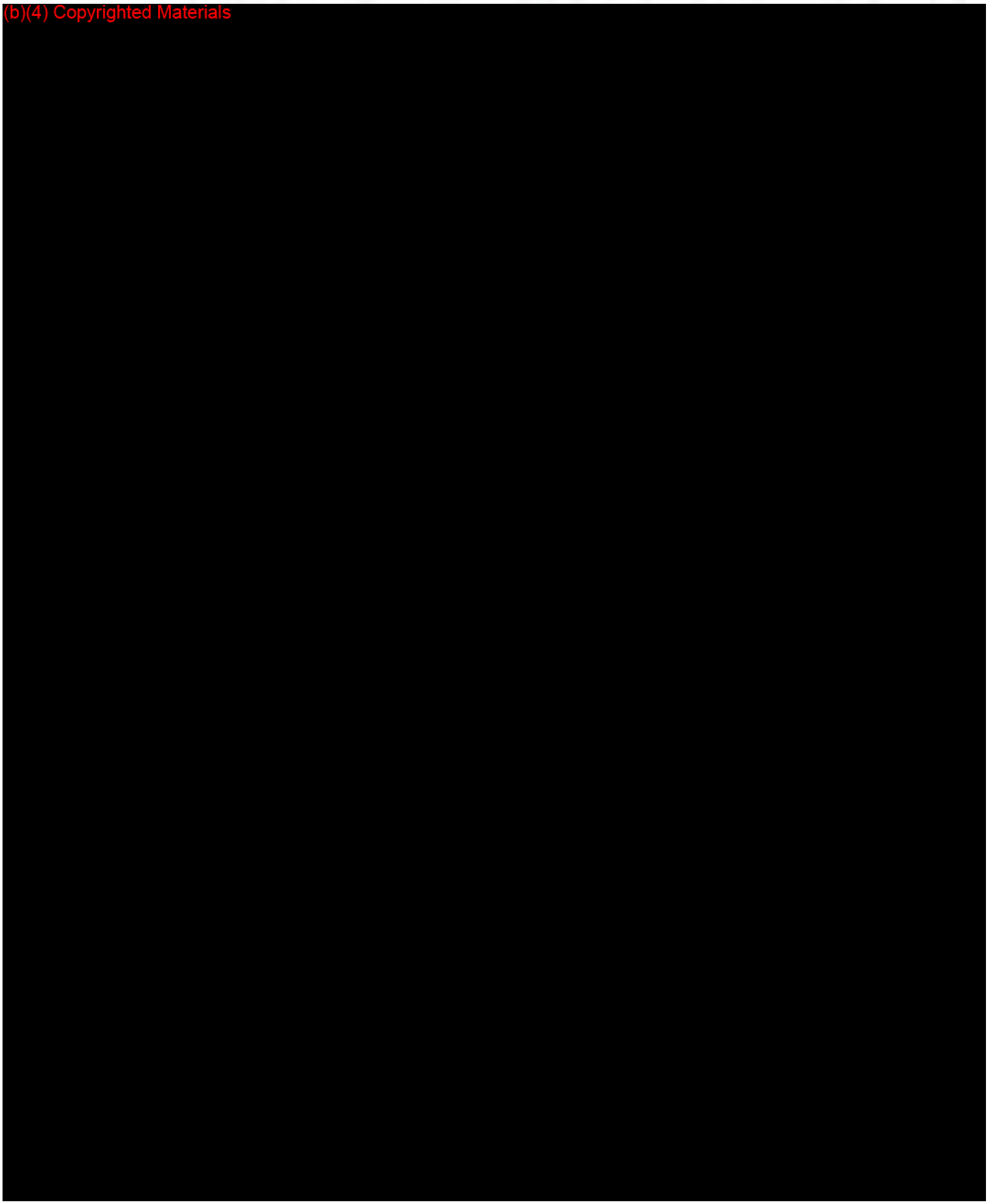

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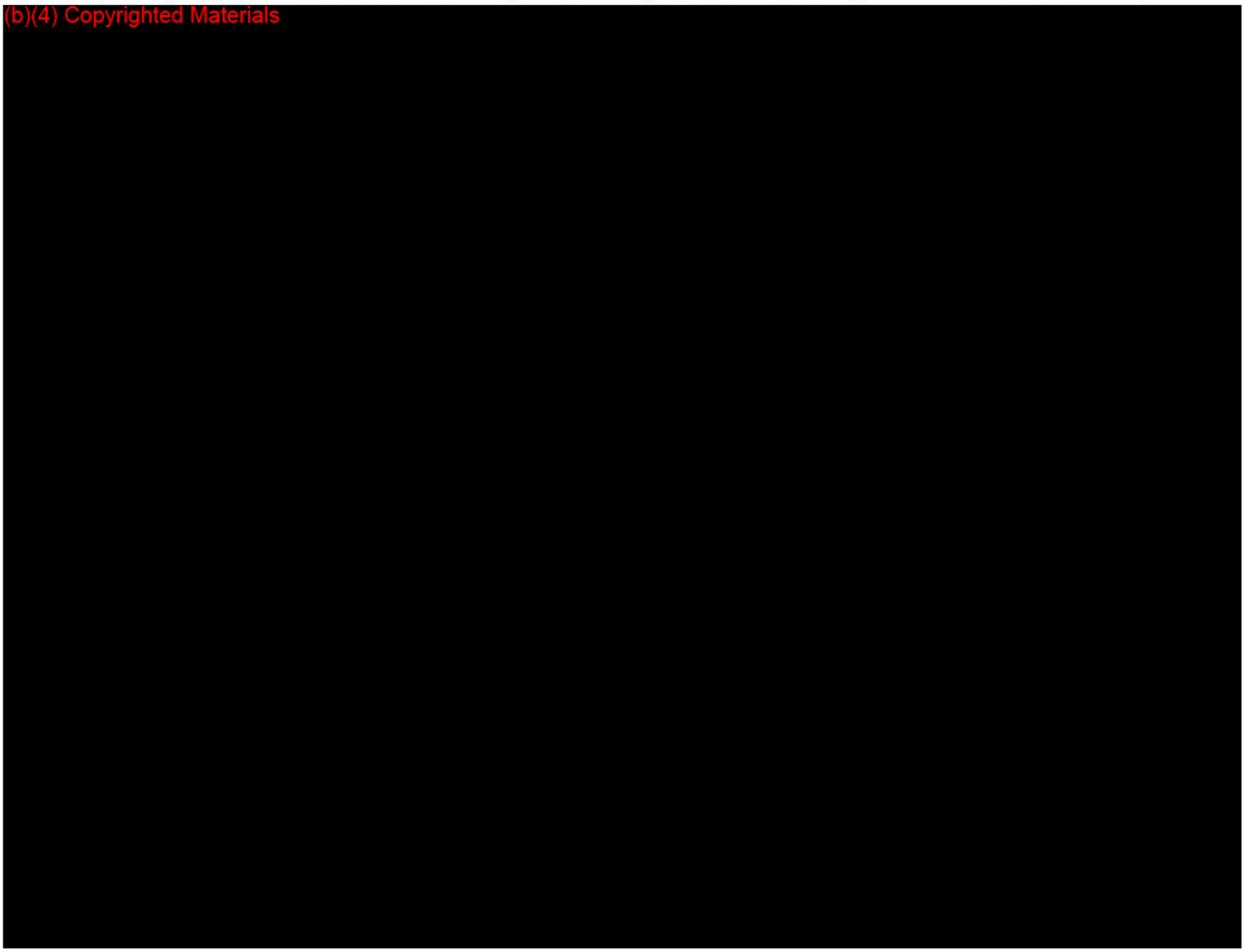

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Appendix 8 – Human IgG Elisa

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Human/Monkey Anti-Type I and Type II Collagen IgG Antibody Assay Kit with TMB

Catalog # 1031T, 1032T, 1033T, 1035T, 2051T, 2052T, 2053T, 2055T

For Research Use Only - Not Human or Therapeutic Use

INTRODUCTION

Species	Type I Collagen Color Coding - Catalog #	Type II Collagen Color Coding - Catalog #
Chick	(CI) Gold - 1031	(CII) Yellow - 2051
Bovine	(BI) Dark Blue - 1032	(BII) Green - 2052
Porcine	(PI) Brown - 1033	(PII) Pink - 2053
Human	(HI) Silver - 1035	(HII) Blue - 2055
Uncoated	Clear	Clear
Standard	Red	Red

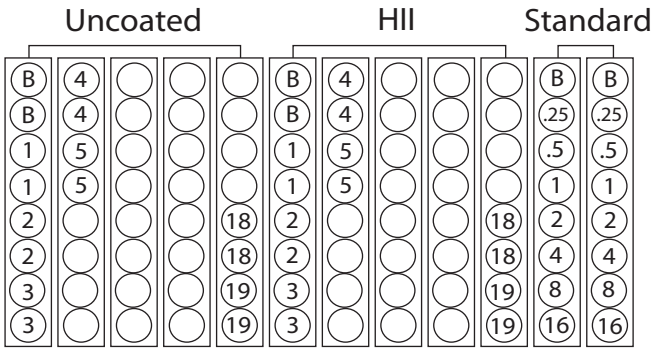
Human sera, especially from patients with autoimmune diseases, contain high levels of immunoreactive components, which yield high background levels in ELISA systems. These non-specific reactions are caused by adhesive immunoglobulins contained in human serum, which strongly adhere to plastic surfaces by hydrophilic binding, and blocking agents such as bovine serum albumin (BSA) and Tween 20, are not capable of blocking these non-specific reactions at all. However, these false positive reactions caused by serum sample itself have not been understood, and are considered as a real antibody-antigen reaction in many cases, even now. In order to obtain a real value of antigen-antibody reaction, it is critical 1) to choose proper blocking agents which block these kinds of non-specific reactions effectively, 2) to determine a unique non-specific background value of individual samples using antigen-non-coated wells and 3) to subtract the background value from the value determined in antigen-coated wells. In addition, it is apparent to determine the non-specific reactions caused by secondary antibody as well. Chondrex's ELISA system incorporates unique blocking agents that inhibit the hydrophobic binding of these serum components onto plastic surfaces and are designed to determine the background values of individual samples using antigen-non-coated wells.

In general, antibodies to collagen in human sera are highly specific to heterologous collagen such as bovine or chick type I and/or type II collagen and cross-react to other species and types of collagen including human collagen, regardless of the disease. For example, serum antibodies even from healthy normal controls react to various species and types of collagen. To determine the human serum antibodies with a significant diversity in the antigen specificity, Chondrex provides various species of type I and type II collagen-coated strips as well as uncoated wells (see table above). This ELISA kit contains enough materials to run two plates on two separate occasions (see assay procedure) and may be used for monkey sera as well as human sera.

Standard ELISA Kit with One Species of Type I or Type II Collagen

Figure 1 shows a standard ELISA kit consisting of five 8-well strips which are uncoated and serve as a control for background levels of individual samples, five 8-well strips coated with one species of type I or type II collagen to determine specific antibody levels, and two 8-well strips for reference standards. "B" represents blank wells to determine non-specific reactions caused by the secondary antibody. Standards and samples are run in duplicate.

Figure 1 - Standard ELISA kit coated with a single species of type II collagen



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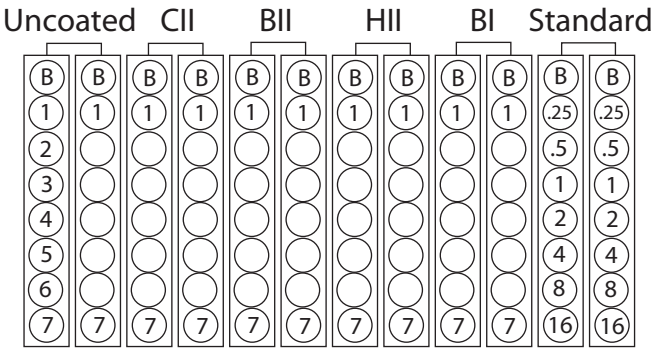
Custom ELISA Kit with Multiple Species of Collagen

Figure 2 shows an example of a custom kit for assaying antibody levels to various species of type I or type II collagen in human serum. This custom ELISA plate consists of two uncoated 8-well strips, two each of 8-well strips coated with chick (CII), bovine (BII) and human (HII) type II collagen, as well as bovine (BI) type I collagen and two 8-well strips for reference standards. "B" represents blank wells to determine non-specific reactions caused by the secondary antibody.

Figure 2 - Custom ELISA system for assaying species specificity of collagen antibodies in human sera



KIT COMPONENTS

Item	Quantity	Amount	Storage
Standard Antibody	1 vial	1.1 ml, 16 units/ml	-20°C
Secondary Antibody (Biotin-Conjugated Goat Anti-Human IgG)	2 vials	50 µl, lyophilized	-20°C
Solution A - Blocking Buffer	1 bottle	20 ml	-20°C
Solution B - Sample/Standard Dilution Buffer	1 bottle	50 ml	-20°C
Solution C - Secondary Antibody Dilution Buffer	1 bottle	20 ml	-20°C
Solution D - Streptavidin Peroxidase Dilution Buffer	1 bottle	20 ml	-20°C
Streptavidin Peroxidase	2 vials	50 µl	-20°C
TMB Solution (contains DMSO)	2 vials	0.2 ml	-20°C
Chromagen Dilution Buffer	1 bottle	20 ml	-20°C
Stop Solution - 2N Sulfuric Acid	1 bottle	10 ml	-20°C
Wash Buffer, 20X	2 bottles	50 ml	-20°C
Type I or Type II Collagen-Coated 8-Well Strips	10 each	8-well strips	-20°C
Uncoated 8-Well Strips	10 each	8-well strips	-20°C
Reference Standard Strips (two strips per run)	4 each	8-well strips	-20°C

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NOTES BEFORE USING ASSAY

1. It is recommended that the standard and samples be run in duplicate.

2. Partially used reagents may be kept at –20°C.

3. Crystals may form in the 20X wash buffer when stored at cold temperatures. If crystals have formed, it is necessary to warm the wash buffer by placing the bottle in warm water until crystals have dissolved completely.

4. Measure exact volume of buffers using a serological pipette prior to diluting. Extra buffer is provided.

ASSAY PROCEDURE

1. **Dilute Wash Buffer**: Dilute 50 ml of 20X wash buffer in 950 ml of distilled water (1X wash buffer). Wash the plate with 1X wash buffer at least 3 times using a wash bottle with manifold or an automated plate washer. Empty the plate by inverting it and blot on a paper towel to remove excess liquid. *Do not allow the plate to dry out.*

2. **Add Blocking Buffer**: Add 100 µl of Blocking Buffer (Solution A) to all wells. Incubate for 1 hour at room temperature.

3. **Prepare Standard Dilutions**: Undiluted standard is 16 units/ml. Prepare serial dilutions of the standard by mixing 250 µl of 16 units/ml standard with 250 µl of Sample/Standard Dilution Buffer (Solution B) - 8 units/ml. Then repeat this procedure to make five more serial dilutions of standard - 4, 2, 1, 0.5 and 0.25 units/ml solutions. The 16 units/ml standard may be stored at -20°C for use in a second assay. We recommend making fresh serial dilutions for each assay.

4. **Prepare Sample Dilutions**: Dilute samples 1:100 or more with Solution B. For example, dilute 20 µl of sample with 1.98 ml of Solution B (1:100). Keep this as a stock solution for future assays. If necessary, dilute the samples further with Solution B, 1:200-1:1000.

   Note: Human serum samples have a high lipid content in general. In order to avoid non-specific reactions caused by lipids, centrifuge samples at 10,000 rpm for 5 minutes using a tabletop centrifuge. Take a desired volume of serum sample carefully by pipette and then wipe the pipette surface with paper.

5. **Wash**: Wash the plate with 1X wash buffer at least 3 times using a wash bottle with manifold or an automated plate washer. Empty the plate by inverting it and blot on a paper towel to remove excess liquid. *Do not allow the plate to dry out.*

6. **Add Standards and Samples**: Add 100 µl of standards, Solution B (blank), and samples to collagen coated and uncoated wells in duplicate. Incubate at room temperature for 2 hours.

7. **Wash**: Wash the plate with 1X wash buffer at least 3 times using a wash bottle with manifold or an automated plate washer. Empty the plate by inverting it and blot on a paper towel to remove excess liquid. *Do not allow the plate to dry out.*

8. **Add Secondary Antibody**: Dissolve one vial of secondary antibody in 10 ml Secondary Antibody Dilution Buffer (Solution C). Add 100 µl of secondary antibody solution to each well and incubate at room temperature for 1 hour.

9. **Wash**: Wash the plate with 1X wash buffer at least 3 times using a wash bottle with manifold or an automated plate washer. Empty the plate by inverting it and blot on a paper towel to remove excess liquid. *Do not allow the plate to dry out.*

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10. **Add Streptavidin Peroxidase**: Dilute one vial of Streptavidin Peroxidase in 10 ml of Streptavidin Peroxidase Dilution Buffer (Solution D). Add 100 µl of streptavidin peroxidase solution to each well and incubate at room temperature for 1 hour.

11. **Wash**: Wash the plate with 1X wash buffer at least 3 times using a wash bottle with manifold or an automated plate washer. Empty the plate by inverting it and blot on a paper towel to remove excess liquid. *Do not allow the plate to dry out.*

12. **TMB**: Dilute one vial of TMB in 10 ml Chromagen Dilution Buffer just prior to use. Add 100 µl of TMB solution to each well immediately after washing the plate. Incubate for 15 minutes at room temperature.

13. **Stop**: Add 50 µl of 2N sulfuric acid (Stop Solution) to each well.

14. **Read Plate**: Read the OD values at 450 nm. If the OD values of samples are greater than the OD values of the highest standard, re-assay the samples at a higher dilution. A 630 nm filter can be used as a reference.

CALCULATION OF ANTIBODY TITERS

1. Average the duplicate OD values for the standards, blanks (B) and test samples in uncoated wells and collagen coated wells.

2. Subtract the blank (B) values from the averaged OD values of the standards and test samples in uncoated wells and collagen coated wells.

   Note: Individual antigens have unique background values. Therefore, "blank" wells should be used for each different antigen.

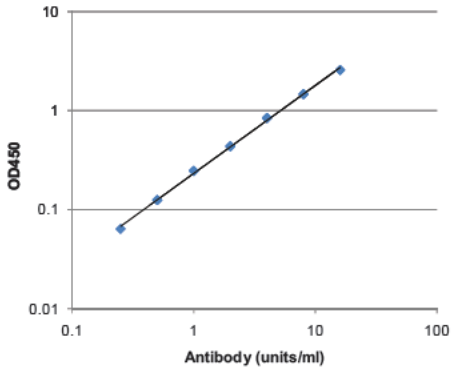
3. Subtract the OD values of samples tested in uncoated wells (background values) from their counterpart OD values in collagen coated wells from step 2 to eliminate values associated with non-specific reactions.

4. Plot the OD values of standards against the units/ml of antibody standard. Using a log/log plot will linearize the data. Figure 3 shows a representative experiment where the standard range is from 0.25 to 16 units/ml.

5. The units/ml of antibody in test samples can be calculated using regression analysis.

   Note: 100 units is approximately 1 µg IgG antibody/ml.

Figure 3 - A typical standard curve



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Appendix 9 – Photographs of subject's wounds

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(b)(4) Pictures of Patients' Wounds

(b)(4) Pictures of Patients' Wounds

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(b)(4) Pictures of Patients' Wounds

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Appendix 20-5 (b)(4) Testing

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Appendix 1 - (b)(4) Testing

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Appendix 20-6 (K[illegible])
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LANDSPÍTALI
UNIVERSITY HOSPITAL

COD SKIN EXTRA CELLULAR MATRIX

USED ON HARD TO HEAL WOUNDS

Gudbjorg Palsdottir[1] RN MS, Baldur Baldursson[2] MD PhD, Hilmar Kjartansson[3] MD
1. Clinical nurse specialist in wound care Landspitali University Hospital (LSH) Reykjavik Iceland 2.Dermatologist LSH / Kerecis Ltd 3.Internal medicine and emergency medicine LSH / Kerecis Ltd

Introduction

Extra Cellular Matrix (ECM) is the material that surrounds the cells in all animal tissues, such as in the skin, the urine bladder and the intestines. ECM products are manufactured by removing all cells and antigenic materials from a tissue, leaving behind intact decellularized tissue.

There has been growing use of ECM products in chronic wound care in the last decade. The product studied is the only product on the market today of non-mammalian origin.

In this study we used a novel product, a fish derived ECM*. The product is intact decellularized fish skin of the Atlantic cod and holds similar composition as mammalian skin. In contrast to mammalian products, the fish skin contains natural Omega3 fatty acids. The structure of the fish ECM supports the in-growth of cells in the wound and also protects the wound from various proteinases that otherwise may impair the wound healing.

Aim

To describe the use of an ECM wound dressing made from intact decellularized cod skin* on hard to heal wounds. To gather data regarding the efficacy and safety of the product.

Methods

Hard to heal wounds of varying aetiology that had not healed despite standard treatment for at least 3 weeks were identified. Information on the aetiology of the wound, duration, frequency of antibiotic treatment and type of earlier treatment were collected. Patients were treated with cod skin ECM* once a week for a period of 2 weeks or longer. Photographs were taken prior, during and at the end of treatment.

Case 1
75 years old male with mixed venous arterial ulcer. Duration of ulcer before treatment was 12 months. He was treated with ECM*, foam and compression. Wound healed completely 2 months after treatment started.

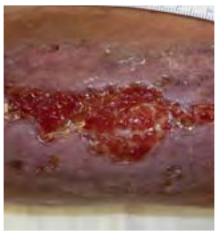


Fig 1: Beginning of treatment

Fig 2: ECM* in wound

Fig 3: ECM* after one week in wound

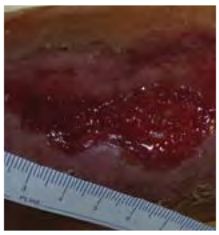


Fig 4: Wound after 2 weeks of treatment with ECM*

Case 2
55 year old male with infected surgical ulcer on ankle. Duration of ulcer before treatment was 10 weeks. He was treated with ECM, foam and compression.

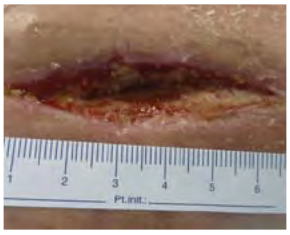


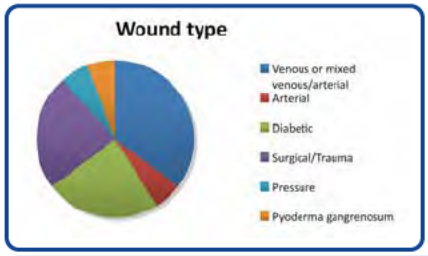
Fig 5: Beginning of treatment

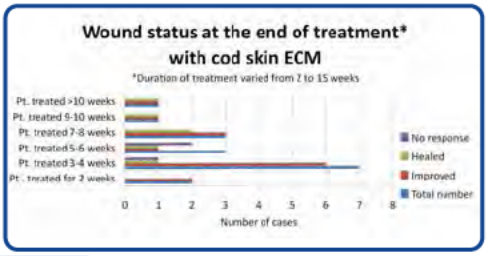
Fig 6: ECM* after one week in wound

Fig 7: Wound after 3 weeks of treatment with ECM*

Results

Of the 17 wounds treated with cod skin ECM, 14 decreased significantly in size. Six wounds healed completely. All but one wound showed a change with increased granulation tissues. None of the patients receiving the treatment showed allergic reaction or discomfort in any way. The application of marine derived ECM was without complications and the material was manageable.





Conclusion: Intact decellularized cod skin extracellular matrix is safe and effective to use on hard to heal wounds of varying aetiology. The material is pliable and easy to use.

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

*Trademarks: The name of the intact decellularized fish skin ECM technology is MariGen™ Omega3 Matrix. The chronic wound treatment product is MariGen™ Wound by Kerecis ltd.

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Section 21: Certificate of Compliance ClinicalTrials.gov

21 Certificate of Compliance ClinicalTrials.gov

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance

Under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

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07/19/2013

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For Devices: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)

MariGen Wound Dressing

Continuation Page for #5

APPLICATION / SUBMISSION INFORMATION

6. Type of Application/Submission Which This Certification Accompanies

☐ IND ☐ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☒ 510(k) ☐ PDP ☐ Other

7. Include IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/ Other Number *(If number previously assigned)*

If BLA was selected in item 6, provide Supplement Number

8. Serial Number Assigned to Application/Submission Which This Certification Accompanies

CERTIFICATION STATEMENT / INFORMATION

9. Check only one of the following boxes *(See instructions for additional information and explanation)*

☐ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

☒ C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met.

Certification Statement / Information section continued on page 2

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

CERTIFICATION STATEMENT / INFORMATION *(Continued)*

10. If you checked box C, in number 9, provide the National Clinical Trial (NCT) Number(s) for any "applicable clinical trial(s)," under 42 U.S.C. § 282(J)(1)(a)(i), section 402(j)(1)(a)(i) of the Public Health Service Act, referenced in the application/ submission which this Certification accompanies. *(Add continuation page as necessary.)*

NCT Number(s): _____

Continuation Page for #10

The undersigned declares, to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.

Warning: A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. Name and Title of the Person who Signs Number 15

Name	Title
Gudmundur F Sigurjonsson	Executive Chairman

12. Address

Address 1 *(Street address, P.O. box, company name c/o)*	
Eyrargata 2	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	
City: Isafjordur	State/Province/Region: Isafjordur
Country: Iceland	ZIP or Postal Code: 400

13. Telephone and Fax Numbers *(Include country code if applicable and area code)*

(Tel): +354 562 2601

(Fax): _____

14. Date of Certification

07/18/2013

15. Signature of Sponsor/Applicant/Submitter or an Authorized Representative *(Sign)*

Sign

This section applies only to requirements of the Paperwork Reduction Act of 1995.

*****DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*****

The burden time for this collection of information is estimated to average 15 minutes and 45 minutes (depending on the type of application/ submission) per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"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 number."

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

Barlow, Lenny *

From: Barlow, Lenny *
Sent: Thursday, October 24, 2013 5:54 PM
To: 'gfsigurjonsson@kerecis.com'
Cc: DCCLetters
Subject: k132343 Correspondence
Attachments: k132343.pdf

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

Records processed under FOIA Request # 2015-9691; Released by CDRH on 04-26-2016

COVER SHEET MEMORANDUM

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

From: Reviewer Name Stephen Curtis

Subject: 510(k) Number K132343

To: The Record

Please list CTS decision code: SE - Substantially Equivalent

☐ Refused to Accept (Note: this is considered the first review cycle. See screening checklist.)

☐ Hold (Additional Information or Telephone Hold)

☒ Final Decision (SE, SE with Limitations, NSE (select code below), 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)*	X	
510(k) Summary or 510(k) Statement *(Attach Summary or Statement)*	X	
Truthful and Accurate Statement *(Must be present for a Final Decision)*	X	
Is the device Class III?		X
[redacted]firm reference standards? (If yes, please attach Form 3654.)		X
Is this a combination product?		X
Is this a reprocessed single use device? (See Guidance for Industry and FDA Staff - MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices.)		X
Is this device intended for pediatric use only?		X
Is this a prescription device? (If both prescription & OTC, check both boxes.)	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 conducted in the United States and Form FDA 3674 was not included or was incomplete, then applicant must be contacted to obtain completed form.)		
Does this device include an Animal Tissue Source?	X	
All Pediatric Patients age <= 21		X
Neonate/Newborn (Birth to 28 days)		X
Infant (29 days to < 2 years)		X
Child (2 years to <12 years)		X
Adolescent (12 years to <18 years)		X
Transitional Adolescent A (18 years to <21 years); Special considerations are being given to this group, different from [redacted]ts age >= 21 (different device design or tesating, different protocol procedures, etc.)		X
[redacted]isitional Adolescent B (18 years to <21 years); No special considerations compared to adults >= 21 years)		X

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

Nanotechnology		X
Is device subject to the Tracking Regulation? (Medical Device Tracking Guidance)		X

Regulation Number:	Unclassified
Class:	Unclassified
Product Code:	KGN
Additional Product Codes:	

Digital Signature Concurrence Table
(Not all signatures may be required)

Branch Chief Sign-Off	David Krause -S 2013.10.22 13:43:26 -04'00'
Division Sign-Off	Mark N. Melkerson -S 2013.10.23 08:22:21 -04'00'

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