March 21, 2016

LATEX DECLARATION

This declaration is to inform users that the below Gentherm products are not made with natural rubber latex or synthetic derivatives of natural rubber latex:

Plasti-Pad® Reusable Hyper/Hypothermia Blankets
Gelli-Roll® Reusable Hyper/Hypothermia Pads
Maxi-Therm® Single-Patient Use/Disposable Hyper/Hypothermia Blankets
Maxi-Therm® Lite Single-Patient Use/Disposable Hyper/Hypothermia Blankets
Kool-Kit® Disposable Blankets/Pads
FilteredFlo® Convective Air Therapy Blankets (sterile and non-sterile blankets)
FilteredFlo® Warming Tube™
Localized Cold Therapy Pads (sterile and non-sterile pads)
SurfaceTemp® Patient Warming & Pressure Redistribution Pad

Sincerely,

GENTHERM MEDICAL LLC

Christina Miracle
Director of Quality Assurance & Regulatory Affairs

#10087.2

12011 Mosteller Road Cincinnati OH 45241
P 1.513.772.8810 F 1.513.772.9119 www.gentherm.com

Superseded

www.cszinc.com

Cincinnati Sub-Zero

October 11, 2011

LATEX FREE DECLARATION

The purpose of this declaration is to confirm that Cincinnati Sub-Zero Products, Inc. does not manufacture or distribute any products which contain Latex that would have direct contact with hospital patients or staff. This includes, but is not limited to, the following products and accessories:

Blanketrol® Hyper-Hypothermia Systems
Norm-O-Temp® Hyperthermia Systems
WarmAir® Convective Air Therapy Systems
Hemotherm® Dual Reservoir Cooler/Heater Systems
Electri-Cool® Localized Cold Therapy Systems
Micro-Temp® Localized Heat Therapy Systems
PlastiPad® Reusable Hyper-Hypothermia Blankets
Maxi-Therm® Single-Patient Use/Disposable Hyper-Hypothermia Blankets
Maxi-Therm® Lite Single-Patient Use/Disposable Hyper-Hypothermia Blankets
Gelli-Roll® Therapeutic Warming Blankets
FilteredFlo® Convective Air Therapy Blankets
WarmAir® Warming Tube™ Convective Air Therapy Blankets
Temp-Pad Localized Cold Therapy Pads
Cool-Temp® Localized Cold Therapy Pads
Steri-Probe® Temperature Probes
Reusable Connecting Hoses

Please feel free to contact me if you need additional information or clarification.

Yours very truly,

CINCINNATI SUB-ZERO PRODUCTS, INC.

Pradeep Gupta
Director of Medical Quality & Regulatory Compliance

12011 Mosteller Road • Cincinnati, OH 45241
(p) 513-772-8810 (f) 513-772-9119

#10087

CSZ Verification Test Report

Test Number: T20150922-1a
Revision: B

Test Title: Design Verification - Latex Eliza for Antigenic Protein (LEAP) Test per ASTM D6499.	**Requested By:** Jason Utter	
Product / Project Name: Various	**Test Plan Developed By:** Jason Utter	**Date:** 10-5-15
Reference number(s) (CRM/CAPA/NCM/ECN): N/A	**Test Plan Approved By:** *Engineering:* Dan Wittmer	*Date:* 10/6/15
	Quality: Anthony Sabatini	*Date:* 10/6/15

Revision Level	Description of Change	Author	Date
A	Original	JRU	10/05/15
B	Added Results and Conclusions.	JRU	11/16/15

Part I. Test Plan

Tested ID Number(s) & Date of Manufacture (i.e. Lot # or Serial Number):

a) List Tested Product ID numbers:

   a. 82461 – FilteredFlo Upper Body Blanket
   b. 82542 – FilteredFlo Sterile Cardiac Blanket
   c. 50230 – Adult Maxi-Therm Blanket
   d. 82176 – Adult Maxi-Therm Lite Blanket
   e. 82196 – Adult Plastipad
   f. 50137 – Sterile CoolTemp Pad
   g. 82600 – Head Wrap

b) List non-tested Product ID Numbers that are impacted by the results of the test. Include justification for non-tested product ID numbers:

   a. The blankets tested are a worst case representative sample from each blanket product line. The testing conducted should be considered valid for all other blankets within that family unless otherwise noted. The following products are impacted by the tests conducted on the blankets listed above:
   b. FilteredFlo blankets
      i. 82243 – FilteredFlo Adult Blanket
      ii. 82244 – FilteredFlo Pediatric Blanket
      iii. 82344 – FilteredFlo Torso Blanket
      iv. 82442 – FilteredFlo Lower Body Blanket
      v. 82443 – FilteredFlo Upper Body Blanket
      vi. 82460 – FilteredFlo Lower Body Blanket
      vii. 82462 – FilteredFlo Adult Blanket

c. Maxi-Therm Blankets
    i. 50231 – Pediatric Maxi-Therm
    ii. 50232- Infant Maxi-Therm
d. Maxi-Therm Lite Blankets
    i. 82170 – Maxi-Therm Lite 25" x 4"
    ii. 82171 – Maxi-Therm Lite, 22" x 17.25"
    iii. 82173 – Maxi-Therm Lite, 25" x 19"
    iv. 82174 – Maxi-Therm Lite, Pediatric, 33" x 25"
    v. 82300 – Maxi-Therm Lite Staff Vest
    vi. 82800 – Maxi-Therm Lite Patient Vest
e. Plastipad
    i. 82193 – Infant Plastipad
    ii. 82194 – Pediatric Plastipad
f. Cold Therapy
    i. 50624 – Pad, 3x18, Temp-Pad® Sterile
    ii. 50625 – Pad, 5x10, Temp-Pad® Sterile
    iii. 50633 – Pad, 5x10, Temp-Pad® Sterile w/Straps
    iv. 50627 – Pad, 8x14, Temp-Pad® Sterile
    v. 50634 – Pad, 8x14, Temp-Pad® Sterile w/Straps
    vi. 50628 – Pad, 11x12, Temp-Pad® Sterile
    vii. 50635 – Pad, 11x12, Temp-Pad® Sterile w/Straps
    viii. 50629 – Pad, 12x15, Temp-Pad® SterileCT-99, Pad Cool Temp Knee/Shoulder
    ix. 50651 – Pad, 8x14, Temp-Pad®
    x. 50733 – Pad, 5x10, Temp-Pad® w/Straps
    xi. 50734 – Pad, 8x14, Temp-Pad® w/Straps
    xii. 50735 – Pad, 11x12, Temp-Pad® w/Straps
    xiii. 50737 – Pad, Cool Temp Knee/Shoulder (Non-Sterile)
    xiv. 50715 – Pad, 11x12, Over-The-Counter Temp-Pad® w/Straps
    xv. 82601 – Pad, Head Wrap

Objective(s):

a) Define test criteria and expected results:
    a. Each tested blanket will pass the Latex Eliza for Antigenic Protein (LEAP) Test per ASTM D6499.

Acceptance Criteria:

a) Define criteria for acceptance:
    a. Each tested blanket will pass testing per ASTM D6499.

Test Conducted By: LEAP Testing Service Nelson Laboratories	**Date:** 10/29/2015
Test Analyzed By: (Engineer)	**Date:** 11/16/15
Test Analyzed By: (Engineer) Brandon Wyatt	**Date:** 11/19/15
Approved By: (Engineering Manager)	**Date:** 12/1/15
Approved By: (Quality)	**Date:** 19 NOV 2015

Part III: Tested Product Disposition

a) Indicate the appropriate disposition for all products, including required retesting to the appropriate Q-sheet. Reference DWI-068.
   a. All blankets used by this test were scrapped by the testing laboratory.

Released Serial Numbers or Lot Numbers:	▪ S/N XXX-XXXXX ▪ Lot # XXXXX
Disposition:	☐ Use as Marketing Samples ☐ Approve for Shipment ☐ Other
Disposition Approved By: *	
Quality: N/A	Date: N/A
Production: N/A	Date: N/A
Engineering: N/A	Date: N/A

* Indicate N/A if not applicable

Part II. Test Execution

Test Equipment / Measuring Devices Used:

a) List test equipment used to perform test (include serial numbers):

   a. Test Equipment provided by Nelson Laboratories.

b) List measuring devices used to perform test (include last calibration dates and calibration due dates):

   a. Measuring devices provided by Nelson Laboratories.

Test Standards Used:

a) List standards used to conduct test (including standard revision level):

   a. This test was conducted per ASTM D6499-12.

Photograph and/or Diagram of the Test Set-Up:

a) List apparatus and show measurement points.

   a. Please reference the attached Nelson Laboratories test report.

Test Results:

a) List and attach originals of raw or hand-written data obtained during the test

   a. Please reference Appendix D for the full Nelson Laboratories test report.

b) Attach training records

   a. Training records can be found in Appendix A of the test report.

c) Document results. Identify / describe any data anomalies discovered during the test.

   a. Please reference the attached Nelson Laboratories test report in Appendix D. Testing was conducted by LEAP Testing Service, a subcontractor used by Nelson Laboratories. All blankets tested passed testing per ASTM D6499-12. All samples tested were below the detection limit for the Inhibition Assay Concentration. Therefore, the blankets tested do not contain latex above the detection level of the test.

d) State if acceptance criteria were met or not.

   a. The acceptance criteria of this test were met. It has been verified that all blankets tested were below the detectable limit of 0.03 µg/g of antigenic latex protein per gram of sample per the ASTM D6499 Latex Eliza for Antigenic Protein (LEAP) Test.

Protocol Deviations:

a) List all deviations from the originally approved protocol by line item.

   a. There were no deviations from the originally approved protocol.

Conclusion:

a) State if test objectives were met or not

   a. The test objectives were met. It has been verified that all blankets tested were below the detectable limit of 0.03 µg/g of antigenic latex protein per gram of sample per the ASTM D6499 Latex Eliza for Antigenic Protein (LEAP) Test.

b) If the Disposition of products involved in the test are intended to be "approved for shipment" or "use as Marketing samples", explain the remedial actions taken to restore any tested product or product used in testing. Provide rationale for any DHR retesting that is not required. Reference DWI-068.

   a. All blankets used by this test were scrapped by the testing laboratory.

Contains Nonbinding Recommendations

Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex

Guidance for Industry and Food and Drug Administration Staff

Document issued on: December 2, 2014

The draft of this document was issued on March 11, 2013.

- For questions regarding medical products regulated by the Center for Devices and Radiological Health (CDRH), contact Michael T. Bailey (301-796-6530 or michael.bailey@fda.hhs.gov); or Geetha C. Jayan (301-796-6300 or geetha.jayan@fda.hhs.gov).
- For questions regarding medical products regulated by the Center for Biologics Evaluation and Research (CBER), contact the CBER Office of Communication, Outreach and Development (1-800-835-4709 or 240-402-7800, or ocod@fda.hhs.gov).
- For questions regarding medical products regulated by the Center for Drug Evaluation and Research (CDER), contact Richard T. Lostritto (301-796-1697 or richard.lostritto@fda.hhs.gov).
- For questions regarding medical products regulated by the Center for Veterinary Medicine (CVM), contact Cory D. Evans, (240-402-0639 or cory.evans@fda.hhs.gov).

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research
Center for Veterinary Medicine

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to http://www.regulations.gov . Submit written comments to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2013-D-0168Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1768 to identify the guidance you are requesting.

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Contains Nonbinding Recommendations

Guidance for Industry and Food and Drug Administration Staff

Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

The purpose of this guidance is to make recommendations on the appropriate language to include in the labeling of a medical product to convey that natural rubber latex was not used as a material in the manufacture of the product, product container, and/or packaging. FDA is concerned that statements submitted for inclusion in medical product labeling, such as "latex-free," "does not contain natural rubber latex," or "does not contain latex" are not accurate because it is not possible to reliably assure that there is an absence of the allergens associated with hypersensitivity reactions to natural rubber latex in the medical product. Use of these terms may give users allergic to natural rubber latex a false sense of security when using a medical product. FDA is recommending that a consistent, scientifically accurate statement be used by all manufacturers who wish to convey that natural rubber latex was not used as a material in the manufacture of a medical product, its container and/or packaging.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

2. Scope

This guidance document applies to all FDA regulated medical products (i.e., devices, drugs, biologics, and veterinary products) for which: (1) natural rubber latex or synthetic derivatives of natural rubber latex were not used as materials in their manufacture; or (2) any container and/or packaging was not made with natural rubber latex or synthetic derivatives of natural rubber latex. This guidance contains labeling recommendations for manufacturers who wish to include a statement in medical product labeling indicating that natural rubber latex or synthetic derivatives of natural rubber latex were not used as manufacturing materials in the medical product, its container and/or packaging.

3. Background

Contact with devices containing natural rubber has been associated with anaphylaxis in individuals allergic to natural rubber latex proteins.[1] Our medical device regulations include provisions that require certain labeling statements on medical devices if the device or device packaging is composed of or contains natural rubber that contacts humans. See 21 CFR 801.437. The biologics regulations (21 CFR 610.61(l)) require that the package label or package insert declare the presence of known sensitizing substances, but do not specifically mention natural rubber latex. Specific regulations for labeling of natural rubber latex content in medical products or their containers do not exist for drugs or veterinary products.

At this time there are no regulations requiring a company to state that natural rubber latex was not used as a material in the manufacture of a medical product, its container and/or packaging. However, some manufacturers have included the promotional statements "latex-free" or "does not contain latex" in medical product labeling to inform users that natural rubber latex, dry natural rubber or synthetic derivatives of natural rubber latex were not used. FDA believes that these labeling statements are not sufficiently specific, not necessarily scientifically accurate and may be misunderstood or applied too widely, and therefore, it is inappropriate to include such statements in medical product labeling.

First, the term "latex" in the labeling statements "latex-free" and "does not contain latex" could refer to natural rubber latex or synthetic latex (not derived from natural rubber latex). Labeling statements that do not clearly state the material of concern are not sufficiently specific and therefore should not be included in medical product labeling.

Second, users may consider the terms "free" and "does not contain" to mean that the medical product is completely devoid of natural rubber latex. However, there are no analytical methods currently available that can identify all proteins and components in natural rubber latex that may lead to allergic reactions in medical product users. In addition, the use of the

[1] Ahmed SM, Aw TC, and Adisesh A. Toxicological and immunological aspects of occupational latex allergy. Toxicol Rev 2004; 23(2):123-34

term "free" or "does not contain" does not address the potential for accidental contamination of a medical product and/or its container with natural rubber latex during or after manufacturing.

Although there are a number of tests to measure the various compounds related to natural rubber latex allergies, FDA is aware of no test method or combination of test methods available at this time that can demonstrate the absence of proteins or components from natural rubber latex that may cause allergic reactions in susceptible individuals. A brief description of three currently available test methods used to assess levels of total protein or natural rubber latex proteins in medical products are provided below:

1. ASTM D5712 – Standard Test Method for Analysis of Aqueous Extractable Protein in Natural Rubber and its Products Using the Modified Lowry Method.

   This is an FDA- recognized standard.[2] The purpose of this test method is to determine the protein content in natural rubber latex materials. This test method does not specifically measure antigenic or allergenic natural rubber latex proteins, but rather the total aqueous extractable protein content in the sample.

2. ASTM D6499 – Standard Test Method for the Immunological Measurement of Antigenic Protein in Natural Rubber and its Products.

   This is an FDA- recognized standard[2]. The purpose of this test method is to determine the amount of antigenic protein in natural rubber and its products using rabbit antisera specific for natural rubber latex proteins. However, the standard clearly states that "Although this method detects antigenic proteins, it should not be considered as a measure of allergenic proteins. Correlation of protein/antigen levels with the level of allergenic proteins has not been fully established."

3. ASTM D7427 – Standard Test Method for Immunological Measurement of Four Principal Allergenic Proteins (Hev b 1, 3, 5 and 6.02) in Natural Rubber and its Products Derived from Latex.

   This standard has not been recognized by the FDA as of the time of issuance of this guidance. The purpose of this test method is to determine the amount of four specific known natural rubber latex allergenic proteins. (At least thirteen natural rubber latex allergens have been identified.) Per the test method, "the sum of the four allergen levels shall be viewed as an indicator of the allergen burden and not as a measure of the total allergen content that can be released from the product."

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[2] FDA recognizes national and international consensus standards for use in development of medical products. A database of all recognized standards can be found at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm. Please see the following site for more information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm.

The specificity and sensitivity of currently available analytical methods are not sufficient to demonstrate that a medical product is completely "free" of natural rubber latex proteins which have primarily been associated with causing severe allergic reactions (Type I allergic reactions). FDA recognizes that the complete absence of all natural rubber latex allergens is unlikely to be necessary for the safe use of medical products by individuals with natural rubber latex allergies. Threshold allergen levels, exposure below which no adverse reaction occurs in the majority of sensitive individuals, have been identified for some non-natural rubber latex allergens (e.g., hymenoptera venoms and specific foods).

However, threshold allergen levels are unavailable for natural rubber latex-allergic individuals. For example, there are at least 13 distinct allergens identified for natural rubber latex allergy and the sensitivity to each varies, not only among individuals, but among groups of individuals (e.g., health care providers, industry workers, children with meningomyelocele). Furthermore, thresholds are likely to be route-specific and multiple routes of exposure (e.g., respiratory, percutaneous, oral, and parenteral) have been implicated in natural rubber latex sensitization and reactivity. There is no one threshold level of exposure that can be considered safe, but rather many levels that are a function of the allergen, the risk group, the exposure route, the immune status of the individual and, perhaps, other factors as yet unidentified. Therefore, any preventative strategy should address the possible different threshold levels for sensitization and for triggering a reaction in an at-risk individual.

Ideally, all threshold levels should be established for each allergen under all conditions, and the lowest threshold level identified for each. This information is unlikely to become available without a concerted scientific effort. Even if this is achieved, the correlation of data from ASTM methods D5712 (total protein), D6499 (overall allergen levels), and D7427 (four specific allergens) to the established minimum threshold levels would be uncertain.

For the reasons stated above, FDA finds that the use of statements, such as "latex-free," "does not contain latex," or other similar labeling statements are, at this time, not scientifically supportable.

FDA strongly recommends that these statements not be used in medical product labeling.

4. Recommended Labeling Statement

Currently, there are no regulations requiring a manufacturer to state that natural rubber latex was not used as a material in their medical product, its container and/or its packaging. If a manufacturer elects to include a statement in medical product labeling indicating that natural rubber latex or synthetic derivatives of natural rubber latex were not used as materials in the manufacture of their medical product and container, FDA recommends the use of the statement **"Not made with natural rubber latex."** If this statement is made without any qualification, it would apply to the medical product, its container, and any packaging. In certain cases, statements regarding "not made with natural rubber latex" may be appropriate only for certain components. In this case a manufacturer may elect to make a statement that

the specific component is not made with natural rubber latex. For example, if the particular presentation or part of the presentation (e.g., vial stopper or syringe) is not made with natural rubber latex, FDA recommends the statement "**The <vial stopper> is not made with natural rubber latex.**"

These statements **"Not made with natural rubber latex"** and **"The <vial stopper> is not made with natural rubber latex"** communicate that natural rubber latex was not used as a material in the finished product or as a material in a specific component, respectively. At the same time, the statement does not make the unsupportable claim that the medical product is "free" of or "does not contain" natural rubber latex (i.e., materials or contamination), which may promote a false sense of safety to users who are allergic to natural rubber latex. Finally, use of a consistent scientifically supportable labeling statement will reduce confusion among FDA staff, medical product manufacturers, and medical product users.

Manufacturers who currently include statements such as "latex-free" or "does not contain latex" in medical product labeling should update their medical product labeling to show the recommended labeling statement **"Not made with natural rubber latex"** or **"The <vial stopper> is not made with natural rubber latex"** as appropriate. Alternatively, manufacturers should consider removing "latex-free" type statements from medical products, their containers, and packaging. Manufacturers may contact the Center that regulates the medical product for guidance on the appropriate regulatory mechanism to update the labeling.