Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER:	(smw)
FOLDER:	K092150 - 930 pages
COMPANY:	BIOMET, INC. (BIOMET)
PRODUCT:	BONE CEMENT (LOD)
SUMMARY:	Product: COBALT MV WITH GENTAMICIN (AKA COBALT G-MV) BONE CEMENT
DATE REQUESTED:	Oct 19, 2015
DATE PRINTED:	Oct 19, 2015
Note:	Printed

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K092150

BIOMET
MANUFACTURING CORP.

OCT 27 2009

510(k) Summary

Preparation Date: July 15, 2009

Applicant/Sponsor: Biomet Manufacturing Corp.

Contact Person: Susan Alexander

Proprietary Name: Cobalt™ MV with Gentamicin Bone Cement (also known as Cobalt™ G-MV)

Common Name: PMMA Bone Cement

Classification Name: Polymethylmethacrylate (PMMA) Bone Cement (21 CFR §888.3027)

Product Code: MBB (bone cement, antibiotic), LOD (bone cement)

Legally Marketed Devices to Which Substantial Equivalence is Claimed:

Cobalt™ G-HV Bone Cement	K051532	Biomet Manufacturing Corp.
Simplex® P with Tobramycin Bone Cement	K014199	Stryker Howmedica Osteonics

Device Description: Cobalt™ G-MV Bone Cement is a methyl methacrylate-styrene copolymer based acrylic medium viscosity bone cement with gentamicin. Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components that when mixed form rapidly-setting radiopaque bone cement for use in orthopedic surgery.

Intended Use: Cobalt™ G-MV Bone Cement is an acrylic cement-like substance which allows seating and fixation of the prosthesis to the bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between the prosthesis and the bone.

Indications for Use: Cobalt™ G-MV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Summary of Technologies: The technological characteristics of Cobalt™ G-MV Bone Cement are the same as, or similar to, the predicate devices.

Non-Clinical Testing: Non-clinical laboratory testing was performed to determine substantial equivalence. The results indicated that the device was functional within its intended use.

Clinical Testing: None provided as a basis for substantial equivalence.

All trademarks are property of Biomet, Inc. unless otherwise noted.
Simplex® is a registered trademark of Stryker Howmedica Osteonics.

Mailing Address:
P.O. Box 587
Warsaw, IN 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574.267.8137
www.biomet.com

Shipping Address:
56 East Bell Drive
Warsaw, IN 46582

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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

Biomet, Inc.
% Ms. Susan Alexander
56 East Bell Drive
P.O. Box 587
Warsaw, Indiana 46581

OCT 27 2009

Re: K092150
Trade/Device Name: Cobalt™ MV with Gentamicin (aka Cobalt™ G-MV) Bone Cement
Regulation Number: 21 CFR 888.3027
Regulation Name: Polymethylmethacrylate (PMMA) bone cement
Regulatory Class: II
Product Code: LOD, MBB
Dated: October 7, 2009
Received: October 8, 2009

Dear Ms. Alexander:

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 #2014-8120; Released by CDRH on 12-8-2015

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/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
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 #2014-8120; Released by CDRH on 12-8-2015

Indications for Use

510(k) Number (if known): _____

Device Name: Cobalt™ MV with Gentamicin (aka Cobalt™ G-MV) Bone Cement

Indications For Use:

Cobalt™ MV with Gentamicin Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-the-Counter Use NO (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)

(Division Sign-Off)
Division of Surgical, Orthopedic,
and Restorative Devices

510(k) Number K092150

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K092150/A001

BIOMET

FDA CDRH DMC
JUL 06 2015
Received

02 July 2015

To Whom It May Concern:

The following table contains a listing of 510(k) clearances originally obtained for Biomet Orthopedics extremity and cement products; however on June 29, 2015 these products and submissions were sold to DJO Global. Therefore, all U.S. regulatory responsibility (e.g. device listings, facility registrations, device modifications) now resides with DJO.

Sincerely,

Lynnette Jackson

Lynnette Jackson
Vice President, Global Regulatory Affairs
Biomet

Notary: 2 July 2015

NOTARY PUBLIC STATE OF INDIANA NOTARY SEAL
REBECCA R. HOMAN
Kosciusko County
My Commission Expires
August 10, 2019

Mailing Address:
P.O. Box 587
Warsaw, IN 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574.267.8137
www.biomet.com

Shipping Address:
56 East Bell Drive
Warsaw, IN 46582

REBECCA R. HOMAN NOTARY SEAL PUBLIC STATE OF INDIANA

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

510(k)	Title	Clearance Date
K051496	Cobalt HV Bone Cement	8/4/2005
K051532	Cobalt G HV Bone Cement	8/3/2005
K091608	Cobalt MV Bone Cement	9/17/2009
K092150	Cobalt MV Bone Cement with Gentamicin	10/27/2009
K051975	Discovery Elbow Porous Coated	9/6/2005
K090473	Discovery Elbow X-Small	3/25/2009
K013042	Discovery Elbow	10/10/2001

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

DJA x00001

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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

Biomet, Inc.
% Ms. Susan Alexander
56 East Bell Drive
P.O. Box 587
Warsaw, Indiana 46581

OCT 27 2009

Re: K092150
Trade/Device Name: Cobalt™ MV with Gentamicin (aka Cobalt™ G-MV) Bone Cement
Regulation Number: 21 CFR 888.3027
Regulation Name: Polymethylmethacrylate (PMMA) bone cement
Regulatory Class: II
Product Code: LOD, MBB
Dated: October 7, 2009
Received: October 8, 2009

Dear Ms. Alexander:

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

DJA x00002

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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/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
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

DJA x00003

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Indications for Use

510(k) Number (if known):_____

Device Name: Cobalt™ MV with Gentamicin (aka Cobalt™ G-MV) Bone Cement

Indications For Use:

Cobalt™ MV with Gentamicin Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-the-Counter Use NO (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)

(Division Sign-Off)
Division of Surgical, Orthopedic,
and Restorative Devices

510(k) Number K092150

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

DJA x00032

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

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

October 09, 2009

BIOMET, INC.
56 EAST BELL DR. P.O. BOX 587
WARSAW, INDIANA 46581-0587
UNITED STATES
ATTN: SUSAN ALEXANDER

510k Number: K092150

Product: COBALT MV WITH GENTAMICIN

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Pleaseremember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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

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

Sincerely,

510(k) Staff

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

September 28, 2009

510k Number: K092150
Product: COBALT MV WITH GENTAMICIN (AKA

BIOMET, INC.
56 EAST BELL DR. P.O. BOX 587
WARSAW, INDIANA 46581-0587
UNITED STATES
ATTN: SUSAN ALEXANDER

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModernizationAct/ucm136685.htm.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

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

DJA x00034

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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

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

Sincerely yours,

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

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

DJA x00064

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

July 16, 2009

BIOMET, INC.
56 EAST BELL DR. P.O. BOX 587
WARSAW, INDIANA 46581-0587
UNITED STATES
ATTN: SUSAN ALEXANDER

510k Number: K092150
Received: 7/16/2009
Product: COBALT MV WITH GENTAMICIN (AKA

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

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC)(HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

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

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form (http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3674.pdf) accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

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

DJA x00065

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007" (http://www.fda.gov/oc/initiatives/fdaaa/guidance_certifications.html). According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements". This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1655.pdf. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice www.fda.gov/cdrh/devadvice/". If you have questions on the status of your submission, please contact DSMICA at (240) 276-3150 or the toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsma/dsmastaf.html. If you have procedural questions, please contact the 510(k) Staff at (240)276-4040.

Sincerely yours,

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

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

DJA x00066

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K092150

BIOMET®
MANUFACTURING CORP.

July 15, 2009

FDA CDRH DMC
JUL 16 2009
Received

Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

RE: 510(k) Premarket Notification
Cobalt™ G-MV Bone Cement
Device User Fee ID Number: MD6043278-956733

Dear Sir or Madam:

Enclosed is a 510(k) notification for Cobalt™ MV with Gentamicin (also known as Cobalt™ G-MV) Bone Cement. We believe this PMMA bone cement with antibiotic is substantially equivalent* to other PMMA bone cements with antibiotic on the market.

This submission has been prepared in keeping with the FDA document "Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s" (August 12, 2005). Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html, an electronic copy is being provided with this submission and it is an exact duplicate of the original paper submission.

Type of 510(k): Traditional

Common or Usual Name: PMMA Bone Cement with antibiotic

Applicant/Manufacturer/Specification Holder:
Biomet Manufacturing Corp.
56 East Bell Drive
P.O. Box 587
Warsaw, Indiana 46581-0587
FDA Registration Number: 1825034

K3

Contact Person:
Susan Alexander
Regulatory Affairs Specialist
Biomet Manufacturing Corp.
P.O. Box 587
Warsaw, Indiana 46581-0587
Phone: 574.267.6639
Fax: 574.372.1683
Email: sue.alexander@biomet.com

Alternate Contact Person:
Tracy Bickel Johnson
Director, Clinical and Regulatory Affairs
Biomet Orthopedics, Inc.
P.O. Box 587
Warsaw, Indiana 46581-0587
Phone: 574.267.6639
Fax: 574.372.1683
Email: tracy.johnson@biomet.com

OR
#

Mailing Address:
P.O. Box 587
Warsaw, IN 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574.267.8137
www.biomet.com

Shipping Address:
56 East Bell Drive
Warsaw, IN 46582

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

DJA x00067

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Device Information:

Classification Name	Polymethylmethacrylate (PMMA) Bone Cement, 21 CFR §888.3027
Device Classification	II
Panel	Orthopedics
Device Product Code	MBB, LOD
Previous FDA Status	None
Basis for Submission	New device

Design and Use of the Device:

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 tissue or other biological device?		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 include clinical information?		X
Is the device implanted?	X	

Confidentiality: With the exception of the 510(k) Summary and Indications for Use Form, Biomet Manufacturing Corp. considers the contents of this submission confidential until released by the sponsor.

To assist in the review of this submission, the table on the following page gives the location in this submission of the items requested in FDA document *"Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s"* (August 12, 2005).

Permission to fax or e-mail information related to this submission is granted by the Sponsor.

Sincerely,

Susan Alexander

Susan Alexander
Regulatory Affairs Specialist
Biomet Manufacturing Corp.

*Any statement made in conjunction with this submission regarding and/or a determination of substantial equivalence to any other product is intended only to relate to whether the product can be lawfully marketed without pre-market approval or reclassification and is not intended to be interpreted as an admission or any other type of evidence in patent infringement litigation. [Establishment Registration and Premarket Notification Procedures, Final Regulation, Preamble, August 23, 1977, 42 FR 42520 (Docket No. 76N-0355)]

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

DJA x00068

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Section	Item	Location in Submission
1	Medical Device User Fee Cover Sheet (Form FDA 3601)	Appendix
2	CDRH Premarket review Submission Cover Sheet	Not submitted
3	510(k) Cover Letter	Cover Letter
4	Indications for Use Statement	Indications for Use Section
5	510(k) Summary	510(k) Summary Section
6	Truthful and Accuracy Statement	Appendix
7	Class III Summary and Certification	Not Applicable
8	Financial Certification or Disclosure Statement	Not Applicable
9	Declarations of Conformity and Summary Reports	Not Applicable
10	Executive Summary	Executive Summary Section
11	Device Description	Device Description Section
12	Substantial Equivalence Discussion	Substantial Equivalence Section
13	Proposed Labeling	Device Description Section – Tab B
14	Sterilization and Shelf Life	Device Description Section
15	Biocompatibility	Device Description Section
16	Software	Not Applicable
17	Electromagnetic Compatibility and Electrical Safety	Not Applicable
18	Performance Testing – Bench	Mechanical Testing Section
19	Performance Testing – Animal	None Conducted
20	Performance Testing – Clinical	None Conducted
21	Other	
	Certificate of Compliance with ClinicalTrials.gov Data Bank	Appendix
	Standard Data Reports for 510(k)	Device Description Section – Tab D

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

DJA x00069

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Executive Summary
Cobalt™ G-MV Bone Cement

Introduction
Cobalt™ MV with gentamicin (also known as Cobalt™ G-MV) Acrylic Bone Cement is a methyl methacrylate-styrene copolymer based acrylic bone cement with a medium viscosity. Cobalt™ G-MV includes gentamicin, a broad spectrum antibiotic. Biomet has developed this bone cement to expand its product line and to provide orthopedic surgeons the option of a medium viscosity, antibiotic-loaded bone cement with excellent handling characteristics. In addition, the cement features a color additive to serve as an optical marking during orthopedic surgery.

Device Description
Cobalt™ G-MV is formed when two separate, pre-measured sterilized components, a powder copolymer and liquid monomer, are mixed to form a fast-setting radiopaque bone cement for use in orthopedic surgery. Mixing of the two sterile components initially produces a paste that is used to anchor the prosthesis, or to fill an osseous defect. The powder contains 10% zirconium dioxide as an x-ray contrast medium. The hardened bone cement allows stable fixation of the prosthesis and transfers mechanical stresses produced during movement from the prosthesis to the bone via the large interface between the cement and the bone. FD&C blue #2 Aluminum Lake color additive serves as an optical marking of the bone cement at the site of the operation. The gentamicin component is a broad spectrum antibiotic.

Cobalt™ G-MV Bone Cement can be mixed in an open bowl or in a vacuum mixer, and is applied to the operative site either manually or with a bone cement gun.

Risk Assessment
Biomet performed a risk assessment for Cobalt™ G-MV and identified no additional risks outside the risks identified in *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)*. The risks associated with Cobalt™ G-MV Bone Cement are the same as those associated with the predicate Simplex® P with Tobramycin (K014199). The risk assessment is included in the design history file for Cobalt™ G-MV and can be accessed at any future FDA inspection.

Intended Use
Cobalt™ G-MV Bone Cement is an acrylic cement-like substance which allows seating and fixation of the prosthesis to the bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between the prosthesis and the bone.

Indications for Use
Cobalt™ G-MV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

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

DJA x00070

Device Comparison Table

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
510(k) No.	New	K051532	K014199
Cement Design	Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Cobalt™ HV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Surgical Simplex® P provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.
Cement Materials	Powder component/ liquid monomer	Powder component/ liquid monomer	Powder component/ liquid monomer
Powder Component	Methyl methacrylate-styrene copolymer 29.83g Poly(methyl methacrylate) 6.00g Zirconium dioxide 4.00g FD&C Blue No. 2 Aluminum Lake 0.05g Residual benzoyl peroxide (0.44g) Benzoyl peroxide (hydrous 75%) 0.12g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methylmethacrylate-methacrylate copolymer with FD&C Blue No. 2 Aluminum Lake 33.86 – 33.42g --- Zirconium dioxide 5.94g --- --- Benzoyl peroxide, (hydrous 75%) 0.20 – 0.64g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methyl methacrylate-styrene-copolymer 30.00g Polymethyl methacrylate 6.00g Barium Sulfate, U.S.P. 4.00g --- Residual benzoyl peroxide (0.51g) Tobramycin Sulfate 1.0g active
Liquid Monomer Component	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 97.4% v/v N, N-dimethyl-p-toluidine 2.6% v/v Hydroquinone 75 ± 15ppm

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

DJA x00071

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
Sterilization	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Gamma Irradiation Liquid Monomer Component Membrane Filtration
Packaging	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile paper-foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in sterile packet, enclosed in a sterile protective package Liquid Monomer Component Pre-sterilized ampoule, enclosed in a pre-sterilized ampoule package
Anatomical Sites	Osseous tissue	Osseous tissue	Osseous tissue

Mechanical Testing

Extensive *in vitro* testing was performed in accordance with *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* to demonstrate the equivalence of Cobalt™ G-MV Bone Cement to the predicate Simplex® P with Tobramycin Bone Cement (K014199). Testing information is included in the **Mechanical Testing** section of this submission.

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

DJA x00072

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Indications for Use

510(k) Number (if known):_____

Device Name: Cobalt™ MV with Gentamicin (aka Cobalt™ G-MV) Bone Cement

Indications For Use:

Cobalt™ MV with Gentamicin Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-the-Counter Use NO (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

DJA x00073

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

BIOMET
MANUFACTURING CORP.

510(k) Summary

Preparation Date: July 15, 2009

Applicant/Sponsor: Biomet Manufacturing Corp.

Contact Person: Susan Alexander

Proprietary Name: Cobalt™ MV with Gentamicin Bone Cement (also known as Cobalt™ G-MV)

Common Name: PMMA Bone Cement

Classification Name: Polymethylmethacrylate (PMMA) Bone Cement (21 CFR §888.3027)

Product Code: MBB (bone cement, antibiotic), LOD (bone cement)

Legally Marketed Devices to Which Substantial Equivalence is Claimed:

Cobalt™ G-HV Bone Cement	K051532	Biomet Manufacturing Corp.
Simplex® P with Tobramycin Bone Cement	K014199	Stryker Howmedica Osteonics

Device Description: Cobalt™ G-MV Bone Cement is a methyl methacrylate-styrene copolymer based acrylic medium viscosity bone cement with gentamicin. Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components that when mixed form rapidly-setting radiopaque bone cement for use in orthopedic surgery.

Intended Use: Cobalt™ G-MV Bone Cement is an acrylic cement-like substance which allows seating and fixation of the prosthesis to the bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between the prosthesis and the bone.

Indications for Use: Cobalt™ G-MV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Summary of Technologies: The technological characteristics of Cobalt™ G-MV Bone Cement are the same as, or similar to, the predicate devices.

Non-Clinical Testing: Non-clinical laboratory testing was performed to determine substantial equivalence. The results indicated that the device was functional within its intended use.

Clinical Testing: None provided as a basis for substantial equivalence.

All trademarks are property of Biomet, Inc. unless otherwise noted.
Simplex® is a registered trademark of Stryker Howmedica Osteonics.

Mailing Address:
P.O. Box 587
Warsaw, IN 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574.267.8137
www.biomet.com

Shipping Address:
56 East Bell Drive
Warsaw, IN 46582

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

DJA x00074

Device Description – Cobalt™ G-MV Bone Cement

Introduction

Cobalt™ MV with Gentamicin (also known as Cobalt™ G-MV) Acrylic Bone Cement is a methyl methacrylate-styrene copolymer based acrylic bone cement with a medium viscosity.

Device Description

Cobalt™ G-MV bone cement is formed when two separate, pre-measured sterilized components, a powder copolymer and liquid monomer, are mixed to form a radiopaque, rapidly-setting bone cement for use in orthopedic surgery. Mixing of the two sterile components initially produces a paste that is used to anchor the prosthesis, or to fill an osseous defect. The hardened bone cement allows stable fixation of the prosthesis and transfers mechanical stresses produced during movement from the prosthesis to the bone via the large interface between the cement and the bone.

The powder component, supplied in a gas-permeable packet, consists of 40 grams of powder with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams	(74.575%)
• Polymethyl methacrylate	6.00 grams	(15.000%)
• Zirconium Dioxide	4.00 grams	(10.000%)
• FD&C Blue No. 2 Aluminum Lake	0.05 grams	(0.125%)
• Benzoyl Peroxide	0.35-1.00 grams	(0.300%)
• Gentamicin sulfate (equivalent to 0.50g gentamicin)	0.84 grams	

The liquid component is supplied in a flexible packet. It consists of 20ml of liquid (monomer) with the following composition:

• Methyl methacrylate (stabilized with hydroquinone)	18.424 grams	(98.0%)
• N,N-dimethyl-p-toluidine	0.376 grams	(2.0%)

The powder contains 10% zirconium dioxide as an x-ray contrast medium. To assist in distinguishing between bone and cement within the surgical field, blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder to produce a bluish tint in the final cement. This color additive may be used safely at a level not to exceed 0.1 percent by weight of the bone cement, per 21 CFR 74.3102 (**Tab A**). The target concentration for this colorant in the powder component of Cobalt™ G-MV is 0.125% by weight. As the weight of the powder component is 40g, and the weight of the liquid component is 18.8g (20ml x 0.94g/ml), the total weight of a single unit of cement is 58.8g. Therefore, the target concentration of the colorant FD&C Blue No.2 Aluminum Lake in Cobalt™ G-MV Bone Cement, after mixing the powder and liquid components, is 0.0849% (0.125% x 40g/58.8g).

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables below for temperature variations.)

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

DJA x00075

The temperature versus set time curves and tables set out below and in the package insert (**Tab B** of this section) provide information for temperature variations. Cobalt™ G-MV Bone Cement can be mixed in an open bowl or in a vacuum mixer, and is applied to the operative site either manually or with a bone cement gun.

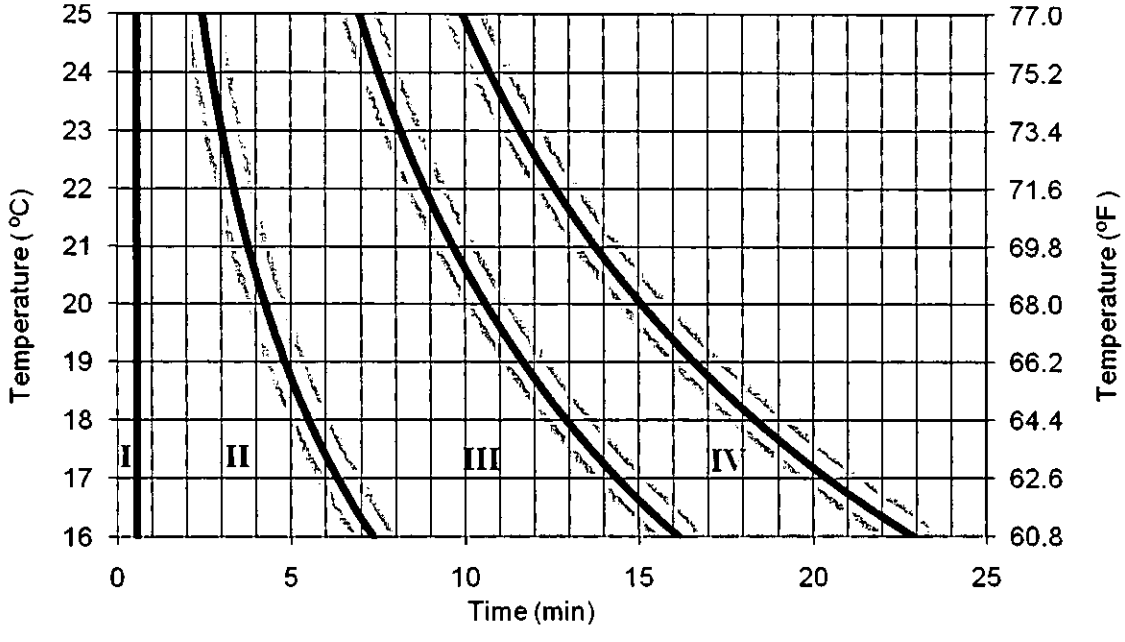
Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

Vacuum Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

Handling and Setting Times vs. Temperature for Open Bowl Mixing of Cobalt™ G-MV Bone Cement

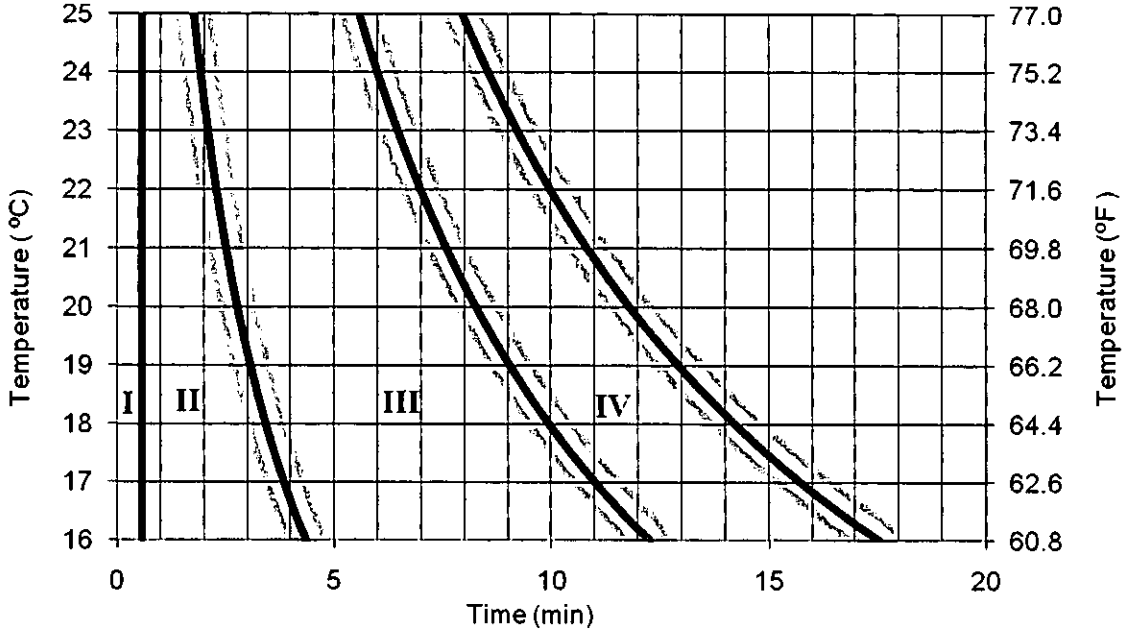


I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

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

DJA x00076

Handling and Setting Times vs. Temperature for Vacuum Mixing of Cobalt™ G-MV Bone Cement



I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

Polymerization is an exothermic reaction with temperatures rising as high as 90°C, which occurs while the cement is hardening *in situ.* The released heat may damage bone or other tissues surrounding the implant. Although the spontaneous generation of heat accelerates the reaction, the polymerization of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

A complete listing of the implants is contained in **Tab C** along with engineering drawings of the implant.

Mechanical Testing

Extensive *in vitro* testing was performed in accordance with *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* to demonstrate the equivalence of Cobalt™ G-MV Bone Cement to the predicate Simplex® P with Tobramycin (K014199). Complete test reports characterizing the chemical, handling, physical, and mechanical properties of Cobalt™ G-MV Bone Cement compared to its predicate device, Simplex® P with Tobramycin (K014199), are located in the **Mechanical Testing** section of this submission. Also provided in the **Mechanical Testing** section are a Mechanical Properties Summary Table and tables demonstrating Cobalt™ G-MV's conformance to consensus standards.

A summary of test reports for Cobalt™ G-MV is included below and in the **Mechanical Testing** section of this submission. Cobalt™ G-MV was tested in accordance with, and conforms to, the standards set forth in ASTM F 451 and ISO 5833 . In addition, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) and met the requirements. (Please see the **Materials and Biocompatibility** discussion in this section for further information.)

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

DJA x00077

Test Report	Purpose	Results Summary

(b)(4)

[redacted]

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

DJA x00078

Test Report	Purpose	Results Summary

(b)(4)

[redacted]

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

DJA x00079

Test Report	Purpose	Results Summary
(b)(4) [redacted]		

Materials and Biocompatibility

Changes made to the concentrations of the powder and monomer components might adversely affect monomer elution. Due to this possibility, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) to ensure that the formulation change did not adversely affect the monomer elution. According to USP Specifications, the sample meets the test requirements if the cell culture treated with the sample is less than or equal to grade 2 (mild reactivity). The sample of Cobalt™ G-MV Bone Cement met the USP requirements for this test. The testing demonstrated that the formulation change did not affect monomer elution. The test report is included in the **Mechanical Testing** section of this submission.

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

DJA x00080

Testing Laboratory:
Pacific BioLabs (formerly Northview Pacific Laboratories)
551 Linus Pauling Drive
Hercules, CA 94547
FDA Registration No. 29-14117

Biocompatibility

Component	Material	Applicable Standard
Powder (copolymer)	• Methyl methacrylate-styrene copolymer • Poly(methyl methacrylate) • Zirconium dioxide • Benzoyl peroxide • FD&C Blue No.2 Aluminum Lake • Gentamicin Sulfate	ASTM F 451-99a ASTM F 451-08 ISO 5833:2002
Liquid (monomer)	• Methyl methacrylate (stabilized with hydroquinone) • N,N-dimethyl-p-toluidine	ASTM F 451-99a ASTM F 451-08 ISO 5833:2002

Standards Data Reports (Forms FDA3654) have been completed for the material standards cited in this submission and are attached in **Tab D**.

Sterility Information
Cobalt™ G-MV powder and the packet containing the powder are provided sterile by gas sterilization methods as follows:

Gas Type:	Ethylene Oxide (EtO)
Residuals:	meet the AMMI/ANSI/ISO 10993-7:1995 and AAMI TIR No. 19-1998
Sterility Assurance Level:	10^{-6}
Sterility Validation Method:	AMMI/ANSI/ISO 11135:1994
Pyrogen-Free:	No claims will be made
Labeling:	All packages will display a black/dark brown to green chemical indication dot along with a statement that the device has been sterilized by Ethylene Oxide (EtO).
Contract Sterilization Site:	Centurion Sterilization Services A Division of Tri-State Hospital Supply Corp. 301 Catrell Drive Howell, Michigan 48843 Registration Number: 1824619

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

DJA x00081

The Cobalt™ G-MV liquid component is sterile filtered and aseptically filled. The interior of the Softpac pouch is Gamma sterilized prior to the asceptic fill. The exterior of the pouch containing the liquid is sterilized by exposure to vaporous hydrogen peroxide, as well as the outside of the liquid packet and inside of the overwrap. The filtration and vaporous hydrogen peroxide sterilization methods are as follows:

Gamma

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: Gamma Irradiation Product Adaption, File #229
Sterilization Site:
STERIS Isomedix
1880 Industrial Drive
Libertyville, Illinois 60048

Filtration

Filter Size: membranes of porosity not greater than 0.22μm
Sterility Validation Method: U.S.P. test methods
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, IN 46582

Vaporous Hydrogen Peroxide

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: EN 550, revised protocol
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, In 46582

These are the same sterilization methods used for the predicate Cobalt™ G-HV cleared in K051532.

[continued next page ...]

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

DJA x00082

Packaging

Cobalt™ G-MV is double packaged. The packaged powder and liquid components are placed into a fiberboard outer box after the individual components are packaged as discussed below.

Powder

The powder component's inner gas permeable pouch is made of Tyvek®/Mylar® and enclosed in a foil-lined protective overwrap pouch, also made of foil. The packaging of Cobalt™ G-MV powder is similar to that of the predicate Cobalt™ G-HV Bone Cement's powder component (K051532). Since FDA's clearance of Cobalt™ G-HV in 2005, Biomet has changed the exterior packaging for its bone cements from a paper/foil/polymer laminated pouch to a foil/polymer laminated pouch comprised of TPC-0814B. This change utilized internal documentation pursuant to FDA's guidance document, *"Deciding when to Submit a 510(k) for a Change to an Existing Device (K97-1).* The exterior foil packaging has been validated and poses no new risks. A copy of the validation for TPC-0814B is on file at Biomet and can be accessed at any future FDA inspection. The inside packaging for Cobalt™ G-MV is the same as the predicate Cobalt™ G-HV's inside packaging, which has not changed since it was cleared.

Liquid (Monomer)

The liquid monomer's inner container is a Cryovac T6050B co-extruded film pouch (LLDPE sealant layer, polypropylene skin, and barrier of EVOH sandwiched between nylon layers). The outer container is a Tyvek® pouch. The packaging for the liquid monomer is the same as that of its predicate, Cobalt™ G-HV (K051532).

Sterilization

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The exterior surfaces of the cement liquid packages are sterilized by exposure to vaporous hydrogen peroxide that takes place at Biomet Manufacturing Corp. The label will include an EtO sterility identifier.

The sterilization of the liquid component of Cobalt™ G-MV Bone Cement is identical to that of the predicate Cobalt™ G-HV Bone Cement's liquid component (K051532). Please refer to the following table for a comparison of the packaging and sterilization of Cobalt™ G-MV Bone Cement to its predicates.

[continued next page ...]

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

DJA x00083

Powder Component Packaging and Sterilization				
		Cobalt™ G-MV (New)	**Cobalt™ G-HV (K051532)**	**Simplex® P w/ Tobramycin (K014199)**
INNERMOST POUCH	**Material**	Tyvek®/Mylar	Tyvek®/Mylar	Multi-layer clear plastic barrier film
	Sterility	Contents & exterior sterile (EtO)	Contents & exterior sterile (EtO)	Contents & exterior sterile (Gamma)
OVERWRAP	**Material**	Foil	Foil	Plastic pouch with breathable header
	Sterility	Contents sterile	Contents sterile	Contents sterile
Liquid Component Packaging and Sterilization				
INNER CONTAINER	**Material**	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Glass ampoule
	Sterility	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & sterilization of ampoule prior to aseptic fill)
	Comment	Very good barrier. Durable package.	Very good barrier. Durable package.	Impermeable barrier, but fragile. Hazardous to open; glass shards may fall into monomer upon opening.
OUTER CONTAINER	**Material**	Tyvek® pouch	Tyvek® pouch	Rigid plastic blister with breathable lid
	Sterility	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (EtO)
	Comment	Vaporous hydrogen peroxide permeable	Vaporous hydrogen peroxide permeable	EtO permeable lid stock

Shelf Life

Cobalt™ G-MV Bone Cement has a one-year shelf life. Please see **Tab E** for the Sterilization and Shelf Life Justification.

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

DJA x00084

Labeling
A copy of the package insert may be found behind **Tab B**, where a representative package label is included as well. In addition, a copy of the outer carton for one of Biomet's PMMA bone cements (Cobalt™ HV, K051496) is provided. The outer carton for Cobalt G-MV will be similar to this, with the same warnings and caution statements.

Surgical Technique
The Surgical Technique for Cobalt™ G-MV is the same as, or similar to, its predicates and is included in the package insert (**Tab B**).

Cobalt™ G-MV copolymer powder is double packaged. The inner gas permeable packet and its contents, as well as the inside of the foil laminate protective overwrap, are sterilized with ethylene oxide. The packet containing the sterile filtered liquid monomer is packaged in a protective gas-permeable overwrap pouch. The interior of the Softpac pouch is Gamma sterilized prior to the asceptic fill. The outside of the liquid packet and inside of overwrap pouch are sterilized by exposure to vaporous hydrogen peroxide.

(At least one extra unit of Cobalt™ G-MV Bone Cement should be available before starting a surgical procedure).

A unit is prepared by mixing the entire contents of one (1) packet of powder (40 g copolymer) with one (1) packet of liquid (20 ml monomer). One or two units will usually suffice, although this will depend upon the specific surgical procedure and the techniques employed. Each unit is prepared separately.

The following are required for preparation of the bone cement:

- Sterile working area
- Sterile plastic bowl approved for use with monomers
- Sterile mixing spoons or spatulas.

Note: For vacuum mixing, refer to manufacturer instructions.

A circulating nurse or assistant opens the peelable film package and the blister pack, and the sterile powder packet and liquid packet are aseptically placed on a sterile table. The powder packet and the liquid packet are opened under sterile conditions. Since each packet of powder contains a pre-measured quantity of copolymer to react with a pre-measured quantity of monomer, care should be taken to mix the entire contents of one powder packet with the entire contents of one liquid packet. Partial amounts should not be used.

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

DJA x00085

MIXING INSTRUCTIONS FOR BOWL MIXING

Note: Cement can also be mixed in a vacuum mixing system. Refer to manufacturer instructions.

Pour the liquid into a bowl. Add the powder. Stir with a spatula vigorously, but carefully, for about 30 seconds.

CEMENT MAY BE APPLIED IN A PRE-DOUGH STATE, BUT IF A DOUGH-LIKE MASS DOES NOT STICK TO RUBBER GLOVES AS DESIRED, WAIT ANOTHER 2-6 MINUTES depending on the ambient temperature (SEE CURVES).

At this state knead for about 15-30 seconds. Thus, it becomes more homogeneous, and mixed air bubbles disappear for the most part. On the other hand, if the kneading process is extended too long, the polymerization may proceed to a point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The working time may be affected by temperature (see curves and tables for working and hardening times). Additionally, the moisture content in any bone cement powder has an effect on polymerization; cement powder with higher moisture content will set faster, while drier cement powder will result in slower set-times. The outer foil pouch acts as a moisture barrier for Cobalt™ G-MV Bone Cement. To minimize fluctuation of set-times, do not remove the powder component's moisture barrier until it is time to mix the cement. Maintaining a constant and moderate (40-55% RH) humidity in the operating room will also lead to more consistent cement handling performance. The ideal working consistency of the Cobalt™ G-MV Bone Cement for manual application to bone is best determined by the surgeon based upon experience in using the preparation. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Excessive cement must be removed while it is still soft. If additional cement is required during the surgical procedure, another packet of liquid and packet of powder may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

The completion of polymerization occurs in the patient and is associated with the liberation of heat. To more rapidly dissipate the heat, the polymerizing cement may be irrigated with a cool physiologic saline solution.

STORAGE

Store package in a dry, ventilated place between 6°C and 23°C (42.8° to 73.4°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73.4 °F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

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

DJA x00086

The copolymer powder does not withstand heat sterilization treatment. If a packet is accidentally opened, it must not be used.

CAUTION

Federal Law restricts this device to sale, distribution, and use by or on the order of a physician.

HOW SUPPLIED

Carton consisting of:

1 packet of copolymer powder containing 40 g
1 packet of liquid monomer containing 20 ml

The following tables and graphs were generated using standard methods including a temperature-controlled environment. Warming of bone cement by any manual manipulation and the eventual application to the surgical site will accelerate the onset and completion of the final hardening phase. The extent of acceleration depends on the timing of manipulation and application. Early and extended warming will have the largest effect on cement hardening.

Typical working data for mixing Cobalt™ G-MV Bone Cement

Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

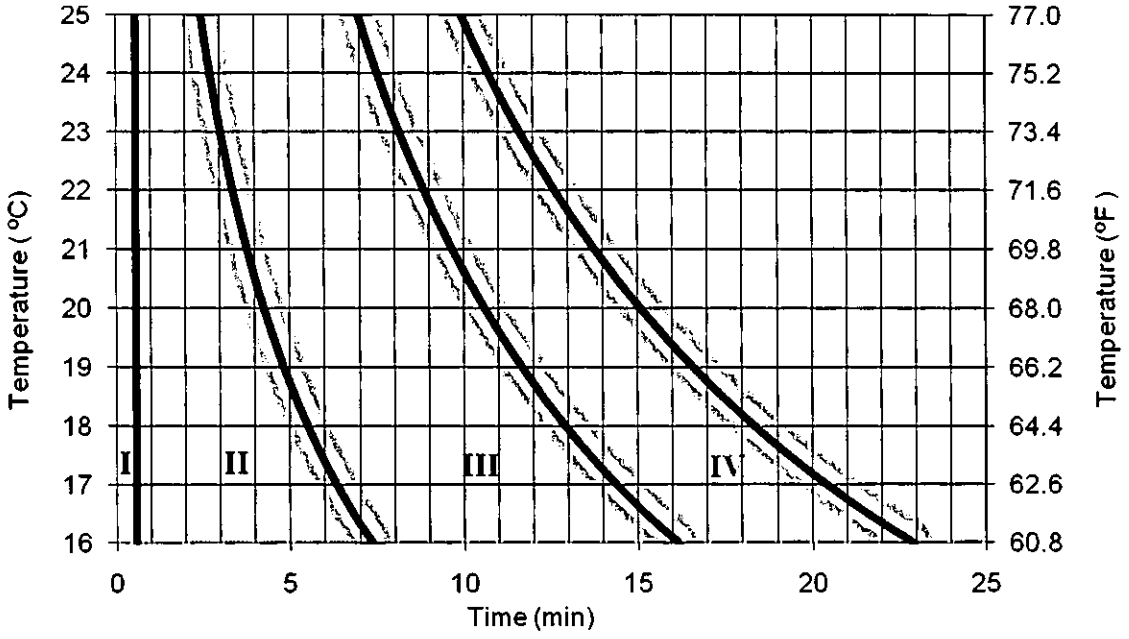
Vacuum Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

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

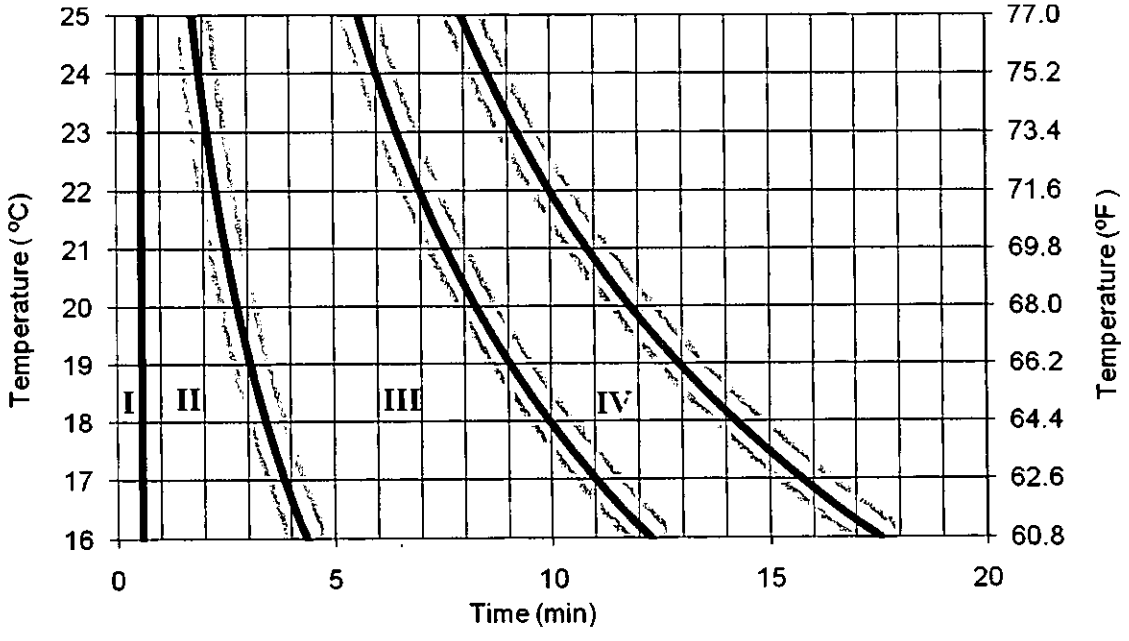
DJA x00087

Handling and Setting Times vs. Temperature for Open Bowl Mixing of Cobalt™ G-MV Bone Cement



I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

Handling and Setting Times vs. Temperature for Vacuum Mixing of Cobalt™ G-MV Bone Cement



I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00088

Electronic Code of Federal Regulations
e-CFR™

e-CFR Data is current as of April 3, 2009

Title 21: Food and Drugs
PART 74—LISTING OF COLOR ADDITIVES SUBJECT TO CERTIFICATION
Subpart D—Medical Devices

Browse Previous | Browse Next

§ 74.3102 FD&C Blue No. 2.

(a) *Identity.* The color additive FD&C Blue No. 2 shall conform in identity to the requirements of §74.102 (a)(1).

(b) *Specifications.* (1) The color additive FD&C Blue No. 2 for use in coloring surgical sutures shall conform to the following specifications and shall be free from impurities other than those named to the extent that such impurities may be avoided by current good manufacturing practice:

Sum of volatile matter at 135 °C (275 °F) and chlorides and sulfates (calculated as sodium salts), not more than 15 percent.

Water insoluble matter, not more than 0.4 percent.

Isatin-5-sulfonic acid, not more than 0.4 percent.

Isomeric colors, not more than 18 percent.

Lower sulfonated subsidiary colors, not more than 5 percent.

Lead (as Pb), not more than 10 parts per million.

Arsenic (as As), not more than 3 parts per million.

Total color, not less than 85 percent.

(2) The color additive FD&C Blue No. 2–Aluminum Lake on alumina for use in bone cement shall be prepared in accordance with the requirements of §82.51 of this chapter.

(c) *Uses and restrictions.* (1) The color additive FD&C Blue No. 2 may be safely used for coloring nylon (the copolymer of adipic acid and hexamethylene diamine) surgical sutures for use in general surgery subject to the following restrictions:

(i) The quantity of color additive does not exceed 1 percent by weight of the suture;

(ii) The dyed suture shall conform in all respects to the requirements of the United States Pharmacopeia XX (1980); and

(iii) When the sutures are used for the purposes specified in their labeling, the color additive does not

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00089

migrate to the surrounding tissues.

(2) The color additive FD&C Blue No. 2–Aluminum Lake on alumina may be safely used for coloring bone cement at a level not to exceed 0.1 percent by weight of the bone cement.

(3) Authorization and compliance with these uses shall not be construed as waiving any of the requirements of sections 510(k), 515, and 520(g) of the Federal Food, Drug, and Cosmetic Act with respect to the medical device in which the color additive FD&C Blue No. 2 and the color additive FD&C Blue No. 2–Aluminum Lake on alumina are used.

(d) *Labeling.* The labels of the color additive FD&C Blue No. 2 and the color additive FD&C Blue No. 2–Aluminum Lake on alumina shall conform to the requirements of §70.25 of this chapter.

(e) *Certification.* All batches of FD&C Blue No. 2 and its lake shall be certified in accordance with regulations in part 80 of this chapter.

[64 FR 48290, Sept. 3, 1999]

Browse Previous | Browse Next

For questions or comments regarding e-CFR editorial content, features, or design, email ecfr@nara.gov.

For questions concerning e-CFR programming and delivery issues, email webteam@gpo.gov.

Section 508 / Accessibility

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOIA-TUS@fda.hhs.gov or 301-796-8114

DJA x00090

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Biomet Orthopedics
56 East Bell Drive
P.O. Box 587
Warsaw, Indiana 46581 USA

01-50-1195
Date: **06/09**

COBALT™ MV WITH GENTAMICIN BONE CEMENT

Medium Viscosity Radiopaque Bone Cement containing Gentamicin
Methyl Methacrylate – Styrene Copolymer & Poly (methyl methacrylate)

Attention Operating Surgeon

DESCRIPTION
Cobalt™ MV with Gentamicin Bone Cement provides two separate, pre-measured sterilized components, which when mixed form a radiopaque rapidly setting bone cement.

One component is supplied in a gas-permeable packet. It consists of 40 g powder (copolymer) with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams
• Poly(methyl methacrylate)	6.00 grams
• Zirconium dioxide	4.00 grams
• FD&C Blue No. 2 Aluminum Lake	0.05 grams
• Benzoyl peroxide	0.35-1.00 grams
• Gentamicin sulfate (equivalent to 0.50 g Gentamicin)	0.84 grams

The other component is supplied in a flexible pouch. It consists of 20 ml of liquid (monomer) with the following composition:

• Methylmethacrylate (stabilized with hydroquinone)	18.424 grams
• N,N-dimethyl-p-toluidine	0.376 grams

The liquid monomer is sterile filtered. The interior of the monomer pouch is sterilized by exposure to gamma radiation. The exterior of the pouch containing the liquid is sterilized with vaporous hydrogen peroxide. The powder is sterilized with ethylene oxide. The gas-permeable packets containing the powder are sterilized with ethylene oxide.

Blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder component to produce a bluish tint in the final cement. This renders it possible to distinguish between bone and cement within the surgical field.

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which, after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables for temperature variations.)

Polymerization is an exothermic reaction with temperatures rising as high as 90°C, which occurs while the cement is hardening *in situ*. The released heat may damage bone or other tissues surrounding the implant. Although the spontaneous generation of heat accelerates the reaction, the polymerization of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

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

DJA x00091

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

MATERIALS:
Methyl methacrylate-Styrene copolymer (containing Benzoyl peroxide)
Poly (methyl methacrylate)
Benzoyl peroxide
Zirconium dioxide
FD&C Blue No.2 Aluminum Lake
Gentamicin sulfate
Methylmethacrylate (stabilized with hydroquinone)
N,N-dimethyl-p-toluidine

ACTION
Cobalt™ MV with Gentamicin Bone Cement is an acrylic cement-like substance which allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between prosthesis and bone. Insoluble zirconium dioxide provides the radiopaque quality of the formulation.

INDICATIONS
Cobalt™ MV with Gentamicin Bone Cement is indicated for use in arthroplastic procedures of the hip, knee, and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended to affix a new prosthesis in the second stage of a two-stage revision after the initial infection has been cleared.

CONTRAINDICATIONS
Cobalt™ MV with Gentamicin Bone Cement must not be used during pregnancy or the nursing period. Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients allergic to gentamicin or to other constituents of the bone cement. A hypersensitivity to any aminoglycoside is a contraindication to the use of gentamicin. A history of hypersensitivity or serious toxic reactions to aminoglycosides may also contraindicate the use of any other aminoglycoside because of known cross-sensitivity of patients to drugs in this class. The use of Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients with infectious arthritis, and in active infection of the joint or joints to be replaced.

Relative contraindications include the following:

1. Uncooperative patient or patient with neurologic disorder who is incapable of following directions
2. Metabolic disorders which may impair bone formation
3. Osteomalacia
4. Distant foci of infections which may spread to the implant site
5. Rapid joint destruction, marked bone loss or bone resorption, vascular insufficiency, muscular atrophy, or neuromuscular disease.
6. Hypotension
7. Congestive heart failure
8. Renal impairment

WARNINGS
Note: Adulteration of this bone cement may negatively affect performance characteristics.

Prior to using the Cobalt™ MV with Gentamicin Bone Cement surgeons should, by specific training and experience, be thoroughly familiar with the properties, handling characteristics, and application of the PMMA bone cement. (See Precautions and Mixing Technique) Because the handling and curing characteristics of this cement varies with temperature and mixing technique, they are best determined by the surgeon's actual experience. It is advisable for the surgeon to go through the entire mixing, handling and setting process *in vitro* before using the material in an actual surgical procedure.

Adverse cardiovascular reactions can include hypotension, hypoxemia, cardiac arrhythmia, bronchspasm, cardiac arrest, myocardial infarction, pulmonary embolism, cerebrovascular accident and possible death. Hypotensive reactions can occur between 10 seconds and 165 seconds after application of PMMA bone cement and can last for 30 seconds to 5 or more minutes. Some hypotensive reactions have progressed to cardiac arrest. The blood pressure, pulse and respiration of patients should be monitored carefully during

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

DJA x00092

and immediately following the application of the PMMA bone cement. Any significant alteration in these vital signs should be corrected with appropriate measures. In addition, over-pressurization of the PMMA bone cement should be avoided during the insertion of the PMMA bone cement and implant in order to minimize the occurrence of pulmonary embolism.

The risk of pulmonary fat embolism and the severity of all Bone Cement Implantation Syndrome (BCIS) complications can be reduced by meticulous irrigation and drying of the intramedullary canal Care should be taken to clean and aspirate the proximal portion of the femoral medullary canal just prior to insertion of bone cement. In high-risk patients, for example those sustaining hip fractures, care should be taken not to over-pressurize the cement and to insert the prosthesis slowly.

Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur, as the serum levels required to cause damage are not reached. Serious allergic reactions have been reported rarely in patients on systemic gentamicin therapy. Therefore, the incidence of these serious allergic events may also occur in patients with gentamicin-loaded bone cement.

Device volatility and flammability and electrocautery devices: The operating room should be adequately ventilated to eliminate monomer vapors. Ignition of monomer vapors caused by use of electrocautery devices in surgical sites near freshly implanted bone cements has been reported.

Irritation of the respiratory tract, eyes, and the liver: Caution should be exercised during the mixing of the liquid and powder components of the PMMA bone cement to prevent excessive exposure to the concentrated vapors of the liquid component, which may produce irritation of the respiratory tract, eyes, and possibly the liver. **Personnel wearing contact lenses should not mix PMMA bone cement or be near the mixing of the PMMA bone cement.**

1. DO NOT USE if there is loss of sterility of the cement.
2. Discard and DO NOT USE opened or damaged packages of the bone cement. Use only product packaged in unopened and undamaged containers.
3. Loosening and fracture of either the cement or the prosthesis, or both, can occur due to disease, trauma, and inadequate cementing technique, mechanical failure of the materials or latent infection.
4. The liquid and powder components of this cement must be mixed thoroughly before using. Inadequate mixing will lead to inhomogeneity that will compromise the mechanical properties and clinical performance of the cement.
5. DO NOT USE bone cement after expiration date.

The surgeon should decide whether the benefits expected from an arthroplasty outweigh any possible long-term adverse effects.

PRECAUTIONS

Strict adherence to good surgical principles and technique are required during use of the cement. Deep wound infection is a serious postoperative complication and may require total removal of the prostheses and embedded cement. Deep wound infection may be latent and not manifest itself for several years postoperatively.

1. **Contact dermatitis:** The liquid component (monomer) has caused contact dermatitis in those handling and mixing PMMA bone cement. Strict adherence to the instructions for mixing the powder and liquid components may reduce the incidence of contact dermatitis.
2. **Hypersensitivity reaction for operating room personnel:** The liquid component of the PMMA bone cement is a powerful lipid solvent. It should not contact rubber or latex gloves. Should contact occur, the gloves may dissolve and tissue damage may occur. Wearing a second pair of gloves and strict adherence to the mixing instructions may diminish the possibility of hypersensitivity reactions. The mixed bone cement should not make contact with gloved hand until the cement has acquired the consistency of dough. This usually occurs between one and two minutes after the liquid and powder components are mixed.
3. **Hypersensitivity reactions for patients:** The gentamicin content of Cobalt™ MV with Gentamicin Bone Cement may cause hypersensitivity reactions in isolated cases.

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

DJA x00093

4. **Inadequate post-operative fixation:** Inadequate fixation or unanticipated postoperative events may affect the PMMA bone cement/bone interface and lead to micro-motion of cement against the bone surface. A fibrous tissue layer may develop between the PMMA bone cement and the bone that may cause loosening of the prosthesis. Thus, continued, periodic follow-up is advised for all patients.
5. **Exothermic reaction:** Polymerization of the PMMA bone cement is an exothermic reaction that occurs while the PMMA bone cement is hardening *in situ*. The released heat may damage bone or other tissue adjacent the implant.
6. **Extrusion:** Extrusion of the PMMA bone cement beyond the region of its intended application may occur resulting in the following complications: hematuria; dysuria; bladder fistula; delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended use; local neuropathy; local vascular erosion and occlusion; and intestinal obstruction because of adhesions and stricture of the ileum from the heat released during the exothermic polymerization.
7. **USE IN PREGNANCY: The safety and effectiveness of the PMMA bone cement in pregnant women has not been established. PMMA bone cement may adversely affect fetal health.**
8. **PEDIATRIC USE: The safety and effectiveness of the PMMA bone cement in children has not been established. PMMA bone cement may adversely affect bone growth.**
9. **Expiration dating:** PMMA bone cement should not be used after the expiration date because the effectiveness of the device may be compromised.
10. **Disposal:** Expired cement should be mixed according to Instructions for Use prior to disposal. Because of the volatility and flammability of the liquid monomer of the PMMA bone cement, liquid monomer that has leaked or is leaking from the package should be collected and evaporated in a well-ventilated hood or absorbed by an inert material and transferred in a suitable container (one that does not react with the PMMA bone cement) for disposal.
11. **Incompatibility:** Aqueous (e.g. antibiotic containing) solutions must not be mixed with the bone cement, as this reduces the strength considerably.
12. **Monitoring:** Patients receiving gentamicin should be periodically monitored with peak and trough levels of the antibiotic, serum electrolytes, serum renal function, urinalysis, and audiograms (in elderly and/or dehydrated patient in whom there is a higher risk of adverse events associated with gentamicin use).
13. **Use of gentamicin should be avoided in the following situation.**
    Concurrent/sequential use of:
    - Other neurotoxic/nephrotoxic antibiotics
    - Other aminoglycosides
    - Cephaloridine
    - Viomycin
    - Polymixin B
    - Colistin
    - Cisplatin
    - Vancomycin

13. **Dose in patients with renal impairment:** Since no adjustment can be made to the dose in the gentamicin-loaded cement, a risk versus benefit assessment should be made before use in patients with renal impairment.
14. **Drug resistant bacteria:** Using Cobalt™ MV with Gentamicin Bone Cement under conditions other than the indicated use is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Avoid over pressurization of the bone cement because this may lead to extrusion of the bone cement beyond the site of its intended application and damage to the surrounding tissues.

ADVERSE EVENTS

The most serious adverse events, including death, reported with the use of acrylic bone cements are:

- Cardiac arrest
- Myocardial infarction
- Pulmonary embolism
- Cerebrovascular accident
- Sudden death

The most frequent adverse events reported are:

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

DJA x00094

- Transitory fall in blood pressure
- Thrombophlebitis
- Hemorrhage and hematoma
- Loosening or displacement of the prosthesis
- Superficial or deep wound infection
- Trochanteric bursitis
- Short-term cardiac conduction irregularities

Nephrotoxicity

- Usually in patients with pre-existing renal damage
- Also in patients with normal renal function to whom amino-glycosides are administered for longer periods or in higher doses than recommended
- The symptoms may manifest after cessation of the therapy

Neurotoxicity

- Manifested as both auditory and vestibular ototoxicity, including irreversible hearing loss
- Numbness
- Skin tingling
- Muscle twitching
- Convulsions

Other adverse events reported are:

- Heterotopic new bone formation
- Trochanteric separation

Other potential adverse events reported include:

- Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur as the serum levels remain well below levels required to cause damage. Concurrent administration of muscle relaxants and ether may potentiate the neuromuscular blocking properties of gentamicin. However, the low serum concentrations significantly reduce the risk of occurrence of this adverse event. The use of antibiotic-loaded bone cement may lead to development of resistant microorganisms and the physician should weigh the risks vs. benefits to the patient before using Cobalt™ MV with Gentamicin Bone Cement in each case.
- Pyrexia due to an allergy or histological reaction to bone cement
- Hematuria
- Dysuria
- Bladder fistula
- Local neuropathy
- Local vascular erosion and occlusion
- Adhesions and stricture of the ileum due to the heat released during polymerization.
- Delayed sciatic nerve entrapment due to extrusion of the bone cement beyond the region of its intended application.

Adverse reactions affecting the cardiovascular system have been attributed to leakage of unpolymerized liquid monomer into the circulatory system. Data indicate that the monomer undergoes rapid hydrolysis to methacrylic acid and that a significant fraction of the circulating methacrylate is in the form of the free acid, rather than of the methyl ester. Correlation between changes in circulating concentrations of the methyl methacrylate/methacrylic acid and changes in blood pressure has not been established.

Hypotensive episodes reported are more marked in patients with elevated or high normal blood pressure in hypovolemia and in patients with pre-existing cardiovascular abnormalities. Elevations in plasma histamine levels subsequent to introduction of cement have also been reported.

Reports of sometime fatal cardiac arrest suggest that elderly osteoporotic patients undergoing hip replacement surgery for fractures of the femoral neck are at greater risk than those receiving elective joint replacement for arthritic disease. Risk is also higher in patients with pre-existing cardiovascular disease. Although the etiology of cardiac arrest is unclear, it may well be either direct embolic effects or secondary to hypoxia produced by pulmonary embolic phenomena. Introduction of liquid cement under pressure into a clean medullary canal has been shown to appreciably enhance the filling of the bone cavities with marked

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

DJA x00095

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

improvement in the security of the bone cement interface. Care must be exercised in introducing the cement continuously from distal to proximal to avoid laminations in the cement.

DOSAGE AND ADMINISTRATION

Cobalt™ MV with Gentamicin copolymer powder is double packaged. The inner gas permeable packet and its contents, as well as the inside of the foil laminate protective overwrap, are sterilized with ethylene oxide. The packet containing the sterile filtered liquid monomer is packaged in a protective gas-permeable overwrap pouch. The outside of the liquid packet and inside of overwrap pouch are sterilized by exposure to vaporous hydrogen peroxide.

(At least one extra unit of Cobalt™ MV with Gentamicin Bone Cement should be available before starting a surgical procedure).

A unit is prepared by mixing the entire contents of one (1) packet of powder (40 g copolymer) with one (1) packet of liquid (20 ml monomer). One or two units will usually suffice, although this will depend upon the specific surgical procedure and the techniques employed. Each unit is prepared separately.

The following are required for preparation of the bone cement:

- Sterile working area
- Sterile plastic bowl approved for use with monomers
- Sterile mixing spoons or spatulas.

Note: For vacuum mixing, refer to manufacturer instructions.

A circulating nurse or assistant opens the peelable film package and the blister pack, and the sterile powder packet and liquid packet are aseptically placed on a sterile table. The powder packet and the liquid packet are opened under sterile conditions. Since each packet of powder contains a pre-measured quantity of copolymer to react with a pre-measured quantity of monomer, care should be taken to mix the entire contents of one powder packet with the entire contents of one liquid packet. Partial amounts should not be used.

MIXING INSTRUCTIONS FOR BOWL MIXING

Note: Cement can also be mixed in a vacuum mixing system. Refer to manufacturer instructions.

Pour the liquid into a bowl. Add the powder. Stir with a spatula vigorously, but carefully, for about 30 seconds.

CEMENT MAY BE APPLIED IN A PRE-DOUGH STATE, BUT IF A DOUGH-LIKE MASS THAT DOES NOT STICK TO RUBBER GLOVES AS DESIRED, WAIT ANOTHER 2 MINUTES - 6 MINUTES depending on the ambient temperature (SEE CURVES).

At this state knead for about 15 seconds -30 seconds. The cement becomes more homogeneous, and mixed air bubbles disappear for the most part. On the other hand, if the kneading process is extended too long, the polymerization may proceed to the point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The working time may be affected by temperature (see curve and table for working and hardening times). Additionally, the moisture content in any bone cement powder has an effect on polymerization; cement powder with higher moisture content will set faster, while drier cement powder will result in slower set-times. The outer foil pouch acts as a moisture barrier for Cobalt™ MV with Gentamicin Bone Cement. To minimize fluctuation of set-times, do not remove the powder component's moisture barrier until it is time to mix the cement. Maintaining a constant and moderate (40%RH-55%RH) humidity in the operating room will also lead to more consistent cement handling performance. The ideal working consistency of the Cobalt™ MV with Gentamicin Bone Cement for manual application to bone is best determined by the surgeon based upon experience in using the preparation. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Excessive cement must be removed while it is still soft. If additional cement is required during the surgical procedure, another

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

DJA x00096

packet of liquid and packet of powder may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

The completion of polymerization occurs in the patient and is associated with the liberation of heat. To more rapidly dissipate the heat, the polymerizing cement may be irrigated with a cool physiologic saline solution.

STORAGE

Store package in a dry, ventilated place between 6°C and 23°C (42.8°F to 73.4°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73.4°F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

The copolymer powder does not withstand heat sterilization treatment. If a packet is accidentally opened, it must not be used.

HOW SUPPLIED

Carton consisting of:
1 packet of copolymer powder containing 40 g
1 packet of liquid monomer containing 20 ml

The following tables and graphs were generated using standard methods including a temperature-controlled environment. Warming of bone cement by any manual manipulation and the eventual application to the surgical site will accelerate the onset and completion of the final hardening phase. The extent of acceleration depends on the timing of manipulation and application. Early and extended warming will have the largest effect on cement hardening.

Typical working data for mixing Cobalt™ MV with Gentamicin Bone Cement

Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

Vacuum Mixing at Ambient Temperatures

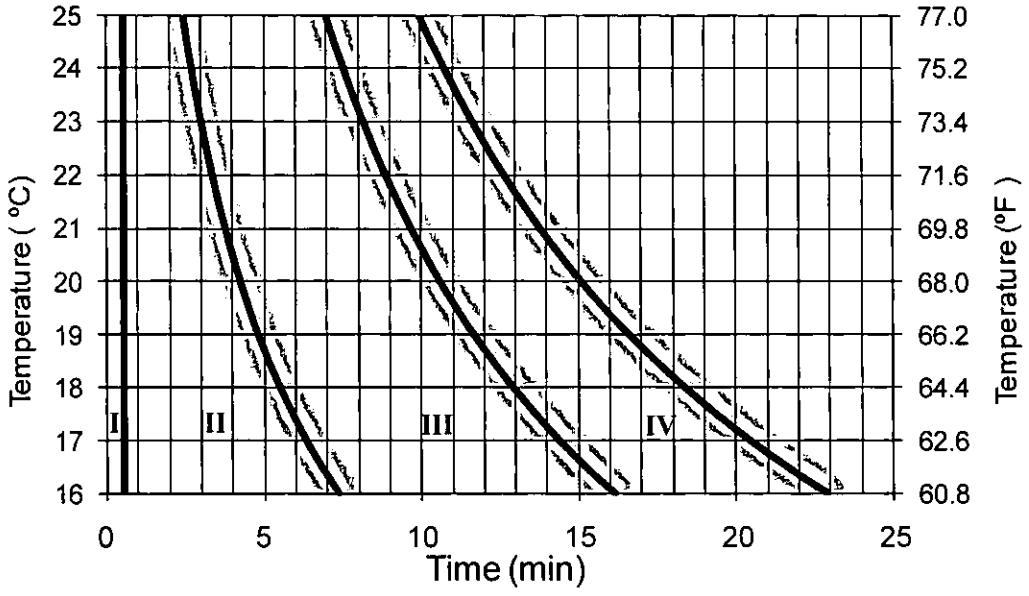
Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

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

DJA x00097

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

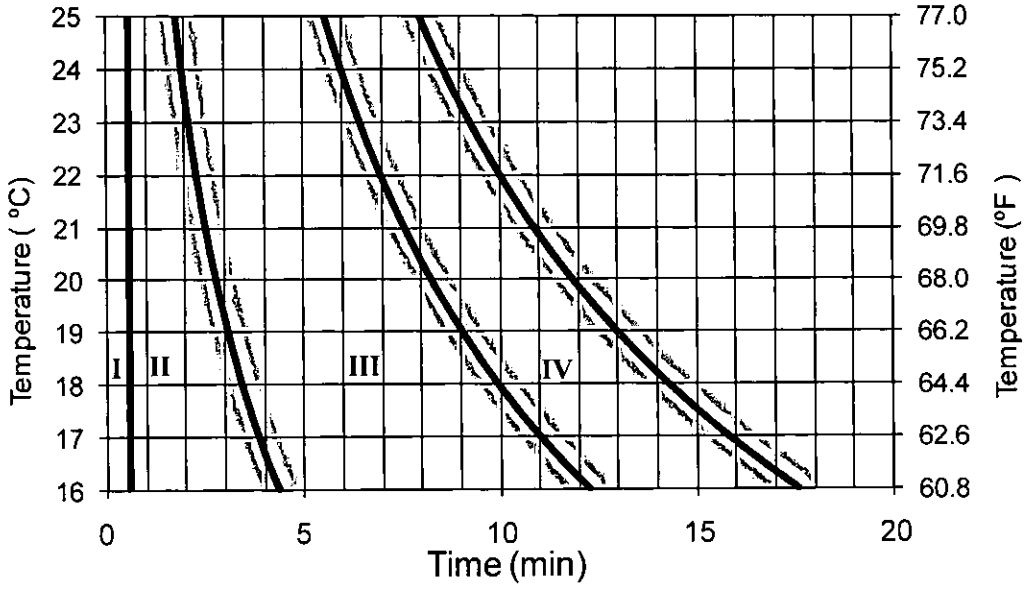
Handling and Setting Times vs. Temperature for
Open Bowl Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

Handling and Setting Times vs. Temperature for
Vacuum Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

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

DJA x00098

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

CAUTION: Federal Law (USA) restricts this device to sale, distribution, or use by or on the order of a physician.

Comments regarding this device can be directed to Attn: Regulatory Dept., Biomet, Inc., P.O. Box 587, Warsaw, IN 46581, FAX: 574-372-3968.

All trademarks herein are the property of Biomet, Inc. or its subsidiaries unless otherwise indicated.

Manufacturer

Date of Manufacture

Do Not Reuse

Caution

STERILE EO — Sterilized using Ethylene Oxide

STERILE R — Sterilized using Irradiation

STERILE — Sterile

STERILE A — Sterilized using Aseptic Processing Techniques

STERILE — Sterilized using Steam or Dry Heat

Use By

WEEE Device

REF — Catalogue Number

LOT — Batch Code

FLAMMABLE — Flammable

EC REP — Authorised Representative in the European Community

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

DJA x00099

COBALT™ G-MV

high contrast bone cement

REF 402439 LOT 123123

COBALT(TM) G-MV BONE CEMENT · 40/20
SOFTPAC SYSTEM
PMMA/MMA **1 PACK**
(STERILE: ETO, FILTRATION, VAPOROUS HYDROGEN PEROXIDE)

40 GRAMS POWDER (STERILE)
METHYL METHACRYLATE-STYRENE COPOLYMER
POLY(METHYL METHACRYLATE) / ZIRCONIUM DIOXIDE
BENZOYL PEROXIDE / FD&C BLUE #2 ALUMINUM LAKE
GENTAMICIN SULFATE

20ML LIQUID (STERILE)
METHYL METHACRYLATE MONOMER WITH HYDROQUINONE STABILIZER
N, N-DIMETHYL-P-TOLUIDINE

STERILE

2009-01

EXPIRY DATE:
2010-01

BIOMET ORTHOPEDICS, INC.
56 EAST BELL DRIVE
P.O. Box 587
WARSAW, IN 46581-0587 USA

BIOMET ORTHOPEDICS, INC.
REF 402439
LOT 123123
COBALT(TM) G-MV BONE CEMENT · 40/20
SOFTPAC SYSTEM
PMMA/MMA **1 PACK**

BIOMET ORTHOPEDICS, INC.
REF 402439
LOT 123123
COBALT(TM) G-MV BONE CEMENT · 40/20
SOFTPAC SYSTEM
PMMA/MMA **1 PACK**

DJA x00100

EXPIRE DATE: 2010-01

AFFIX TO PATIENT RECORDS

BIOMET ORTHOPEDICS, INC.
REF 402439
LOT 123123
COBALT(TM) G-MV BONE CEMENT - 40/20
SOFTPAC SYSTEM
PMMA/MMA 1 PACK

EXPIRE DATE: 2010-01

AFFIX TO PATIENT RECORDS

BIOMET ORTHOPEDICS, INC.
REF 402439
LOT 123123
COBALT(TM) G-MV BONE CEMENT - 40/20
SOFTPAC SYSTEM
PMMA/MMA 1 PACK

EXPIRE DATE: 2010-01

AFFIX TO PATIENT RECORDS

EXPIRE DATE: 2010-01

AFFIX TO PATIENT RECORDS

DJA x00101

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

BIOMET®

Sterile Packaged Product

COBALT™ HV

high contrast bone cement

Warning:

- Flammable liquid
- Store in a cool, dry, dark place
- Contents of pouches within this box STERILE unless damaged or opened
- Do not resterilize
- See package insert for dosage and administration

Caution: Federal law (USA) restricts this device to sale by, or on the order of a physician.

Made in the USA.

BIOMET®

COBALT™ HV

high contrast bone cement

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

DJA x00102

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Product Listing
Cobalt™ G-MV Bone Cement

Part Number	Description	Pack Quantity
402439	Cobalt™ G-MV Bone Cement – 40/20	1 pack

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

(b)(4) Drawing

(b)(4) Drawing

(b)(4) Drawing

(b)(4) Drawing

(b)(4) Drawing

DJA x00108

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

A brief note about Standards Data Reports (Form FDA 3654) included in this 510(k):

Cobalt™ G-MV was tested both in-house and at outside laboratories, depending on the test. Form 3654's question, "Was a third party lab responsible for testing conformity ..." allows only a "yes" or "no" answer. In the case of Cobalt™ G-MV, the answer is "yes" ... in some cases. The testing locations are identified in the test reports included in the **Mechanical Testing** section of this 510(k).

Although ISO 5833, Implants for Surgery - Acrylic Resin Cements, is cited in the guidance document, *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* this particular standard could not be located in the Standards database on FDA's Web site.

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

DJA x00109

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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]

F 451-08, Standard Specification for Acrylic Bone Cement

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 020	
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?	☒	☐
oes 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 the standard? 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: Class II Special Controls Guidance Document: Polymethylmethacrylate (PMMA) Bone Cement; Guidance for Industry and FDA (July 17, 2002)

[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 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 of 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

DJA x00110

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
F 451-99A, STANDARD SPECIFICATION FOR ACRYLIC BONE CEMENT

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
ALL		☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

❖ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

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

Center for Devices and Radiological Health
1350 Piccard Drive
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

DJA x00111

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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]

F 451-99a, Standard Specification for Acrylic Bone Cement

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 020	
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?	☒	☐
oes 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 the standard? 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: Class II Special Controls Guidance Document: Polymethylmethacrylate (PMMA) Bone Cement; Guidance for Industry and FDA (July 17, 2002)

[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 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 of 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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
F 451-99A, STANDARD SPECIFICATION FOR ACRYLIC BONE CEMENT

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
ALL		☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

* Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

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

Center for Devices and Radiological Health
1350 Piccard Drive
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

DJA x00113

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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 5833:2002, Implants for Surgery - Acrylic Resin Cements

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☐	☒
FDA Recognition number [3]	# Unknown	
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 the standard? 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: Class II Special Controls Guidance Document: Polymethylmethacrylate (PMMA) Bone Cement; Guidance for Industry and FDA (July 17, 2002)

[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 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 of 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

DJA x00114

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
ISO 5833:2002, IMPLANTS FOR SURGERY - ACRYLIC RESIN CEMENTS

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
ALL		☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED❖

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

❖ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

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

Center for Devices and Radiological Health
1350 Piccard Drive
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

DJA x00115

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

COBALT G-MV BONE CEMENT SHELF-LIFE JUSTIFICATION

The proposed initial shelf-life of one year for Cobalt G-MV Bone Cement is based on the substantial equivalence of the cement's formulation, time-zero performance, packaging and sterilization, compared to legally marketed PMMA bone cements.

The report entitled "FORMULATION COMPARISON: COBALT G-MV BONE CEMENT vs. SIMPLEX P with TOBRAMYCIN BONE CEMENT", establishes the substantial equivalence of the chemistries, for both the powder and liquid components, of Cobalt G-MV and Simplex P W/ tobramycin (cleared in K014199).

The time-zero performance of Cobalt G-MV Bone Cement is documented in many of the reports included in this 510(k) submission. In all of these reports Cobalt G-MV was found to be substantially equivalent to Simplex P W/ tobramycin (cleared in K014199).

The report entitled "PACKAGING/STERILIZATION COMPARISON COBALT G-MV vs. Cobalt HV/G-HV and Simplex P w/tobramycin" establishes the substantial equivalence of packaging materials and sterilization techniques for Cobalt G-MV to the packaging materials and sterilization techniques used with Cobalt G-HV (cleared by FDA in 510 K051532).

Summary

The chemistry and time-zero performance of Cobalt G-MV are substantially equivalent to Simplex P W/ tobramycin, cement with a 5-year shelf-life. Likewise, the packaging materials and sterilization methods employed for Cobalt G-MV powder component are substantially equivalent to those for Cobalt G-HV (K051532), cleared with a one-year shelf-life.

Conclusion

The proposed one-year initial shelf-life for Cobalt GMV Bone Cement is conservative in light of the data in-hand today and rationale presented herein.

6/30/09

Imad Merkhan
Research scientist

6/30/09

Daniel Smith
Director

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

DJA x00116

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Substantial Equivalence
Cobalt™ G-MV Bone Cement

Introduction
Cobalt™ MV with Gentamicin (also known as Cobalt™ G-MV) Acrylic Bone Cement is a methyl methacrylate-styrene copolymer based acrylic bone cement with a medium viscosity. Cobalt™ G-MV includes gentamicin, a broad spectrum antibiotic. Biomet has developed this bone cement to expand its product line and to provide orthopedic surgeons the option of a medium viscosity, antibiotic-loaded bone cement with excellent handling characteristics. In addition, the cement features a color additive to serve as an optical marking during orthopedic surgery.

Cobalt™ G-MV Bone Cement is substantially equivalent to the following cleared devices:

K051532	Cobalt™ G-HV Bone Cement	Biomet, Inc.
K014199	Simplex® P with Tobramycin Bone Cement	Stryker Howmedica Osteonics

A Predicate Device Comparison Table comparing Cobalt™ G-MV Bone Cement to the predicates can be found in **Tab A** of this section and information on the predicate devices may be found in **Tab B**.

Intended Use
Cobalt™ G-MV is an acrylic cement-like substance which allows seating and fixation of the prosthesis to the bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between the prosthesis and the bone. Insoluble barium sulfate provides the radiopaque quality of the formulation.

Cobalt™ G-MV's intended use is exactly the same as the intended use of its predicates.

Indications for Use
The Indications for Use for Cobalt™ G-MV Bone Cement are the same as the predicate Cobalt™ G-HV (K051521), and similar to the predicate Simplex® P with Tobramycin (K014199). Specifically, the Indications for Use Statement is as follows:

> Cobalt™ G-MV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Design
Cobalt™ G-MV is provided in two separate, pre-measured sterilized components, a 40g packet of polymer powder and a 20mL unit of liquid monomer. When these components are mixed they form radiopaque fast-setting bone cement. This is the same essential design of both bone cement predicates, with the variable feature of each being its chemical composition. Cobalt™ G-MV Bone Cement's formula composition is similar to that of Simplex® P with Tobramycin Cement (K014199) with respect to dough time, work time and set time. Cobalt™ G-MV includes the additional feature of a blue color additive to enhance differentiation from bone in the surgical field. This color additive is the same additive approved by FDA per 21 CFR 74.3102 and used in the predicate Cobalt™ G-HV Bone Cement (K051532). These variations do not result in any significant differences in the chemical, handling, physical, and mechanical properties of Cobalt™ G-MV and Simplex® P with Tobramycin.

Cobalt™ G-MV Bone Cement utilizes the broad-spectrum antibiotic gentamicin, as does its predicate Cobalt™ G-HV (K051532).

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

DJA x00117

Materials

The chemical compounds comprising Cobalt™ G-MV Bone Cement are the same as those used in the predicate Simplex® P with Tobramycin (K014199), except for the radiopacifier, the color additive, and the antibiotic. (See **Tab A** for a device comparison.) The radiopacifier, color additive, and antibiotic used in Cobalt G-MV are also used in the predicate Cobalt™ G-HV (K051532).

40g powder component:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams	(74.575%)
• Polymethyl methacrylate	6.00 grams	(15.000%)
• Zirconium Dioxide	4.00 grams	(10.000%)
• FD&C Blue No. 2 Aluminum Lake	0.05 grams	(0.125%)
• Benzoyl Peroxide	0.35-1.00 grams	(0.300%)
• Gentamicin Sulfate (equivalent to 0.50g of gentamicin)	0.84 grams	

20mL liquid component (monomer):

• Methyl methacrylate (stabilized with hydroquinone)	18.424 grams	(98.0%)
• N,N-dimethyl-p-toluidine	0.376 grams	(2.0%)

Packaging

Cobalt™ G-MV is double packaged. The packaged powder and liquid components are placed into a fiberboard outer box after the individual components are packaged.

The packaging of Cobalt™ G-MV powder is similar to that of the predicate Cobalt™ G-HV Bone Cement's powder component (K051532). Since FDA's clearance of Cobalt™ G-HV in 2005, Biomet has changed the exterior packaging for its bone cements from a paper/foil/polymer laminated pouch to a foil/polymer laminated pouch comprised of TPC-0814B. This change utilized internal documentation pursuant to FDA's guidance document, *"Deciding when to Submit a 510(k) for a Change to an Existing Device (K97-1)*. The exterior foil packaging has been validated and poses no new risks. A copy of the validation for TPC-0814B is on file at Biomet and can be accessed at any future FDA inspection. The inside packaging for Cobalt™ G-MV is the same as the predicate Cobalt™ G-HV's (K051532) inside packaging.

The liquid monomer's inner container is a Cryovac T6050B co-extruded film pouch (LLDPE sealant layer, polypropylene skin, and barrier of EVOH sandwiched between nylon layers). The outer container is a Tyvek® pouch. The packaging for the liquid monomer is the same as that of its predicate, Cobalt™ G-HV (K051532).

Sterilization

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The interior of the pouch is sterilized by exposure to gamma irradiation prior to monomer fill. Sterilization for Cobalt™ G-MV is the same as for the predicate Cobalt™ G-HV (K051532).

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

DJA x00118

Mechanical Testing
Extensive *in vitro* testing was performed in accordance with *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* to demonstrate the equivalence of Cobalt™ G-MV Bone Cement to the predicate Simplex® P with Tobramycin (K014199). Please refer to the **Mechanical Testing Section** for the following:

- ⇨ Summary of Chemical, Physical, Handling & Mechanical Testing (**Tab A**)
- ⇨ Conformance to consensus standards tables (**Tab B**)
- ⇨ Test report summary table (**Tab C**)
- ⇨ Test reports characterizing the chemical, handling, physical, and mechanical properties of Cobalt™ G-MV Bone Cement compared to its predicate device, Simplex® P with Tobramycin (K014199) (**Tab D**)

The test results show that the properties of Cobalt™ G-MV are similar to, or better than, those of its predicate, Simplex® P with Tobramycin (K014199).

Clinical Information
No clinical testing was necessary for a determination of substantial equivalence.

Conclusion
The Cobalt™ G-MV Bone Cement described in this submission is substantially equivalent to the predicate devices. There are no issues regarding safety and/or efficacy.

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

DJA x00119

Predicate Device Comparison Table
Cobalt™ G-MV Bone Cement

	Cobalt™ G-MV Bone Cement	Cobalt™ G-HV Bone Cement	*Simplex®* P with Tobramycin
Manufacturer	Biomet	Biomet	Stryker
510(k) Number	New	K051532	K014199
Indications	Cobalt™ G-MV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.	Cobalt™ G-HV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.	Simplex® P with Tobramycin is indicated for the fixation of prostheses to living bone for use in the second stage of a two-stage revision for total joint arthroplasty.
Intended Use	Allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution between the prosthesis and the bone. Gentamicin sulfate, U.S.P. reduces the risk of bacterial colonization of the bone cement.	Allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution between the prosthesis and the bone. Gentamicin sulfate, U.S.P. reduces the risk of bacterial colonization of the bone cement.	Allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution between the prosthesis and the bone. Tobramycin Sulfate, U.S.P. reduces the risk of bacterial colonization of the bone cement.
Product Code	LOD, MBB	LOD	LOD
Technological Characteristics			
Cement Design	Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Cobalt™ G-HV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Simplex® P provides two separate, pre-measured sterilized components which when mixed form moderately setting bone cement.
Cement Materials	Powder component/Liquid Monomer	Powder Component/ Liquid Monomer	Powder Component/ Liquid Monomer

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00120

	Cobalt™ G-MV Bone Cement	Cobalt™ G-HV Bone Cement	Simplex® P with Tobramycin
Powder Component	Methyl methacrylate-styrene copolymer 29.83g	Methylmethacrylate-methacrylate copolymer with FD&C Blue No. 2 Aluminum Lake 33.86 – 33.42g	Methyl methacrylate-styrene-copolymer 30.00g
	Poly(methyl methacrylate) 6.00g	---	Polymethyl methacrylate 6.00g
	Zirconium dioxide 4.00g	Zirconium dioxide 5.94g	Barium Sulfate, U.S.P. 4.00g
	FD&C Blue No. 2 Aluminum Lake 0.05g	---	---
	Residual benzoyl peroxide/40g powder 0.44g	---	Residual benzoyl peroxide/40g powder 0.51g
	Benzoyl peroxide (hydrous 75%) 0.12g	Benzoyl peroxide (hydrous 75%) 0.20 – 0.64g	---
	Gentamicin Sulfate (equivalent to 0.50g Gentamicin) 0.84g	Gentamicin Sulfate (equivalent to 0.50 g Gentamicin) 0.84g	Tobramycin Sulfate 1.0g active
Liquid Monomer Component	Methylmethacrylate (stabilized with hydroquinone) 18.424g	Methylmethacrylate (stabilized with hydroquinone) 18.424g	Methylmethacrylate (monomer) 19.48ml
	N,N-dimethyl-p-toluidine 0.376g	N,N-dimethyl-p-toluidine 0.376g	N. N-dimethyl-p-toluidine 0.52ml
	Hydroquinone 60 ± 20ppm	Hydroquinone 60 ± 20ppm	Hydroquinone 75 ± 15ppm
Sterilization	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Gamma Irradiation Liquid Monomer Component Membrane Filtration

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00121

	Cobalt™ G-MV Bone Cement	Cobalt™ G-HV Bone Cement	Simplex® P with Tobramycin
Packaging	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile paper-foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in sterile packet, enclosed in a sterile protective package Liquid Monomer Component Pre-sterilized ampoule, enclosed in a pre-sterilized ampoule package
Anatomical Sites	Osseous Tissue	Osseous Tissue	Osseous Tissue
Material and Performance Characterization	See Mechanical Testing section	K051532	See Mechanical Testing section
Mechanical Safety	ASTM Standard Specification for acrylic bone cement F 451-99a and ISO 5833 (Implants for surgery – Acrylic resin cements) is met	ASTM Standard Specification for acrylic bone cement F 451-99a and ISO 5833 (Implants for surgery – Acrylic resin cements) is met	ASTM Standard Specification for acrylic bone cement F 451-99a and ISO 5833 (Implants for surgery – Acrylic resin cements) is met

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00122

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

FORMULATION COMPARISON
COBALT G-MV BONE CEMENT vs. SIMPLEX P W/TOBRAMYCIN BONE CEMENT

The nominal formulation of both the powder and liquid components for Cobalt G-MV and Simplex P w/tobramycin (510 K014199) bone cements are shown below. The formula, listed below, of Simplex P w/tobramycin Bone Cement is as stated in its package inserts. However, Cobalt G-MV Bone cement formula, listed below, is in a different format from what is stated in its package insert for comparison reasons. An excerpt from Simplex P w/tobramycin package insert is attached.

Cobalt G-MV Bone Cement:

40 grams of powder (copolymer) with the following composition:

Methyl methacrylate-Styrene copolymer	29.83g~ 74.600 w/w%
Polymethyl methacrylate	6.00g~ 15.000 w/w%
Zirconium Dioxide	4.00g~10.000 w/w%
FD&C blue #2 aluminum lake	0.05g~ 0.125 w/w%
Residual BPO/40g powder	0.44g~ 1.106 w/w%
Added BPO, hydrous 75%	0.12g~ 0.300 w/w%
Gentamicin active (as sulfate)	0.50g

20 ml of liquid (monomer) with the following composition:

Methylmethacrylate (stabilized with hydroquinone)	19.6 ml
N,N-dimethyl-p-toluidine	0.4ml

Simplex P w/tobramycin Bone Cement:

40 grams of powder (copolymer) with the following composition:

Methyl methacrylate-Styrene copolymer	30.00 g ~ 75.000 w/w%
Polymethyl methacrylate	6.00 g ~ 15.000 w/w%
Barium Sulfate	4.00 g ~ 10.000 w/w%
Residual BPO/40g powder	0.51g ~1.275 w/w%
Tobramycin active (as sulfate)	1.00 g

20 ml of liquid (monomer) with the following composition:

Methylmethacrylate (stabilized with hydroquinone)	19.5 ml
N,N-dimethyl-p-toluidine	0.5 ml

Colorants

As can be seen in the preceding tables, colorant is present in the powder component of Cobalt G-MV bone cement only. There is no colorant in Simplex P w/tobramycin. The colorant used in Cobalt cements is listed in the Code of Federal Regulations as acceptable additives to PMMA bone cements.

The listing for FD&C Blue #2 Aluminum Lake appears in 21 CFR 74.3102 and in part (c)(2) states, "*The color additive FD&C Blue No. 2-Aluminum Lake on alumina may be safely used for coloring bone cement at a level not to exceed 0.1 percent by weight of the bone cement.*" (The complete color additive listing is attached.)

Polymers

The package inserts of Cobalt G-MV and Simplex P w/tobramycin both describe the polymeric constituent of their powder components as "Methyl methacrylate-Styrene copolymer and poly methyl methacrylate". This description is factual, but additional information regarding the character of the polymeric constituent of Simplex P can be found in the book Bone Cements: Up-to-Date Comparison of Physical and Chemical Properties of Commercial Materials, by K-D Kühn (Germany: Springer-Verlag, 2000).

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

DJA x00123

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Initiator (Benzoyl Peroxide BPO)
Simplex P w/tobramycin utilizes only residual BPO to initiate polymerization of the monomer liquid. However, Cobalt G-MV employs both residual BPO (80% of total BPO) and added BPO (20% of total BPO).

Radiopacifier (barium sulfate vs. zirconium dioxide)

The radiopacifier used in Cobalt G-MV Bone Cement is zirconium dioxide. However, Simplex P w/tobramycin has barium sulfate. Both radiopacifiers are used in commercial bone cements. The report titled radiopacity shows that Cobalt G-MV Bone Cement has better radiopacity than Simplex P w/tobramycin.

Monomer Liquid

Both monomer formulations include a monomeric component (methyl methacrylate), an accelerant (N,N-dimethyl-P-toluidine) and a stabilizer (hydroquinone).

Hydroquinone

The presence of hydroquinone in the monomer liquids is acknowledged for both cements. The hydroquinone content in Cobalt monomer liquid is 60ppm and the hydroquinone content in Simplex P monomer liquid is 75 ppm.

Antibiotic

The antibiotic used in Cobalt G-MV Bone Cement is gentamicin sulfate. However, Simplex P w/tobramycin has tobramycin sulfate.
Most infections associated with total joint replacement are caused by some kind of Staphylococcus. The spectrums of antibiotic activity for gentamicin and tobramycin are very similar, although a couple of minor differences have been reported. Gentamicin has greater activity against Serratia, while tobramycin has greater activity against Psuedomonas – otherwise their activity is just about the same.
Although Cobalt G-MV has smaller quantity antibiotics than Simplex P w/tobramycin, the report titled "antibiotic elution" shows substantial equivalent in antibiotic elution between Cobalt G-MV and Simplex P w/tobramycin.

Conclusion

The chemistries of Cobalt G-MV and Simplex P w/tobramycin powder and liquid formulations are substantially equivalent.

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

DJA x00124

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG 3 - 2005

Mr. Lonnie Witham
Biomet Manufacturing Corp.
P.O. Box 587
Warsaw, Indiana 46581-0587

Re: K051532
Trade/Device Name: Cobalt™ G HV Bone Cement
Regulation Number: 21 CFR 888.3027
Regulation Name: Polymethylmethacrylate (PMMA) bone cement
Regulatory Class: II
Product Code: LOD
Dated: July 13, 2005
Received: July 14, 2005

Dear Mr. Witham:

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

DJA x00125

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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) 276-0120 . 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 (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Mark Melkerson
Acting 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

DJA x00126

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K051532

1/2

AUG 3 - 2005

510(k) Summary

Cobalt G™ HV Bone Cement

Applicant/Sponsor: Biomet Manufacturing Corp.
P.O. Box 587
Warsaw, Indiana 46581-0587

Contact Person: Lonnie Witham
Telephone: (574) 267-6639
Fax: (574) 372-1683

Proprietary Name: Cobalt G™ HV Bone Cement

Common Name: PMMA Bone Cement

Legally Marketed Devices To Which Substantial Equivalence Is Claimed:
Predicate Device: Palacos® G Bone Cement
Cleared by: Biomet 510(k) Notification (K030086)
Manufacturer: Biomet Inc.; 56 East Bell Drive; Warsaw, IN 46582

Predicate Device: Generation 4® Bone Cement
Cleared by: 510(k) Notification (K993836)
Manufacturer: Biomet Inc.; 56 East Bell Drive; Warsaw, IN 46582
(Relevant to packaging and sterilization processes cleared for this device)

Device Description:
Cobalt G™ HV Bone Cement is a fast setting polymer (polymethylmethacrylate) cement for use in bone surgery. Mixing of the two sterile components, consisting of a powder and a liquid, initially produces a paste that is used to anchor a joint prosthesis or to fill an osseous defect. The hardened bone cement allows stable fixation of the prosthesis and transfers stresses produced on movement to the bone via the large interface. Insoluble zirconium (IV) oxide is included in the cement powder as an x-ray contrast medium. The FD&C Blue No. 2 Aluminum Lake color additive serves as optical marking of the bone cement at the site of the operation. The gentamicin component is a broad-spectrum antibiotic.

The powder component is supplied in a polyethylene-coated paper packet. It consists of 40 grams of powder (copolymer) with the following composition:

• Methylmethacrylate-methylacrylate copolymer with FD&C Blue No. 2 Aluminum Lake	33.42 - 33.86 grams
• Benzoyl peroxide, hydrous 75%	0.20 - 0.64 grams
• Zirconium dioxide	5.94 grams
• Gentamicin sulfate (equivalent to 0.5 grams gentamicin)	0.835 grams

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

DJA x00127

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K051532 2/2

The liquid component is supplied in a flexible packet. It consists of 20 ml of liquid (monomer) with the following composition:

- Methylmethacrylate (stabilized with hydroquinone) 18.424 grams
- N,N-dimethyl-p-toluidine 0.376 grams

Methymethacrylate monomer is the primary constituent of the liquid component. In much smaller quantities are the accelerator, N, N-dimethyl-p-toluidine, and the stabilizer, hydroquinone, both are typical constituents of PMMA bone cement.

When the powder and liquid components are mixed, the accelerator speeds the generation of free radicals and the stabilizer in the liquid reacts with many of the early free radicals, but is soon consumed. Free radicals can then initiate formation of polymer chains.

Polymerization proceeds slowly over the first few minutes. Polymer chains at the surface of the powder beads mingle with monomer and newly formed polymer chains, while smaller beads may dissolve completely. The cement temperature rises as set time of the cement approaches. Polymerization is essentially complete and the bone cement hard within 15 minutes.

Intended Use / Indications for Use:

Cobalt G™ HV Bone Cement with gentamicin is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Summary of the Technological Characteristics:

The components of Cobalt G™ HV Bone Cement are substantially equivalent to the legally marketed device Palacos® G Bone Cement. Both cements are processed and sterilized in an equivalent manner, the primary difference being the addition of color additive FD&C Blue No. 2 Aluminum Lake. The FDA has approved the new color additive (FD&C Blue No. 2 Aluminum Lake) for use in bone cement.

Non-Clinical /Clinical Testing:

The substantial equivalence to Palacos® G was determined by in vitro comparative testing to Cobalt G™ HV Bone Cement and comparatively analyzing the relevant data. The results showed that Cobalt G™ HV Bone Cement possesses chemical, physical, mechanical and handling characteristics necessary to fulfill its intended use. In summary, Cobalt G™ HV Bone Cement (with gentamicin) is equivalent to Palacos® G (with gentamicin) for its primary intended use of fixation of prosthetic components as described in the device labeling. No clinical testing was performed.

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

DJA x00128

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

STATEMENT OF INDICATIONS FOR USE

510(k) Number K051532

Device Name: Cobalt™ G HV Bone Cement

Indications for Use:

Cobalt™ G HV Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

Prescription Use X OR Over-The-Counter-Use
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(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 K051532

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

DJA x00129

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAY 0 6 2003

Ms. Jennifer A. Daudelin
Regulatory Affairs Specialist
Stryker Howmedica Osteonics
59 Route 17 South
Allendale, NJ 07401

Re: K014199
Trade/Device Name: Simplex™ P with Tobramycin
Regulation Number: 888.3027
Regulation Name: Polymethylmethacrylate (PMMA) bone cement
Regulatory Class: II
Product Code: LOD
Dated: February 3, 2003
Received: February 4, 2003

Dear Ms. Daudelin:

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

DJA x00130

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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 (301) 594-4659. 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 (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

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

Enclosure

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

DJA x00131

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

510(k) Summary for Simplex™ P with Tobramycin

K014199

Proprietary Name:	Simplex™ P with Tobramycin Bone Cement
Common Name:	Antibiotic Bone Cement
Classification Name and Reference:	21 CFR 888.3027 Polymethylmethacrylate (PMMA) Bone Cement
Proposed Regulatory Class:	II
Device Product Code:	OR (87) LOD
For Information contact:	Jennifer A. Daudelin Regulatory Affairs Specialist Howmedica Osteonics Corp. 59 Route 17 Allendale, NJ 07401-1677 (201) 831-5379 Fax: (201) 831-6038 Email: Jdaudelin@howost.com
Date Summary Prepared:	April 28, 2003

MAY 0 6 2003

Device Description

Simplex™ P with Tobramycin is an acrylic bone cement intended for the fixation of prostheses to living bone for use in second stage revision for total joint arthroplasty. The cement is packaged in two sterile components; a liquid monomer component and a powder copolymer component. The liquid monomer component is comprised of methyl methacrylate, N.N-dimethyl-p-toluidine, and hydroquinone. The powder copolymer component consists of methylmethacrylate-styrene copolymer, polymethylmethacrylate, barium sulfate U.S.P., and tobramycin sulfate U.S.P. The liquid and powder components are mixed together resulting in the exothermic polymeric formation of a soft, pliable, dough-like mass. As the reaction progresses, a cement-like complex is formed.

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

DJA x00132

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Intended Use

Simplex™ P with Tobramycin is indicated for the fixation of prostheses to living bone for use in the second stage of a two-stage revision for total joint arthroplasty.

Substantial Equivalence

Simplex™ P with Tobramycin is substantially equivalent in intended use, overall materials, mechanical properties, and operational principles to Surgical Simplex® P Radiopaque Bone Cement (Howmedica Osteonics N-17-004).

Performance Data

Information on the safe use of Simplex™ P with Tobramycin was initially gathered through traditional literature searching. Information in published papers was supplemented by contacting authors of the relevant papers for additional unpublished details. Finally, arthroplasty registries were contacted to determine whether they had data that might be relevant to the safe use of this product.

The cumulative results of extensive in vitro and in vivo test data show that a balance is achieved between antibiotic release and mechanical integrity without threats of systemic toxicity or compromised mechanical function.

Additional in vivo studies were performed, which evaluated the antibiotic release from cement polymerized in situ in rabbits. Local concentrations were measured in the femoral bone bed surrounding the cement, following animal sacrifice and excision, as well as systemic levels drawn throughout the study. The values predicted by the model correlate very well with clinical data from hemovac, serum, urine, and bone samples as reported by several clinicians.

In summary, the testing demonstrates that, in terms of safety and mechanical properties, Simplex™ P with Tobramycin bone cement is substantially equivalent to the legally marketed predicate Surgical Simplex® P Bone Cement.

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015
DJA x00133

Indications for Use

510(k) Number (if known): K014199

Device Name: Simplex™ P with Tobramycin

Indications for Use:

Simplex™ P with Tobramycin is indicated for the fixation of prostheses to living bone for use in the second stage of a two-stage revision for total joint arthroplasty.

for Mark N Melkerson

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

510(k) Number K014199

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use_____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

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

DJA x00134

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Cobalt G-MV Bone Cement vs. Simplex® P w/tobramycin

Summary of Chemical, Physical, Handling & Mechanical Testing

(b)(4) Testing

[redacted]

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

DJA x00135

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

(b)(4) Testing

[redacted]

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

DJA x00136

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

(b)(4) Testing

[redacted]

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

DJA x00137

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Mechanical Testing
Tables Demonstrating Conformance of
Cobalt™ G-MV Bone Cement to Consensus Standards

(b)(4) Testing

[redacted]

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

DJA x00138

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Mechanical Testing
Summary of Test Reports – Cobalt™ G-MV Bone Cement

The table below summarizes the testing conducted on Cobalt™ G-MV Bone Cement. Complete test reports are included in the **Mechanical Testing section** of this 510(k).

(b)(4) Testing

[redacted]

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

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

DJA x00415

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Antibiotic Elution

FDA CDRH DMC

JUL 16 2009

Received

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

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00856

Form Approved: OMB No. 0910-511 Expiration Date: January 31, 2010. 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) [redacted]
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)

BIOMET INC
56 EAST BELL DRIVE
P O BOX 587
WARSAW IN 46581-0587
US

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)
351418342

2. CONTACT NAME
Susan Alexander

2.1 E-MAIL ADDRESS
sue.alexander@biomet.com

2.2 TELEPHONE NUMBER (include Area code)
574-371.1152

2.3 FACSIMILE (FAX) NUMBER (Include Area code)
574-372.1683

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/oc/mdufma

Select an application type:
[X] Premarket notification(510(k)); except for third party
[ ] 513(g) Request for Information
[ ] Biologics License Application (BLA)
[ ] Premarket Approval Application (PMA)
[ ] Modular PMA
[ ] Product Development Protocol (PDP)
[ ] Premarket Report (PMR)
[ ] Annual Fee for Periodic Reporting (APR)
[ ] 30-Day Notice

3.1 Select a center
[X] CDRH
[ ] CBER

3.2 Select one of the types below
[X] Original Application

Supplement Types:
[ ] Efficacy (BLA)
[ ] Panel Track (PMA, PMR, PDP)
[ ] Real-Time (PMA, PMR, PDP)
[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)
[ ] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA
[X] NO, I am not a small business
4.1 If Yes, please enter your Small Business Decision Number:

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?
[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/cdrh/mdufma for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.
[ ] This application is the first PMA submitted by a qualified small business, including any affiliates
[ ] This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only
[ ] The sole purpose of the application is to support conditions of use for a pediatric population
[ ] 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

8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION
(b) (4) [redacted] 02-Jun-2009

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

DJA x00857

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT
(As Required by 21 CFR 807.87(j))

I certify, in my capacity as a Development Engineer of Biomet Manufacturing Corp., I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Imad Merkhan

Imad Merkhan

6/16/09
Date

Cobalt™ G-MV Bone Cement
Device

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

DJA x00858

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

TRUTHFUL AND ACCURATE STATEMENT
(As Required by 21 CFR 807.87(j))

I certify, in my capacity as Director of Clinical and Regulatory Affairs, Biomet Manufacturing Corp., I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Tracy Bickel Johnson

7/15/09
Date

Cobalt™ G-MV Bone Cement
Device

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

DJA x00859

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

See OMB Statement on Reverse. Form Approved: OMB No. 0910-0816, Expiration Date: 10-31-2011

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.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
Biomet Manufacturing Corp.

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

3. ADDRESS *(Number, Street, State, and ZIP Code)*
56 East Bell Drive
P.O. Box 587
Warsaw, IN 46581-0587

4. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 574.267.6639
(Fax) 574.372.1683

PRODUCT INFORMATION

5. **FOR DRUGS/BIOLOGICS:** Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s)
FOR DEVICES: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)
(Attach extra pages as necessary)

Common name: PMMA Bone Cement

Trade name: Cobalt G-MV Bone Cement

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)*
NA

8. SERIAL NUMBER ASSIGNED TO APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
NA

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, enacted by 121 Stat. 823, Public Law 110-85, 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, enacted by 121 Stat. 823, Public Law 110-85, 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, enacted by 121 Stat. 823, Public Law 110-85, 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.

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 *(Attach extra pages as necessary)*
NCT Number(s): NA

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. SIGNATURE OF SPONSOR/APPLICANT/SUBMITTER OR AN AUTHORIZED REPRESENTATIVE (Sign)
Susan Alexander

12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11
(Name) Susan A. Alexander
(Title) Regulatory Affairs Specialist

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in Nos. 11 and 12)*
56 East Bell Drive
P.O. Box 587
Warsaw, IN 46581-0587

14. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 574.267.6639, x1152
(Fax) 574.372.1683

15. DATE OF CERTIFICATION
6/29/09

PSC Graphics: (301) 443-1090 EF

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

DJA K00004

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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

COVER SHEET MEMORANDUM

From: Reviewer Name Hany Demian

Subject: 510(k) Number K092150/S

To: The Record

Please list CTS decision code SE

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

☐ Hold (Additional Information or Telephone Hold).

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

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/510(k) Statement (1 PAGE)	*Attach Summary*	X	
Truthful and Accurate Statement.	*Must be present for a Final Decision*	X	
Is the device Class III? If yes, does firm include Class III Summary?	*Must be present for a Final Decision*		X
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)			NA
Is this a combination product? (Please specify category 4, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC		X	
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			X
Is this device intended for pediatric use only?			X
Is this a prescription device? (If both prescription & OTC, check both boxes.)		X	
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			NA
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)			No
Does this device include an Animal Tissue Source?			
All Pediatric Patients age<≈21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days -< 2 years old)			
Child (2 years -< 12 years old)			
Adolescent (12 years -< 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			

Rev. 7/2/07

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

DJA x00005

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)			
Nanotechnology			
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		

Regulation Number	Class*	Product Code
888.3027	II	LOD MBB

(*If unclassified, see 510(k) Staff)

Additional Product Codes:

Review: (Branch Chief) REVB (Branch Code) 10/27/09 (Date)

Final Review: (Division Director) 10/27/09 (Date)

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

DJA x00007

K092150 S1
SE

Date: 10/26/2009
To: The Record
From: Hany Demian, M.S.

Office: ODE
Division: DSORD

510(k) Holder: Biomet
Device Name: Cobalt G-MV Bone Cement
Contact: Susan Alexander
Phone: 574-267-6639

concur 10/27/09

I. Purpose and Submission Summary

Biomet wishes to market Gentamicin-MV Acrylic Bone Cement for a 2 stage revision once the initial infection as been cleared. This is the same bone cement without the antibiotic cleared in K091608. In S1, the sponsor provided additional data and clarifications that address my concerns regarding (BPO, fatigue testing and gentamicin particle size). I recommend SE determination.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or OTC)	x		
Truthful and Accuracy Statement	x		
510(k) Summary or 510(k) Statement	x		
Standards Form			x
	Yes	**No**	**N/A**
Is the device life-supporting or life sustaining?		x	
Is the device an implant (implanted longer than 30 days)?	x		
Does the device design use software?		x	
Is the device sterile?	x		
Is the device reusable (not reprocessed single use)? Are "cleaning" instructions included for the end user?		x	

Indications for Use

Cobalt™ MV with Gentamicin Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

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

DJA x00008

Reviewer's Comments:

This is the standard indications for use for a low amount of antibiotic that has been previously cleared for a 2 stage revision procedure once the initial infection as been cleared. Therefore the indications for use is considered acceptable.

Device Description:

Device Description

Cobalt™ G-MV bone cement is formed when two separate, pre-measured sterilized components, a powder copolymer and liquid monomer, are mixed to form a radiopaque, rapidly-setting bone cement for use in orthopedic surgery. Mixing of the two sterile components initially produces a paste that is used to anchor the prosthesis, or to fill an osseous defect. The hardened bone cement allows stable fixation of the prosthesis and transfers mechanical stresses produced during movement from the prosthesis to the bone via the large interface between the cement and the bone.

The powder component, supplied in a gas-permeable packet, consists of 40 grams of powder with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams	(74.575%)
• Polymethyl methacrylate	6.00 grams	(15.000%)
• Zirconium Dioxide	4.00 grams	(10.000%)
• FD&C Blue No. 2 Aluminum Lake	0.05 grams	(0.125%)
• Benzoyl Peroxide	0.35-1.00 grams	(0.300%)
• Gentamicin sulfate (equivalent to 0.50g gentamicin)	0.84 grams	

The *liquid* component is supplied in a flexible packet. It consists of 20ml of liquid (monomer) with the following composition:

• Methyl methacrylate (stabilized with hydroquinone)	18.424 grams	(98.0%)
• N,N-dimethyl-p-toluidine	0.376 grams	(2.0%)

The powder contains 10% zirconium dioxide as an x-ray contrast medium. To assist in distinguishing between bone and cement within the surgical field, blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder to produce a bluish tint in the final cement. This color additive may be used safely at a level not to exceed 0.1 percent by weight of the bone cement, per 21 CFR 74.3102 (**Tab A**). The target concentration for this colorant in the powder component of Cobalt™ G-MV is 0.125% by weight. As the weight of the powder component is 40g, and the weight of the liquid component is 18.8g (20ml x 0.94g/ml), the total weight of a single unit of cement is 58.8g. Therefore, the target concentration of the colorant FD&C Blue No.2 Aluminum Lake in Cobalt™ G-MV Bone Cement, after mixing the powder and liquid components, is 0.0849% (0.125% x 40g/58.8g).

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables below for temperature variations.)

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

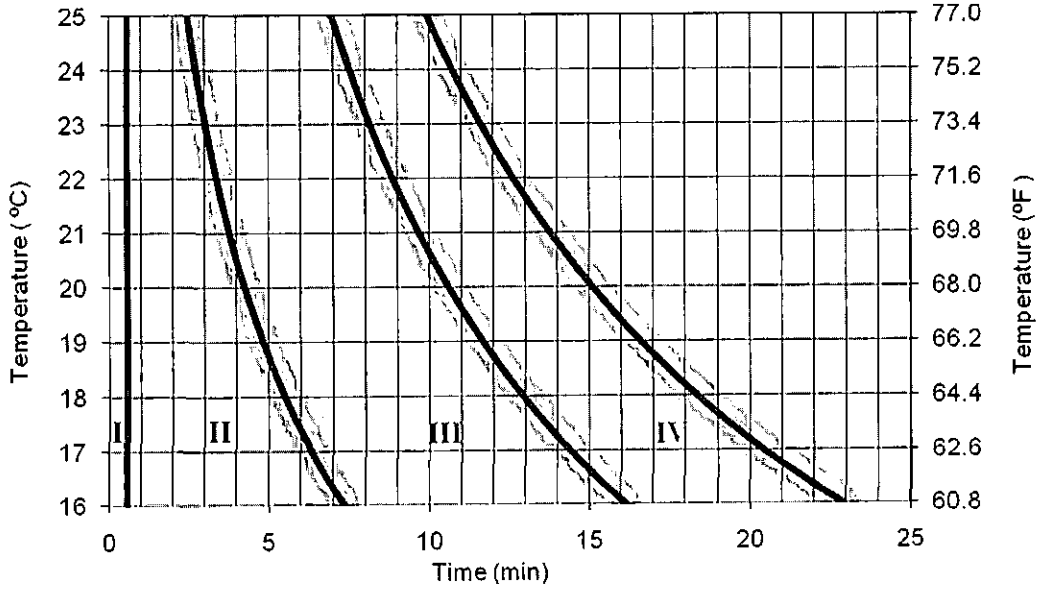
Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

Vacuum Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

Handling and Setting Times vs. Temperature for Open Bowl Mixing of Cobalt™ G-MV Bone Cement

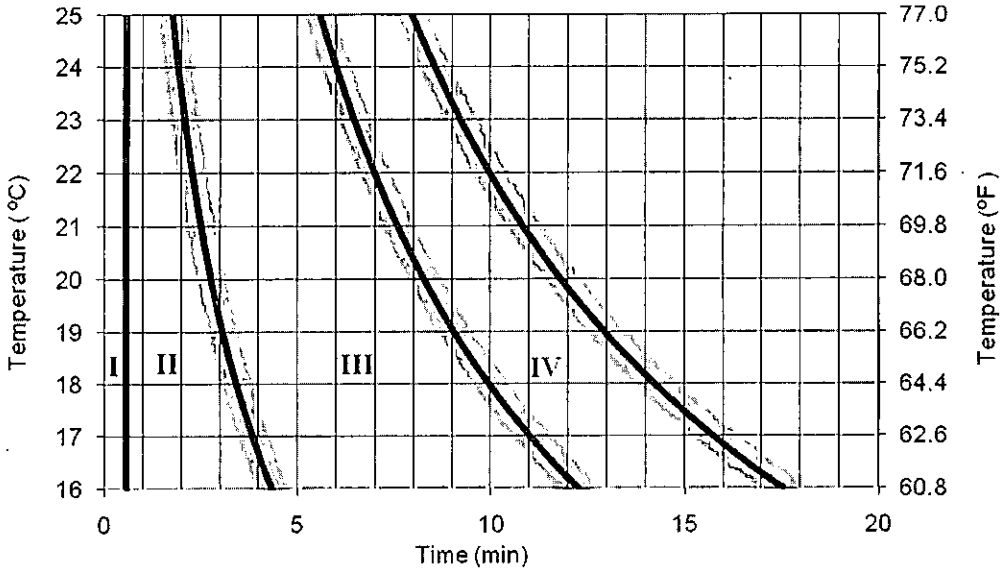


I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

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

DJA x00010

Handling and Setting Times vs. Temperature for Vacuum Mixing of Cobalt™ G-MV Bone Cement



I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

Reviewer's Comments:
The sponsor has provided adequate device description and handling characteristics versus temperatures. This is the same formulation was cleared without the gentamicin sulfate in K091608. In S1, the sponsor provided the upper and lower particle size distribution limits for the gentamicin sulfate powder (63-250 microns.

Performance Testing – Bench

Mechanical Testing
Extensive *in vitro* testing was performed in accordance with *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* to demonstrate the equivalence of Cobalt™ G-MV Bone Cement to the predicate Simplex® P with Tobramycin (K014199). Complete test reports characterizing the chemical, handling, physical, and mechanical properties of Cobalt™ G-MV Bone Cement compared to its predicate device, Simplex® P with Tobramycin (K014199), are located in the **Mechanical Testing** section of this submission. Also provided in the **Mechanical Testing** section are a Mechanical Properties Summary Table and tables demonstrating Cobalt™ G-MV's conformance to consensus standards.

A summary of test reports for Cobalt™ G-MV is included below and in the **Mechanical Testing** section of this submission. Cobalt™ G-MV was tested in accordance with, and conforms to, the standards set forth in ASTM F 451 and ISO 5833 . In addition, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) and met the requirements. (Please see the **Materials and Biocompatibility** discussion in this section for further information.)

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

DJA x00011

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Cobalt G-MV Bone Cement vs. Simplex® P w/tobramycin

Summary of Chemical, Physical, Handling & Mechanical Testing

(b)(4) Testing

[redacted]

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

DJA x00012

(b)(4) Testing

[redacted]

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

DJA x00013

(b)(4) Testing

[redacted]

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

DJA x00014

(b)(4) Testing

[redacted]

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

DJA x00015

(b)(4) Testing

[redacted]

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

DJA x00016

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Labeling

COBALT™ MV WITH GENTAMICIN BONE CEMENT

Medium Viscosity Radiopaque Bone Cement containing Gentamicin
Methyl Methacrylate – Styrene Copolymer & Poly (methyl methacrylate)

Attention Operating Surgeon

DESCRIPTION
Cobalt™ MV with Gentamicin Bone Cement provides two separate, pre-measured sterilized components, which when mixed form a radiopaque rapidly setting bone cement.

One component is supplied in a gas-permeable packet. It consists of 40 g powder (copolymer) with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams
• Poly(methyl methacrylate)	6.00 grams
• Zirconium dioxide	4.00 grams
• FD&C Blue No. 2 Aluminum Lake	0.05 grams
• Benzoyl peroxide	0.35-1.00 grams
• Gentamicin sulfate (equivalent to 0.50 g Gentamicin)	0.84 grams

The other component is supplied in a flexible pouch. It consists of 20 ml of liquid (monomer) with the following composition:

• Methylmethacrylate (stabilized with hydroquinone)	18.424 grams
• N,N-dimethyl-p-toluidine	0.376 grams

The liquid monomer is sterile filtered. The interior of the monomer pouch is sterilized by exposure to gamma radiation. The exterior of the pouch containing the liquid is sterilized with vaporous hydrogen peroxide. The powder is sterilized with ethylene oxide. The gas-permeable packets containing the powder are sterilized with ethylene oxide.

Blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder component to produce a bluish tint in the final cement. This renders it possible to distinguish between bone and cement within the surgical field.

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which, after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables for temperature variations.)

Polymerization is an exothermic reaction with temperatures rising as high as 90°C, which occurs while the cement is hardening *in situ*. The released heat may damage bone or other tissues surrounding the implant. Although the spontaneous generation of heat accelerates the reaction, the polymerization of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

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

DJA x00017

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

MATERIALS:
Methyl methacrylate-Styrene copolymer (containing Benzoyl peroxide)
Poly (methyl methacrylate)
Benzoyl peroxide
Zirconium dioxide
FD&C Blue No.2 Aluminum Lake
Gentamicin sulfate
Methylmethacrylate (stabilized with hydroquinone)
N,N-dimethyl-p-toluidine

ACTION
Cobalt™ MV with Gentamicin Bone Cement is an acrylic cement-like substance which allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between prosthesis and bone. Insoluble zirconium dioxide provides the radiopaque quality of the formulation.

INDICATIONS
Cobalt™ MV with Gentamicin Bone Cement is indicated for use in arthroplastic procedures of the hip, knee, and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended to affix a new prosthesis in the second stage of a two-stage revision after the initial infection has been cleared.

CONTRAINDICATIONS
Cobalt™ MV with Gentamicin Bone Cement must not be used during pregnancy or the nursing period. Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients allergic to gentamicin or to other constituents of the bone cement. A hypersensitivity to any aminoglycoside is a contraindication to the use of gentamicin. A history of hypersensitivity or serious toxic reactions to aminoglycosides may also contraindicate the use of any other aminoglycoside because of known cross-sensitivity of patients to drugs in this class. The use of Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients with infectious arthritis, and in active infection of the joint or joints to be replaced.

Relative contraindications include the following:

1. Uncooperative patient or patient with neurologic disorder who is incapable of following directions
2. Metabolic disorders which may impair bone formation
3. Osteomalacia
4. Distant foci of infections which may spread to the implant site
5. Rapid joint destruction, marked bone loss or bone resorption, vascular insufficiency, muscular atrophy, or neuromuscular disease.
6. Hypotension
7. Congestive heart failure
8. Renal impairment

WARNINGS
Note: Adulteration of this bone cement may negatively affect performance characteristics.

Prior to using the Cobalt™ MV with Gentamicin Bone Cement surgeons should, by specific training and experience, be thoroughly familiar with the properties, handling characteristics, and application of the PMMA bone cement. (See Precautions and Mixing Technique) Because the handling and curing characteristics of this cement varies with temperature and mixing technique, they are best determined by the surgeon's actual experience. It is advisable for the surgeon to go through the entire mixing, handling and setting process *in vitro* before using the material in an actual surgical procedure.

Adverse cardiovascular reactions can include hypotension, hypoxemia, cardiac arrhythmia, bronchspasm, cardiac arrest, myocardial infarction, pulmonary embolism, cerebrovascular accident and possible death. Hypotensive reactions can occur between 10 seconds and 165 seconds after application of PMMA bone cement and can last for 30 seconds to 5 or more minutes. Some hypotensive reactions have progressed to cardiac arrest. The blood pressure, pulse and respiration of patients should be monitored carefully during

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

DJA x00018

and immediately following the application of the PMMA bone cement. Any significant alteration in these vital signs should be corrected with appropriate measures. In addition, over-pressurization of the PMMA bone cement should be avoided during the insertion of the PMMA bone cement and implant in order to minimize the occurrence of pulmonary embolism.

The risk of pulmonary fat embolism and the severity of all Bone Cement Implantation Syndrome (BCIS) complications can be reduced by meticulous irrigation and drying of the intramedullary canal Care should be taken to clean and aspirate the proximal portion of the femoral medullary canal just prior to insertion of bone cement. In high-risk patients, for example those sustaining hip fractures, care should be taken not to over-pressurize the cement and to insert the prosthesis slowly.

Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur, as the serum levels required to cause damage are not reached. Serious allergic reactions have been reported rarely in patients on systemic gentamicin therapy. Therefore, the incidence of these serious allergic events may also occur in patients with gentamicin-loaded bone cement.

Device volatility and flammability and electrocautery devices: The operating room should be adequately ventilated to eliminate monomer vapors. Ignition of monomer vapors caused by use of electrocautery devices in surgical sites near freshly implanted bone cements has been reported.

Irritation of the respiratory tract, eyes, and the liver: Caution should be exercised during the mixing of the liquid and powder components of the PMMA bone cement to prevent excessive exposure to the concentrated vapors of the liquid component, which may produce irritation of the respiratory tract, eyes, and possibly the liver. **Personnel wearing contact lenses should not mix PMMA bone cement or be near the mixing of the PMMA bone cement.**

1. DO NOT USE if there is loss of sterility of the cement.
2. Discard and DO NOT USE opened or damaged packages of the bone cement. Use only product packaged in unopened and undamaged containers.
3. Loosening and fracture of either the cement or the prosthesis, or both, can occur due to disease, trauma, and inadequate cementing technique, mechanical failure of the materials or latent infection.
4. The liquid and powder components of this cement must be mixed thoroughly before using. Inadequate mixing will lead to inhomogeneity that will compromise the mechanical properties and clinical performance of the cement.
5. DO NOT USE bone cement after expiration date.

The surgeon should decide whether the benefits expected from an arthroplasty outweigh any possible long-term adverse effects.

PRECAUTIONS

Strict adherence to good surgical principles and technique are required during use of the cement. Deep wound infection is a serious postoperative complication and may require total removal of the prostheses and embedded cement. Deep wound infection may be latent and not manifest itself for several years postoperatively.

1. **Contact dermatitis:** The liquid component (monomer) has caused contact dermatitis in those handling and mixing PMMA bone cement. Strict adherence to the instructions for mixing the powder and liquid components may reduce the incidence of contact dermatitis.
2. **Hypersensitivity reaction for operating room personnel:** The liquid component of the PMMA bone cement is a powerful lipid solvent. It should not contact rubber or latex gloves. Should contact occur, the gloves may dissolve and tissue damage may occur. Wearing a second pair of gloves and strict adherence to the mixing instructions may diminish the possibility of hypersensitivity reactions. The mixed bone cement should not make contact with gloved hand until the cement has acquired the consistency of dough. This usually occurs between one and two minutes after the liquid and powder components are mixed.
3. **Hypersensitivity reactions for patients:** The gentamicin content of Cobalt™ MV with Gentamicin Bone Cement may cause hypersensitivity reactions in isolated cases.

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

DJA x00019

4. **Inadequate post-operative fixation:** Inadequate fixation or unanticipated postoperative events may affect the PMMA bone cement/bone interface and lead to micro-motion of cement against the bone surface. A fibrous tissue layer may develop between the PMMA bone cement and the bone that may cause loosening of the prosthesis. Thus, continued, periodic follow-up is advised for all patients.
5. **Exothermic reaction:** Polymerization of the PMMA bone cement is an exothermic reaction that occurs while the PMMA bone cement is hardening *in situ*. The released heat may damage bone or other tissue adjacent the implant.
6. **Extrusion:** Extrusion of the PMMA bone cement beyond the region of its intended application may occur resulting in the following complications: hematuria; dysuria; bladder fistula; delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended use; local neuropathy; local vascular erosion and occlusion; and intestinal obstruction because of adhesions and stricture of the ileum from the heat released during the exothermic polymerization.
7. **USE IN PREGNANCY: The safety and effectiveness of the PMMA bone cement in pregnant women has not been established. PMMA bone cement may adversely affect fetal health.**
8. **PEDIATRIC USE: The safety and effectiveness of the PMMA bone cement in children has not been established. PMMA bone cement may adversely affect bone growth.**
9. **Expiration dating:** PMMA bone cement should not be used after the expiration date because the effectiveness of the device may be compromised.
10. ***Disposal:*** Expired cement should be mixed according to Instructions for Use prior to disposal. Because of the volatility and flammability of the liquid monomer of the PMMA bone cement, liquid monomer that has leaked or is leaking from the package should be collected and evaporated in a well-ventilated hood or absorbed by an inert material and transferred in a suitable container (one that does not react with the PMMA bone cement) for disposal.
11. **Incompatibility:** Aqueous (e.g. antibiotic containing) solutions must not be mixed with the bone cement, as this reduces the strength considerably.
12. **Monitoring:** Patients receiving gentamicin should be periodically monitored with peak and trough levels of the antibiotic, serum electrolytes, serum renal function, urinalysis, and audiograms (in elderly and/or dehydrated patient in whom there is a higher risk of adverse events associated with gentamicin use).
13. **Use of gentamicin should be avoided in the following situation.**
    Concurrent/sequential use of:
    - Other neurotoxic/nephrotoxic antibiotics
    - Other aminoglycosides
    - Cephaloridine
    - Viomycin
    - Polymixin B
    - Colistin
    - Cisplatin
    - Vancomycin
13. **Dose in patients with renal impairment:** Since no adjustment can be made to the dose in the gentamicin-loaded cement, a risk versus benefit assessment should be made before use in patients with renal impairment.
14. **Drug resistant bacteria:** Using Cobalt™ MV with Gentamicin Bone Cement under conditions other than the indicated use is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Avoid over pressurization of the bone cement because this may lead to extrusion of the bone cement beyond the site of its intended application and damage to the surrounding tissues.

ADVERSE EVENTS

The most serious adverse events, including death, reported with the use of acrylic bone cements are:

- Cardiac arrest
- Myocardial infarction
- Pulmonary embolism
- Cerebrovascular accident
- Sudden death

The most frequent adverse events reported are:

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

DJA x00020

- Transitory fall in blood pressure
- Thrombophlebitis
- Hemorrhage and hematoma
- Loosening or displacement of the prosthesis
- Superficial or deep wound infection
- Trochanteric bursitis
- Short-term cardiac conduction irregularities

Nephrotoxicity

- Usually in patients with pre-existing renal damage
- Also in patients with normal renal function to whom amino-glycosides are administered for longer periods or in higher doses than recommended
- The symptoms may manifest after cessation of the therapy

Neurotoxicity

- Manifested as both auditory and vestibular ototoxicity, including irreversible hearing loss
- Numbness
- Skin tingling
- Muscle twitching
- Convulsions

Other adverse events reported are:

- Heterotopic new bone formation
- Trochanteric separation

Other potential adverse events reported include:

- Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur as the serum levels remain well below levels required to cause damage. Concurrent administration of muscle relaxants and ether may potentiate the neuromuscular blocking properties of gentamicin. However, the low serum concentrations significantly reduce the risk of occurrence of this adverse event. The use of antibiotic-loaded bone cement may lead to development of resistant microorganisms and the physician should weigh the risks vs. benefits to the patient before using Cobalt™ MV with Gentamicin Bone Cement in each case.
- Pyrexia due to an allergy or histological reaction to bone cement
- Hematuria
- Dysuria
- Bladder fistula
- Local neuropathy
- Local vascular erosion and occlusion
- Adhesions and stricture of the ileum due to the heat released during polymerization.
- Delayed sciatic nerve entrapment due to extrusion of the bone cement beyond the region of its intended application.

Adverse reactions affecting the cardiovascular system have been attributed to leakage of unpolymerized liquid monomer into the circulatory system. Data indicate that the monomer undergoes rapid hydrolysis to methacrylic acid and that a significant fraction of the circulating methacrylate is in the form of the free acid, rather than of the methyl ester. Correlation between changes in circulating concentrations of the methyl methacrylate/methacrylic acid and changes in blood pressure has not been established.

Hypotensive episodes reported are more marked in patients with elevated or high normal blood pressure in hypovolemia and in patients with pre-existing cardiovascular abnormalities. Elevations in plasma histamine levels subsequent to introduction of cement have also been reported.

Reports of sometime fatal cardiac arrest suggest that elderly osteoporotic patients undergoing hip replacement surgery for fractures of the femoral neck are at greater risk than those receiving elective joint replacement for arthritic disease. Risk is also higher in patients with pre-existing cardiovascular disease. Although the etiology of cardiac arrest is unclear, it may well be either direct embolic effects or secondary to hypoxia produced by pulmonary embolic phenomena. Introduction of liquid cement under pressure into a clean medullary canal has been shown to appreciably enhance the filling of the bone cavities with marked

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

DJA x00021

improvement in the security of the bone cement interface. Care must be exercised in introducing the cement continuously from distal to proximal to avoid laminations in the cement.

DOSAGE AND ADMINISTRATION

Cobalt™ MV with Gentamicin copolymer powder is double packaged. The inner gas permeable packet and its contents, as well as the inside of the foil laminate protective overwrap, are sterilized with ethylene oxide. The packet containing the sterile filtered liquid monomer is packaged in a protective gas-permeable overwrap punch. The outside of the liquid packet and inside of overwrap pouch are sterilized by exposure to vaporous hydrogen peroxide.

(At least one extra unit of Cobalt™ MV with Gentamicin Bone Cement should be available before starting a surgical procedure).

A unit is prepared by mixing the entire contents of one (1) packet of powder (40 g copolymer) with one (1) packet of liquid (20 ml monomer). One or two units will usually suffice, although this will depend upon the specific surgical procedure and the techniques employed. Each unit is prepared separately.

The following are required for preparation of the bone cement:

- Sterile working area
- Sterile plastic bowl approved for use with monomers
- Sterile mixing spoons or spatulas.

Note: For vacuum mixing, refer to manufacturer instructions.

A circulating nurse or assistant opens the peelable film package and the blister pack, and the sterile powder packet and liquid packet are aseptically placed on a sterile table. The powder packet and the liquid packet are opened under sterile conditions. Since each packet of powder contains a pre-measured quantity of copolymer to react with a pre-measured quantity of monomer, care should be taken to mix the entire contents of one powder packet with the entire contents of one liquid packet. Partial amounts should not be used.

MIXING INSTRUCTIONS FOR BOWL MIXING

Note: Cement can also be mixed in a vacuum mixing system. Refer to manufacturer instructions.

Pour the liquid into a bowl. Add the powder. Stir with a spatula vigorously, but carefully, for about 30 seconds.

CEMENT MAY BE APPLIED IN A PRE-DOUGH STATE, BUT IF A DOUGH-LIKE MASS THAT DOES NOT STICK TO RUBBER GLOVES AS DESIRED, WAIT ANOTHER 2 MINUTES - 6 MINUTES depending on the ambient temperature (SEE CURVES).

At this state knead for about 15 seconds -30 seconds. The cement becomes more homogeneous, and mixed air bubbles disappear for the most part. On the other hand, if the kneading process is extended too long, the polymerization may proceed to the point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The working time may be affected by temperature (see curve and table for working and hardening times). Additionally, the moisture content in any bone cement powder has an effect on polymerization; cement powder with higher moisture content will set faster, while drier cement powder will result in slower set-times. The outer foil pouch acts as a moisture barrier for Cobalt™ MV with Gentamicin Bone Cement. To minimize fluctuation of set-times, do not remove the powder component's moisture barrier until it is time to mix the cement. Maintaining a constant and moderate (40%RH-55%RH) humidity in the operating room will also lead to more consistent cement handling performance. The ideal working consistency of the Cobalt™ MV with Gentamicin Bone Cement for manual application to bone is best determined by the surgeon based upon experience in using the preparation. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Excessive cement must be removed while it is still soft. If additional cement is required during the surgical procedure, another

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

DJA x00022

packet of liquid and packet of powder may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

The completion of polymerization occurs in the patient and is associated with the liberation of heat. To more rapidly dissipate the heat, the polymerizing cement may be irrigated with a cool physiologic saline solution.

STORAGE

Store package in a dry, ventilated place between 6°C and 23°C (42.8°F to 73.4°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73.4°F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

The copolymer powder does not withstand heat sterilization treatment. If a packet is accidentally opened, it must not be used.

HOW SUPPLIED

Carton consisting of:
1 packet of copolymer powder containing 40 g
1 packet of liquid monomer containing 20 ml

The following tables and graphs were generated using standard methods including a temperature-controlled environment. Warming of bone cement by any manual manipulation and the eventual application to the surgical site will accelerate the onset and completion of the final hardening phase. The extent of acceleration depends on the timing of manipulation and application. Early and extended warming will have the largest effect on cement hardening.

Typical working data for mixing Cobalt™ MV with Gentamicin Bone Cement

Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	18° C	20° C	23° C
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

Vacuum Mixing at Ambient Temperatures

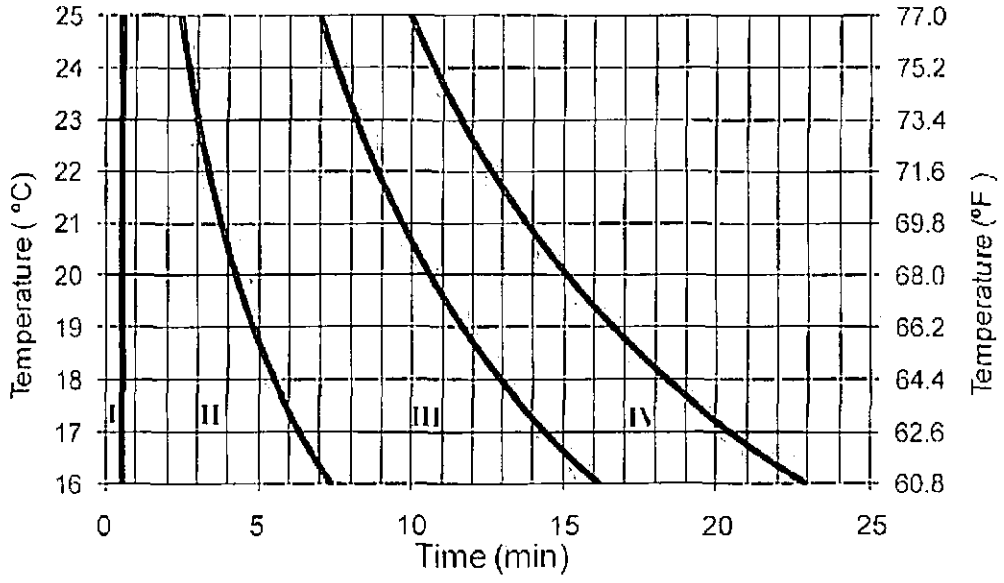
Ambient and component temperature	18° C	20° C	23° C
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

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

DJA x00023

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

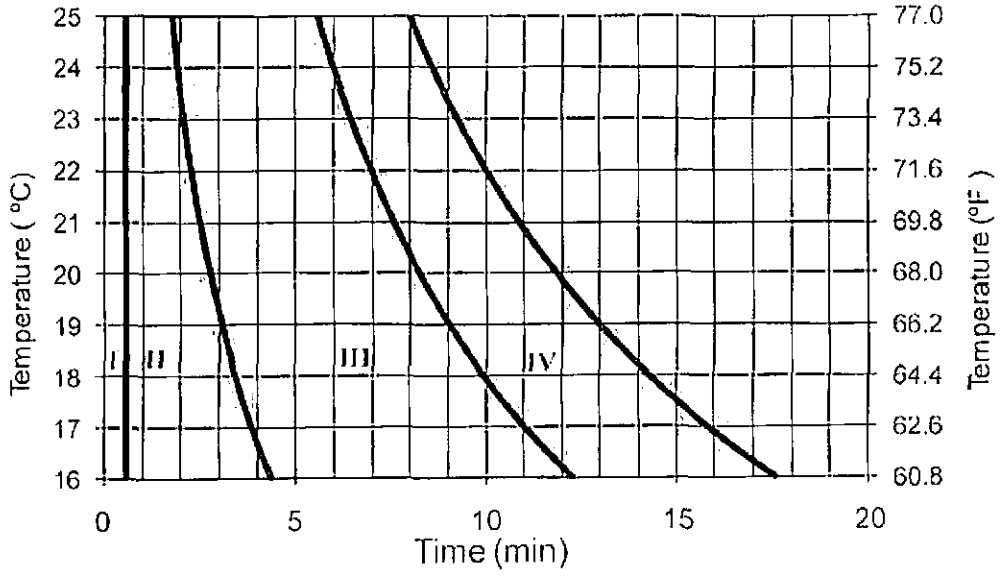
Handling and Setting Times vs. Temperature for
Open Bowl Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

Handling and Setting Times vs. Temperature for
Vacuum Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

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

DJA x00024

Reviewer's Comments:

The sponsor has provided adequate labeling including indications, contraindications, warnings, precautions, adverse events, important information to the user and handling times based on temperatures encountered in the operating room. This labeling was previously cleared for G-HV Bone (K051532) cement for another Biomet Bone Cement containing the same amount of gentamicin bone cement for a 2 stage revision.

Sterilization/Shelf Life/Packaging

Shelf Life

Cobalt™ G-MV Bone Cement has a one-year shelf life. The packaging material and level of BPO support a 1 year shelf life. This is a conservative estimate considering the decomposition rate of BPO, the storage conditions and packaging material.

Sterility Information

Cobalt™ G-MV powder and the packet containing the powder are provided sterile by gas sterilization methods as follows:

Gas Type:	Ethylene Oxide (EtO)
Residuals:	meet the AMMI/ANSI/ISO 10993-7:1995 and AAMI TIR No. 19-1998
Sterility Assurance Level:	10^{-6}
Sterility Validation Method:	AMMI/ANSI/ISO 11135:1994
Pyrogen-Free:	No claims will be made
Labeling:	All packages will display a black/dark brown to green chemical indication dot along with a statement that the device has been sterilized by Ethylene Oxide (EtO).
Contract Sterilization Site:	Centurion Sterilization Services A Division of Tri-State Hospital Supply Corp. 301 Catrell Drive Howell, Michigan 48843 Registration Number: 1824619

The Cobalt™ G-MV liquid component is sterile filtered and aseptically filled. The interior of the pouch is sterilized by exposure to gamma irradiation prior to monomer fill. The exterior of the pouch containing the liquid is sterilized by exposure to vaporous hydrogen peroxide, as well as the outside of the liquid packet and inside of the overwrap. The filtration and vaporous hydrogen peroxide sterilization methods are as follows:

Filtration

Filter Size: membranes of porosity not greater than 0.22μm
Sterility Validation Method: U.S.P. test methods
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, IN 46582

Vaporous Hydrogen Peroxide

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: EN 550, revised protocol
Sterilization Site:
Biomet Manufacturing Corp.

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

DJA x00025

56 East Bell Drive
Warsaw, In 46582

These are the same sterilization methods used for the predicate Cobalt™ HV cleared in K051496.

Packaging

Packaging

Cobalt™ G-MV is double packaged. The packaged powder and liquid components are placed into a fiberboard outer box after the individual components are packaged as discussed below.

Powder

The powder component's inner gas permeable pouch is made of Tyvek®/Mylar® and enclosed in a foil-lined protective overwrap pouch, also made of foil. The packaging of Cobalt™ G-MV powder is similar to that of the predicate Cobalt™ G-HV Bone Cement's powder component (K051532). Since FDA's clearance of Cobalt™ G-HV in 2005, Biomet has changed the exterior packaging for its bone cements from a paper/foil/polymer laminated pouch to a foil/polymer laminated pouch comprised of TPC-0814B. This change utilized internal documentation pursuant to FDA's guidance document, *"Deciding when to Submit a 510(k) for a Change to an Existing Device (K97-1).* The exterior foil packaging has been validated and poses no new risks. A copy of the validation for TPC-0814B is on file at Biomet and can be accessed at any future FDA inspection. The inside packaging for Cobalt™ G-MV is the same as the predicate Cobalt™ G-HV's inside packaging, which has not changed since it was cleared.

Liquid (Monomer)

The liquid monomer's inner container is a Cryovac T6050B co-extruded film pouch (LLDPE sealant layer, polypropylene skin, and barrier of EVOH sandwiched between nylon layers). The outer container is a Tyvek® pouch. The packaging for the liquid monomer is the same as that of its predicate, Cobalt™ G-HV (K051532).

Sterilization

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The exterior surfaces of the cement liquid packages are sterilized by exposure to vaporous hydrogen peroxide that takes place at Biomet Manufacturing Corp. The label will include an EtO sterility identifier.

The sterilization of the liquid component of Cobalt™ G-MV Bone Cement is identical to that of the predicate Cobalt™ G-HV Bone Cement's liquid component (K051532). Please refer to the following table for a comparison of the packaging and sterilization of Cobalt™ G-MV Bone Cement to its predicates.

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

DJA x00026

Sterility Information
Cobalt™ G-MV powder and the packet containing the powder are provided sterile by gas sterilization methods as follows:

Gas Type:	Ethylene Oxide (EtO)
Residuals:	meet the AMMI/ANSI/ISO 10993-7:1995 and AAMI TIR No. 19-1998
Sterility Assurance Level:	10^{-6}
Sterility Validation Method:	AMMI/ANSI/ISO 11135:1994
Pyrogen-Free:	No claims will be made
Labeling:	All packages will display a black/dark brown to green chemical indication dot along with a statement that the device has been sterilized by Ethylene Oxide (EtO).
Contract Sterilization Site:	Centurion Sterilization Services A Division of Tri-State Hospital Supply Corp. 301 Catrell Drive Howell, Michigan 48843 Registration Number: 1824619

The Cobalt™ G-MV liquid component is sterile filtered and aseptically filled. The interior of the Softpac pouch is Gamma sterilized prior to the asceptic fill. The exterior of the pouch containing the liquid is sterilized by exposure to vaporous hydrogen peroxide, as well as the outside of the liquid packet and inside of the overwrap. The filtration and vaporous hydrogen peroxide sterilization methods are as follows:

Gamma

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: Gamma Irradiation Product Adaption, File #229
Sterilization Site:
STERIS Isomedix
1880 Industrial Drive
Libertyville, Illinois 60048

Filtration

Filter Size: membranes of porosity not greater than 0.22μm
Sterility Validation Method: U.S.P. test methods
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, IN 46582

Vaporous Hydrogen Peroxide

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: EN 550, revised protocol
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, In 46582

These are the same sterilization methods used for the predicate Cobalt™ G-HV cleared in K051532.

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

DJA x00027

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The exterior surfaces of the cement liquid packages are sterilized by exposure to vaporous hydrogen peroxide that takes place at Biomet Manufacturing Corp. The label will include an EtO sterility identifier.

The sterilization of the liquid component of Cobalt™ MV Bone Cement is identical to that of the predicate Cobalt™ MV (K091608).

Powder Component Packaging and Sterilization				
		Cobalt™ G-MV (New)	**Cobalt™ G-HV (K051532)**	**Simplex® P w/ Tobramycin (K014199)**
Innermost Pouch	**Material**	Tyvek®/Mylar	Tyvek®/Mylar	Multi-layer clear plastic barrier-film
	Sterility	Contents & exterior sterile (EtO)	Contents & exterior sterile (EtO)	Contents & exterior sterile (Gamma)
Overwrap	**Material**	Foil	Foil	Plastic pouch with breathable header
	Sterility	Contents sterile	Contents sterile	Contents sterile
Liquid Component Packaging and Sterilization				
Inner Container	**Material**	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Glass ampoule
	Sterility	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & sterilization of ampoule prior to aseptic fill)
	Comment	Very good barrier. Durable package.	Very good barrier. Durable package.	Impermeable barrier, but fragile. Hazardous to open; glass shards may fall into monomer upon opening.
Outer Container	**Material**	Tyvek® pouch	Tyvek® pouch	Rigid plastic blister with breathable lid
	Sterility	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (EtO)
	Comment	Vaporous hydrogen peroxide permeable	Vaporous hydrogen peroxide permeable	EtO permeable lid stock

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

DJA x00028

STORAGE

Store package in a dry, ventilated place between 6° and 23°C (43° to 74°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73°F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

Reviewer's Comments:

The packaging and sterilization information is considered adequate based on the sponsor's identification of the packaging material, sterilization method to be used by the end user.

Biocompatibility

Materials and Biocompatibility

Changes made to the concentrations of the powder and monomer components might adversely affect monomer elution. Due to this possibility, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) to ensure that the formulation change did not adversely affect the monomer elution. According to USP Specifications, the sample meets the test requirements if the cell culture treated with the sample is less than or equal to grade 2 (mild reactivity). The sample of Cobalt™ G-MV Bone Cement met the USP requirements for this test. The testing demonstrated that the formulation change did not affect monomer elution. The test report is included in the **Mechanical Testing** section of this submission.

Testing Laboratory:

Pacific BioLabs (formerly Northview Pacific Laboratories)
551 Linus Pauling Drive
Hercules, CA 94547
FDA Registration No. 29-14117

Biocompatibility

Component	Material	Applicable Standard
Powder (copolymer)	• Methyl methacrylate-styrene copolymer • Poly(methyl methacrylate) • Zirconium dioxide • Benzoyl peroxide • Gentamicin Sulfate • FD&C Blue No.2 Aluminum Lake	ASTM F 451-99a ISO 5833:2002
Liquid (monomer)	• Methyl methacrylate (stabilized with hydroquinone) • N,N-dimethyl-p-toluidine	ASTM F 451-99a ISO 5833:2002

Reviewer's Comments:

The sponsor has provided adequate rationale why additional biocompatibility is not needed for this

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

DJA x00029

formulation that has a long history of being biocompatible.

IV. Software

N/A

V. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

N/A

Performance Testing – Animal

None provide and none required for this PMMA Bone Cement.

Performance Testing – Clinical

None provide and is not needed because the materials and similar formulations have a long history of clinical success.

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

DJA x00030

Substantial Equivalence Discussion

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
510(k) No.	New	K051532	K014199
Cement Design	Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Cobalt™ HV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Surgical Simplex® P provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.
Cement Materials	Powder component/ liquid monomer	Powder component/ liquid monomer	Powder component/ liquid monomer
Powder Component	Methyl methacrylate-styrene copolymer 29.83g Poly(methyl methacrylate) 6.00g Zirconium dioxide 4.00g FD&C Blue No. 2 Aluminum Lake 0.05g Residual benzoyl peroxide (0.44g) Benzoyl peroxide (hydrous 75%) 0.12g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methylmethacrylate-methacrylate copolymer with FD&C Blue No. 2 Aluminum Lake 33.86 – 33.42g --- Zirconium dioxide 5.94g --- --- Benzoyl peroxide, (hydrous 75%) 0.20 – 0.64g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methyl methacrylate-styrene-copolymer 30.00g Polymethyl methacrylate 6.00g Barium Sulfate, U.S.P. 4.00g --- Residual benzoyl peroxide (0.51g) Tobramycin Sulfate 1.0g active
Liquid Monomer Component	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 97.4% v/v N, N-dimethyl-p-toluidine 2.6% v/v Hydroquinone 75 ± 15ppm

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

DJA x00031

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
Sterilization	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Gamma Irradiation Liquid Monomer Component Membrane Filtration
Packaging	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile paper-foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in sterile packet, enclosed in a sterile protective package Liquid Monomer Component Pre-sterilized ampoule, enclosed in a pre-sterilized ampoule package
Anatomical Sites	Osseous tissue	Osseous tissue	Osseous tissue

Reviewer's Comments:

The sponsor has provided a comparison to a predicate bone cement. However, additional information is needed regarding the fatigue testing. See the deficiency list at the end of the memo.

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

X. **Recommendation**

Regulation Number: 21 CFR 888.3027
Regulation Name: PMMA Bone Cement;
Regulatory Class: Class II
Product Code: LOD, MBB

Reviewer — Date 10-26-09

Branch Chief — Date 10/27/09

CONCUR

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

DJA x00035

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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

COVER SHEET MEMORANDUM

From: Reviewer Name Hany Demian

Subject: 510(k) Number K092150

To: The Record

Please list CTS decision code TH

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

☐ Hold (Additional Information or Telephone Hold)

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

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 /510(k) Statement	*Attach Summary*	X	
Truthful and Accurate Statement.	*Must be present for a Final Decision*	X	
Is the device Class III? If yes, does firm include Class III Summary?	*Must be present for a Final Decision*		X
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)			NA
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			NO
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			X
Is this device intended for pediatric use only?			X
Is this a prescription device? (If both prescription & OTC, check both boxes.)		X	
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			X
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)			X
Does this device include an Animal Tissue Source?			
All Pediatric Patients age<=21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days -< 2 years old)			
Child (2 years -< 12 years old)			
Adolescent (12 years -< 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			

Rev. 7/2/07

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00036

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)			
Nanotechnology			
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		

Regulation Number	Class*	Product Code
888.3027	II	LOD/MRB

(*If unclassified, see 510(k) Staff)

Additional Product Codes:

Review: (Branch Chief) REVB (Branch Code) 09/25/09 (Date)

Final Review: (Division Director) (Date)

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

DJA x00037

Demian, Hany

To: Alexander, Sue

Subject: K092150 Telephone Hold

concur 09/25/09

Hi Sue, I am placing this document on hold until you adequately addresses the following deficiencies:

1. In your device description and package insert you state you have a range of benzoyl peroxide was 0.35-1.0 grams. You state the your bone cement formulation contains 1.38% w/w of benzoyl peroxide but you have not provide the range of benzoyl peroxide in your release criteria for benzoyl peroxide levels for the product. Please provide the lowest and highest level of benzoyl peroxide in your release criteria and what level tested in all the pre-clinical testing that you have provided in your submission. This information is needed to help determine the handling characteristics and physical and mechanical properties for your bone cement formulation. See the PMMA guidance document for a discussion for benzoyl peroxide levels in bone cement formulations.

2. You have provided limit fatigue testing at 15 MPa and 10 MPa. At 10 MPa you have only performed testing to a run out of 1 million cycles. Please perform fatigue testing in accordance with ASTM F2118 where run-out is considered 5 million cycles.

3. You have stated the gentamicin sulfate will be added to the powder component. However you have not provided the particle size distribution of the gentamicin sulfate. In addition, please identify the supplier for the gentamicin sulfate.

Hany

From: Alexander, Sue [mailto:sue.alexander@biomet.com]
Sent: Wednesday, August 12, 2009 10:23 AM
To: Demian, Hany
Subject: RE: Cobalt MV (K091608)

Okay, thanks very much!

Susan Alexander
Regulatory Affairs Specialist
Biomet Orthopedics

574.371.1152 direct
574.372.1683 fax
sue.alexander@biomet.com
www.biomet.com

DISCLAIMER:
This communication, along with any documents, files or attachments, is intended only for the use of the addressee and may contain legally privileged and confidential information. If you are not the intended recipient, you are hereby notified that any dissemination, distribution or copying of any information contained in or attached to this communication is strictly prohibited. If you have received this message in error, please notify the sender immediately and destroy the original communication and its attachments without reading, printing or saving in any manner.

From: Demian, Hany [mailto:Hany.Demian@fda.hhs.gov]
Sent: Wednesday, August 12, 2009 10:22 AM
To: Alexander, Sue
Subject: RE: Cobalt MV (K091608)

Hi Sue,

same amount of time as a letter.

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

DJA x00038

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K092150
Telephone Hold

Date: 9/23/2009
To: The Record
From: Hany Demian, M.S.

Office: ODE
Division: DSORD

510(k) Holder: Biomet
Device Name: Cobalt G-MV Bone Cement
Contact: Susan Alexander
Phone: 574-267-6639

I. Purpose and Submission Summary

Biomet wishes to market Gentamicin-MV Acrylic Bone Cement for a 2 stage revision once the initial infection as been cleared. This is the same bone cement without the antibiotic cleared in K091608. There are several deficiencies that the sponsor needs to address. See the end of the memo for the list of deficiencies. I recommend placing this document on hold until the sponsor adequately responds to deficiencies cited at the end of the memo.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or OTC)	x		
Truthful and Accuracy Statement	x		
510(k) Summary or 510(k) Statement	x		
Standards Form			x
	Yes	**No**	**N/A**
Is the device life-supporting or life sustaining?		x	
Is the device an implant (implanted longer than 30 days)?	x		
Does the device design use software?		x	
Is the device sterile?	x		
Is the device reusable (not reprocessed single use)? Are "cleaning" instructions included for the end user?		x	

Indications for Use

Cobalt™ MV with Gentamicin Bone Cement is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended for use to affix a new prosthesis in the second phase of a two-stage revision after the initial infection has been cleared.

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

DJA x00039

Reviewer's Comments:

This is the standard indications for use for a low amount of antibiotic that has been previously cleared for a 2 stage revision procedure once the initial infection as been cleared. Therefore the indications for use is considered acceptable.

Device Description:

Device Description

Cobalt™ G-MV bone cement is formed when two separate, pre-measured sterilized components, a powder copolymer and liquid monomer, are mixed to form a radiopaque, rapidly-setting bone cement for use in orthopedic surgery. Mixing of the two sterile components initially produces a paste that is used to anchor the prosthesis, or to fill an osseous defect. The hardened bone cement allows stable fixation of the prosthesis and transfers mechanical stresses produced during movement from the prosthesis to the bone via the large interface between the cement and the bone.

The powder component, supplied in a gas-permeable packet, consists of 40 grams of powder with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams	(74.575%)
• Polymethyl methacrylate	6.00 grams	(15.000%)
• Zirconium Dioxide	4.00 grams	(10.000%)
• FD&C Blue No. 2 Aluminum Lake	0.05 grams	(0.125%)
• Benzoyl Peroxide	0.35-1.00 grams	(0.300%)
• Gentamicin sulfate (equivalent to 0.50g gentamicin)	0.84 grams	

The liquid component is supplied in a flexible packet. It consists of 20ml of liquid (monomer) with the following composition:

• Methyl methacrylate (stabilized with hydroquinone)	18.424 grams	(98.0%)
• N,N-dimethyl-p-toluidine	0.376 grams	(2.0%)

The powder contains 10% zirconium dioxide as an x-ray contrast medium. To assist in distinguishing between bone and cement within the surgical field, blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder to produce a bluish tint in the final cement. This color additive may be used safely at a level not to exceed 0.1 percent by weight of the bone cement, per 21 CFR 74.3102 (**Tab A**). The target concentration for this colorant in the powder component of Cobalt™ G-MV is 0.125% by weight. As the weight of the powder component is 40g, and the weight of the liquid component is 18.8g (20ml x 0.94g/ml), the total weight of a single unit of cement is 58.8g. Therefore, the target concentration of the colorant FD&C Blue No.2 Aluminum Lake in Cobalt™ G-MV Bone Cement, after mixing the powder and liquid components, is 0.0849% (0.125% x 40g/58.8g).

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables below for temperature variations.)

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

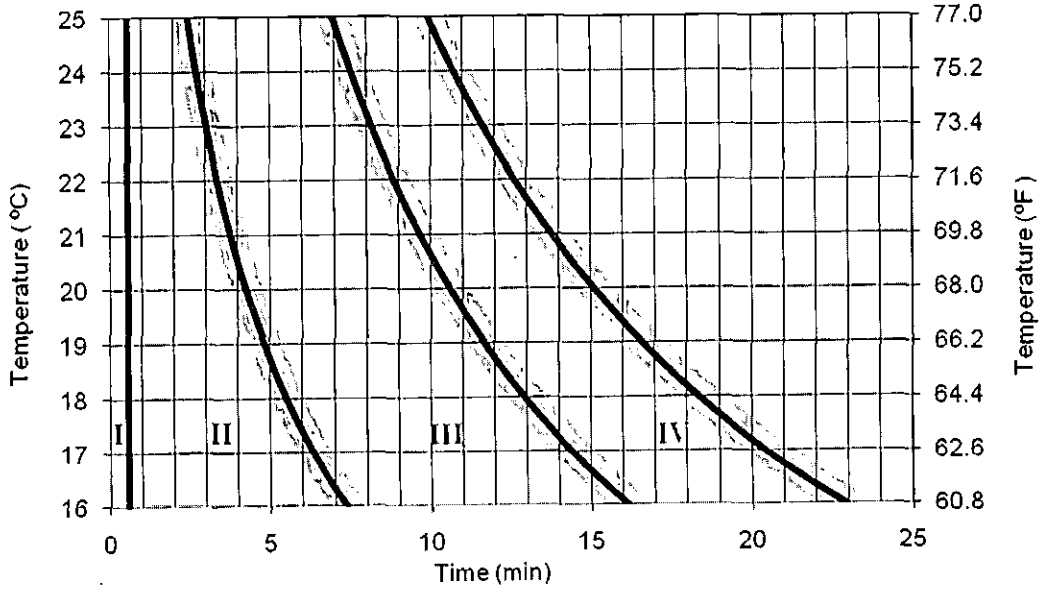
Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

Vacuum Mixing at Ambient Temperatures

Ambient and component temperature	**18° C**	**20° C**	**23° C**
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

Handling and Setting Times vs. Temperature for Open Bowl Mixing of Cobalt™ G-MV Bone Cement

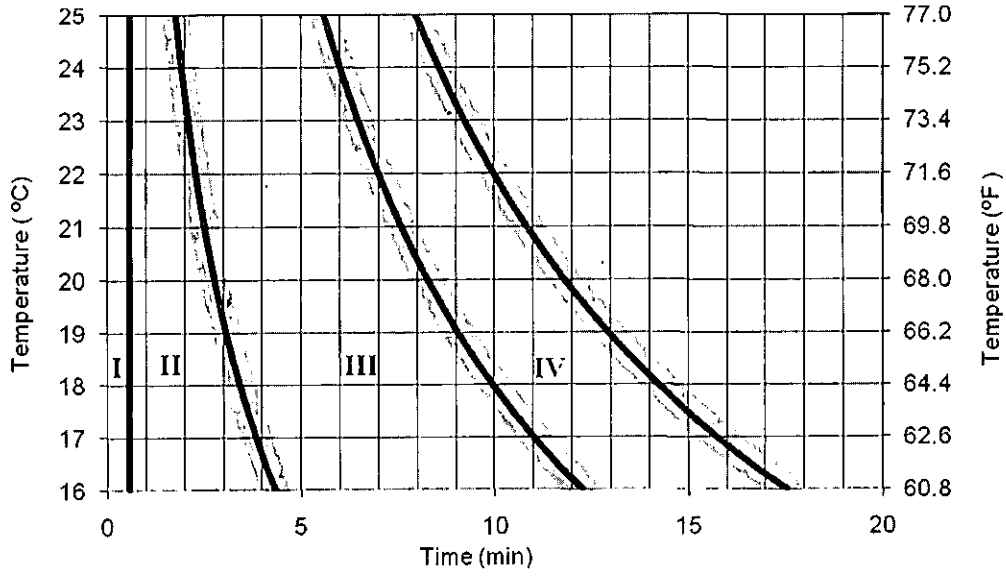


I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

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

DJA x00041

Handling and Setting Times vs. Temperature for Vacuum Mixing of Cobalt™ G-MV Bone Cement



I – Mixing phase
II – Pre-dough phase
III – Post-dough phase
IV – Final hardening phase

Reviewer's Comments:
The sponsor has provided adequate device description and handling characteristics versus temperatures. This is the same formulation was cleared without the gentamicin sulfate in K091608. However, see the end of the memo for the list of deficiencies that the sponsor needs to address.

Performance Testing – Bench

Mechanical Testing
Extensive *in vitro* testing was performed in accordance with *Class II, Special Controls Guidance: Polymethylmethacrylate (PMMA) Bone Cement: Guidance for Industry and FDA (July 17, 2002)* to demonstrate the equivalence of Cobalt™ G-MV Bone Cement to the predicate Simplex® P with Tobramycin (K014199). Complete test reports characterizing the chemical, handling, physical, and mechanical properties of Cobalt™ G-MV Bone Cement compared to its predicate device, Simplex® P with Tobramycin (K014199), are located in the **Mechanical Testing** section of this submission. Also provided in the **Mechanical Testing** section are a Mechanical Properties Summary Table and tables demonstrating Cobalt™ G-MV's conformance to consensus standards.

A summary of test reports for Cobalt™ G-MV is included below and in the **Mechanical Testing** section of this submission. Cobalt™ G-MV was tested in accordance with, and conforms to, the standards set forth in ASTM F 451 and ISO 5833 . In addition, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) and met the requirements. (Please see the **Materials and Biocompatibility** discussion in this section for further information.)

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Cobalt G-MV Bone Cement vs. Simplex® P w/tobramycin

Summary of Chemical, Physical, Handling & Mechanical Testing

(b)(4) Testing

[redacted]

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

DJA x00043

(b)(4) Testing

[redacted]

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

DJA x0044

(b)(4) Testing

[redacted]

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

DJA x00045

(b)(4) Testing

[redacted]

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

DJA x0046

(b)(4) Testing

[redacted]

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

DJA x00047

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Labeling

COBALT™ MV WITH GENTAMICIN BONE CEMENT

Medium Viscosity Radiopaque Bone Cement containing Gentamicin
Methyl Methacrylate – Styrene Copolymer & Poly (methyl methacrylate)

Attention Operating Surgeon

DESCRIPTION
Cobalt™ MV with Gentamicin Bone Cement provides two separate, pre-measured sterilized components, which when mixed form a radiopaque rapidly setting bone cement.

One component is supplied in a gas-permeable packet. It consists of 40 g powder (copolymer) with the following composition:

• Methyl methacrylate-Styrene copolymer	28.95-29.60 grams
• Poly(methyl methacrylate)	6.00 grams
• Zirconium dioxide	4.00 grams
• FD&C Blue No. 2 Aluminum Lake	0.05 grams
• Benzoyl peroxide	0.35-1.00 grams
• Gentamicin sulfate (equivalent to 0.50 g Gentamicin)	0.84 grams

The other component is supplied in a flexible pouch. It consists of 20 ml of liquid (monomer) with the following composition:

• Methylmethacrylate (stabilized with hydroquinone)	18.424 grams
• N,N-dimethyl-p-toluidine	0.376 grams

The liquid monomer is sterile filtered. The interior of the monomer pouch is sterilized by exposure to gamma radiation. The exterior of the pouch containing the liquid is sterilized with vaporous hydrogen peroxide. The powder is sterilized with ethylene oxide. The gas-permeable packets containing the powder are sterilized with ethylene oxide.

Blue pigment (FD&C Blue No. 2 Aluminum Lake) is added to the powder component to produce a bluish tint in the final cement. This renders it possible to distinguish between bone and cement within the surgical field.

When the powder (copolymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerization of the monomer, which then binds together granules of polymer. As polymerization proceeds, a sticky dough-like mass is formed, which, after about 3 minutes can be manipulated for about 5 minutes (at 23°C [73°F]). (See curves and tables for temperature variations.)

Polymerization is an exothermic reaction with temperatures rising as high as 90°C, which occurs while the cement is hardening *in situ*. The released heat may damage bone or other tissues surrounding the implant. Although the spontaneous generation of heat accelerates the reaction, the polymerization of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

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

DJA x00048

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

MATERIALS:
Methyl methacrylate-Styrene copolymer (containing Benzoyl peroxide)
Poly (methyl methacrylate)
Benzoyl peroxide
Zirconium dioxide
FD&C Blue No.2 Aluminum Lake
Gentamicin sulfate
Methylmethacrylate (stabilized with hydroquinone)
N,N-dimethyl-p-toluidine

ACTION
Cobalt™ MV with Gentamicin Bone Cement is an acrylic cement-like substance which allows seating and fixation of prosthesis to bone. After complete polymerization, the cement acts as a buffer for even weight distribution and other stresses between prosthesis and bone. Insoluble zirconium dioxide provides the radiopaque quality of the formulation.

INDICATIONS
Cobalt™ MV with Gentamicin Bone Cement is indicated for use in arthroplastic procedures of the hip, knee, and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary because of revision of previous arthroplasty procedures due to joint infection. The cement is intended to affix a new prosthesis in the second stage of a two-stage revision after the initial infection has been cleared.

CONTRAINDICATIONS
Cobalt™ MV with Gentamicin Bone Cement must not be used during pregnancy or the nursing period. Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients allergic to gentamicin or to other constituents of the bone cement. A hypersensitivity to any aminoglycoside is a contraindication to the use of gentamicin. A history of hypersensitivity or serious toxic reactions to aminoglycosides may also contraindicate the use of any other aminoglycoside because of known cross-sensitivity of patients to drugs in this class. The use of Cobalt™ MV with Gentamicin Bone Cement is contraindicated in patients with infectious arthritis, and in active infection of the joint or joints to be replaced.

Relative contraindications include the following:

1. Uncooperative patient or patient with neurologic disorder who is incapable of following directions
2. Metabolic disorders which may impair bone formation
3. Osteomalacia
4. Distant foci of infections which may spread to the implant site
5. Rapid joint destruction, marked bone loss or bone resorption, vascular insufficiency, muscular atrophy, or neuromuscular disease.
6. Hypotension
7. Congestive heart failure
8. Renal impairment

WARNINGS
Note: Adulteration of this bone cement may negatively affect performance characteristics.

Prior to using the Cobalt™ MV with Gentamicin Bone Cement surgeons should, by specific training and experience, be thoroughly familiar with the properties, handling characteristics, and application of the PMMA bone cement. (See Precautions and Mixing Technique) Because the handling and curing characteristics of this cement varies with temperature and mixing technique, they are best determined by the surgeon's actual experience. It is advisable for the surgeon to go through the entire mixing, handling and setting process *in vitro* before using the material in an actual surgical procedure.

Adverse cardiovascular reactions can include hypotension, hypoxemia, cardiac arrhythmia, bronchspasm, cardiac arrest, myocardial infarction, pulmonary embolism, cerebrovascular accident and possible death. Hypotensive reactions can occur between 10 seconds and 165 seconds after application of PMMA bone cement and can last for 30 seconds to 5 or more minutes. Some hypotensive reactions have progressed to cardiac arrest. The blood pressure, pulse and respiration of patients should be monitored carefully during

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

DJA x00049

and immediately following the application of the PMMA bone cement. Any significant alteration in these vital signs should be corrected with appropriate measures. In addition, over-pressurization of the PMMA bone cement should be avoided during the insertion of the PMMA bone cement and implant in order to minimize the occurrence of pulmonary embolism.

The risk of pulmonary fat embolism and the severity of all Bone Cement Implantation Syndrome (BCIS) complications can be reduced by meticulous irrigation and drying of the intramedullary canal Care should be taken to clean and aspirate the proximal portion of the femoral medullary canal just prior to insertion of bone cement. In high-risk patients, for example those sustaining hip fractures, care should be taken not to over-pressurize the cement and to insert the prosthesis slowly.

Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur, as the serum levels required to cause damage are not reached. Serious allergic reactions have been reported rarely in patients on systemic gentamicin therapy. Therefore, the incidence of these serious allergic events may also occur in patients with gentamicin-loaded bone cement.

Device volatility and flammability and electrocautery devices: The operating room should be adequately ventilated to eliminate monomer vapors. Ignition of monomer vapors caused by use of electrocautery devices in surgical sites near freshly implanted bone cements has been reported.

Irritation of the respiratory tract, eyes, and the liver: Caution should be exercised during the mixing of the liquid and powder components of the PMMA bone cement to prevent excessive exposure to the concentrated vapors of the liquid component, which may produce irritation of the respiratory tract, eyes, and possibly the liver. **Personnel wearing contact lenses should not mix PMMA bone cement or be near the mixing of the PMMA bone cement.**

1. DO NOT USE if there is loss of sterility of the cement.
2. Discard and DO NOT USE opened or damaged packages of the bone cement. Use only product packaged in unopened and undamaged containers.
3. Loosening and fracture of either the cement or the prosthesis, or both, can occur due to disease, trauma, and inadequate cementing technique, mechanical failure of the materials or latent infection.
4. The liquid and powder components of this cement must be mixed thoroughly before using. Inadequate mixing will lead to inhomogeneity that will compromise the mechanical properties and clinical performance of the cement.
5. DO NOT USE bone cement after expiration date.

The surgeon should decide whether the benefits expected from an arthroplasty outweigh any possible long-term adverse effects.

PRECAUTIONS

Strict adherence to good surgical principles and technique are required during use of the cement. Deep wound infection is a serious postoperative complication and may require total removal of the prostheses and embedded cement. Deep wound infection may be latent and not manifest itself for several years postoperatively.

1. **Contact dermatitis:** The liquid component (monomer) has caused contact dermatitis in those handling and mixing PMMA bone cement. Strict adherence to the instructions for mixing the powder and liquid components may reduce the incidence of contact dermatitis.
2. **Hypersensitivity reaction for operating room personnel:** The liquid component of the PMMA bone cement is a powerful lipid solvent. It should not contact rubber or latex gloves. Should contact occur, the gloves may dissolve and tissue damage may occur. Wearing a second pair of gloves and strict adherence to the mixing instructions may diminish the possibility of hypersensitivity reactions. The mixed bone cement should not make contact with gloved hand until the cement has acquired the consistency of dough. This usually occurs between one and two minutes after the liquid and powder components are mixed.
3. **Hypersensitivity reactions for patients:** The gentamicin content of Cobalt™ MV with Gentamicin Bone Cement may cause hypersensitivity reactions in isolated cases.

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

DJA x00050

4. **Inadequate post-operative fixation:** Inadequate fixation or unanticipated postoperative events may affect the PMMA bone cement/bone interface and lead to micro-motion of cement against the bone surface. A fibrous tissue layer may develop between the PMMA bone cement and the bone that may cause loosening of the prosthesis. Thus, continued, periodic follow-up is advised for all patients.
5. **Exothermic reaction:** Polymerization of the PMMA bone cement is an exothermic reaction that occurs while the PMMA bone cement is hardening *in situ*. The released heat may damage bone or other tissue adjacent the implant.
6. **Extrusion:** Extrusion of the PMMA bone cement beyond the region of its intended application may occur resulting in the following complications: hematuria; dysuria; bladder fistula; delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended use; local neuropathy; local vascular erosion and occlusion; and intestinal obstruction because of adhesions and stricture of the ileum from the heat released during the exothermic polymerization.
7. **USE IN PREGNANCY: The safety and effectiveness of the PMMA bone cement in pregnant women has not been established. PMMA bone cement may adversely affect fetal health.**
8. **PEDIATRIC USE: The safety and effectiveness of the PMMA bone cement in children has not been established. PMMA bone cement may adversely affect bone growth.**
9. **Expiration dating:** PMMA bone cement should not be used after the expiration date because the effectiveness of the device may be compromised.
10. **Disposal:** Expired cement should be mixed according to Instructions for Use prior to disposal. Because of the volatility and flammability of the liquid monomer of the PMMA bone cement, liquid monomer that has leaked or is leaking from the package should be collected and evaporated in a well-ventilated hood or absorbed by an inert material and transferred in a suitable container (one that does not react with the PMMA bone cement) for disposal.
11. **Incompatibility:** Aqueous (e.g. antibiotic containing) solutions must not be mixed with the bone cement, as this reduces the strength considerably.
12. **Monitoring:** Patients receiving gentamicin should be periodically monitored with peak and trough levels of the antibiotic, serum electrolytes, serum renal function, urinalysis, and audiograms (in elderly and/or dehydrated patient in whom there is a higher risk of adverse events associated with gentamicin use).
13. **Use of gentamicin should be avoided in the following situation.**
    Concurrent/sequential use of:
    - Other neurotoxic/nephrotoxic antibiotics
    - Other aminoglycosides
    - Cephaloridine
    - Viomycin
    - Polymixin B
    - Colistin
    - Cisplatin
    - Vancomycin
13. **Dose in patients with renal impairment:** Since no adjustment can be made to the dose in the gentamicin-loaded cement, a risk versus benefit assessment should be made before use in patients with renal impairment.
14. **Drug resistant bacteria:** Using Cobalt™ MV with Gentamicin Bone Cement under conditions other than the indicated use is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Avoid over pressurization of the bone cement because this may lead to extrusion of the bone cement beyond the site of its intended application and damage to the surrounding tissues.

ADVERSE EVENTS

The most serious adverse events, including death, reported with the use of acrylic bone cements are:

- Cardiac arrest
- Myocardial infarction
- Pulmonary embolism
- Cerebrovascular accident
- Sudden death

The most frequent adverse events reported are:

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

- Transitory fall in blood pressure
- Thrombophlebitis
- Hemorrhage and hematoma
- Loosening or displacement of the prosthesis
- Superficial or deep wound infection
- Trochanteric bursitis
- Short-term cardiac conduction irregularities

Nephrotoxicity

- Usually in patients with pre-existing renal damage
- Also in patients with normal renal function to whom amino-glycosides are administered for longer periods or in higher doses than recommended
- The symptoms may manifest after cessation of the therapy

Neurotoxicity

- Manifested as both auditory and vestibular ototoxicity, including irreversible hearing loss
- Numbness
- Skin tingling
- Muscle twitching
- Convulsions

Other adverse events reported are:

- Heterotopic new bone formation
- Trochanteric separation

Other potential adverse events reported include:

- Application of gentamicin may have the potential to trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur as the serum levels remain well below levels required to cause damage. Concurrent administration of muscle relaxants and ether may potentiate the neuromuscular blocking properties of gentamicin. However, the low serum concentrations significantly reduce the risk of occurrence of this adverse event. The use of antibiotic-loaded bone cement may lead to development of resistant microorganisms and the physician should weigh the risks vs. benefits to the patient before using Cobalt™ MV with Gentamicin Bone Cement in each case.
- Pyrexia due to an allergy or histological reaction to bone cement
- Hematuria
- Dysuria
- Bladder fistula
- Local neuropathy
- Local vascular erosion and occlusion
- Adhesions and stricture of the ileum due to the heat released during polymerization.
- Delayed sciatic nerve entrapment due to extrusion of the bone cement beyond the region of its intended application.

Adverse reactions affecting the cardiovascular system have been attributed to leakage of unpolymerized liquid monomer into the circulatory system. Data indicate that the monomer undergoes rapid hydrolysis to methacrylic acid and that a significant fraction of the circulating methacrylate is in the form of the free acid, rather than of the methyl ester. Correlation between changes in circulating concentrations of the methyl methacrylate/methacrylic acid and changes in blood pressure has not been established.

Hypotensive episodes reported are more marked in patients with elevated or high normal blood pressure in hypovolemia and in patients with pre-existing cardiovascular abnormalities. Elevations in plasma histamine levels subsequent to introduction of cement have also been reported.

Reports of sometime fatal cardiac arrest suggest that elderly osteoporotic patients undergoing hip replacement surgery for fractures of the femoral neck are at greater risk than those receiving elective joint replacement for arthritic disease. Risk is also higher in patients with pre-existing cardiovascular disease. Although the etiology of cardiac arrest is unclear, it may well be either direct embolic effects or secondary to hypoxia produced by pulmonary embolic phenomena. Introduction of liquid cement under pressure into a clean medullary canal has been shown to appreciably enhance the filling of the bone cavities with marked

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

DJA x00052

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

improvement in the security of the bone cement interface. Care must be exercised in introducing the cement continuously from distal to proximal to avoid laminations in the cement.

DOSAGE AND ADMINISTRATION

Cobalt™ MV with Gentamicin copolymer powder is double packaged. The inner gas permeable packet and its contents, as well as the inside of the foil laminate protective overwrap, are sterilized with ethylene oxide. The packet containing the sterile filtered liquid monomer is packaged in a protective gas-permeable overwrap pouch. The outside of the liquid packet and inside of overwrap pouch are sterilized by exposure to vaporous hydrogen peroxide.

(At least one extra unit of Cobalt™ MV with Gentamicin Bone Cement should be available before starting a surgical procedure).

A unit is prepared by mixing the entire contents of one (1) packet of powder (40 g copolymer) with one (1) packet of liquid (20 ml monomer). One or two units will usually suffice, although this will depend upon the specific surgical procedure and the techniques employed. Each unit is prepared separately.

The following are required for preparation of the bone cement:

- Sterile working area
- Sterile plastic bowl approved for use with monomers
- Sterile mixing spoons or spatulas.

Note: For vacuum mixing, refer to manufacturer instructions.

A circulating nurse or assistant opens the peelable film package and the blister pack, and the sterile powder packet and liquid packet are aseptically placed on a sterile table. The powder packet and the liquid packet are opened under sterile conditions. Since each packet of powder contains a pre-measured quantity of copolymer to react with a pre-measured quantity of monomer, care should be taken to mix the entire contents of one powder packet with the entire contents of one liquid packet. Partial amounts should not be used.

MIXING INSTRUCTIONS FOR BOWL MIXING

Note: Cement can also be mixed in a vacuum mixing system. Refer to manufacturer instructions.

Pour the liquid into a bowl. Add the powder. Stir with a spatula vigorously, but carefully, for about 30 seconds.

CEMENT MAY BE APPLIED IN A PRE-DOUGH STATE, BUT IF A DOUGH-LIKE MASS THAT DOES NOT STICK TO RUBBER GLOVES AS DESIRED, WAIT ANOTHER 2 MINUTES - 6 MINUTES depending on the ambient temperature (SEE CURVES).

At this state knead for about 15 seconds -30 seconds. The cement becomes more homogeneous, and mixed air bubbles disappear for the most part. On the other hand, if the kneading process is extended too long, the polymerization may proceed to the point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The working time may be affected by temperature (see curve and table for working and hardening times). Additionally, the moisture content in any bone cement powder has an effect on polymerization; cement powder with higher moisture content will set faster, while drier cement powder will result in slower set-times. The outer foil pouch acts as a moisture barrier for Cobalt™ MV with Gentamicin Bone Cement. To minimize fluctuation of set-times, do not remove the powder component's moisture barrier until it is time to mix the cement. Maintaining a constant and moderate (40%RH-55%RH) humidity in the operating room will also lead to more consistent cement handling performance. The ideal working consistency of the Cobalt™ MV with Gentamicin Bone Cement for manual application to bone is best determined by the surgeon based upon experience in using the preparation. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Excessive cement must be removed while it is still soft. If additional cement is required during the surgical procedure, another

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

packet of liquid and packet of powder may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

The completion of polymerization occurs in the patient and is associated with the liberation of heat. To more rapidly dissipate the heat, the polymerizing cement may be irrigated with a cool physiologic saline solution.

STORAGE

Store package in a dry, ventilated place between 6°C and 23°C (42.8°F to 73.4°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73.4°F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

The copolymer powder does not withstand heat sterilization treatment. If a packet is accidentally opened, it must not be used.

HOW SUPPLIED

Carton consisting of:
1 packet of copolymer powder containing 40 g
1 packet of liquid monomer containing 20 ml

The following tables and graphs were generated using standard methods including a temperature-controlled environment. Warming of bone cement by any manual manipulation and the eventual application to the surgical site will accelerate the onset and completion of the final hardening phase. The extent of acceleration depends on the timing of manipulation and application. Early and extended warming will have the largest effect on cement hardening.

Typical working data for mixing Cobalt™ MV with Gentamicin Bone Cement

Open Bowl Mixing at Ambient Temperatures

Ambient and component temperature	18° C	20° C	23° C
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	5'30"	4'15"	3'00"
End of application phase	12'50"	10'30"	8'10"
Hardening	18'15"	15'00"	11'40"

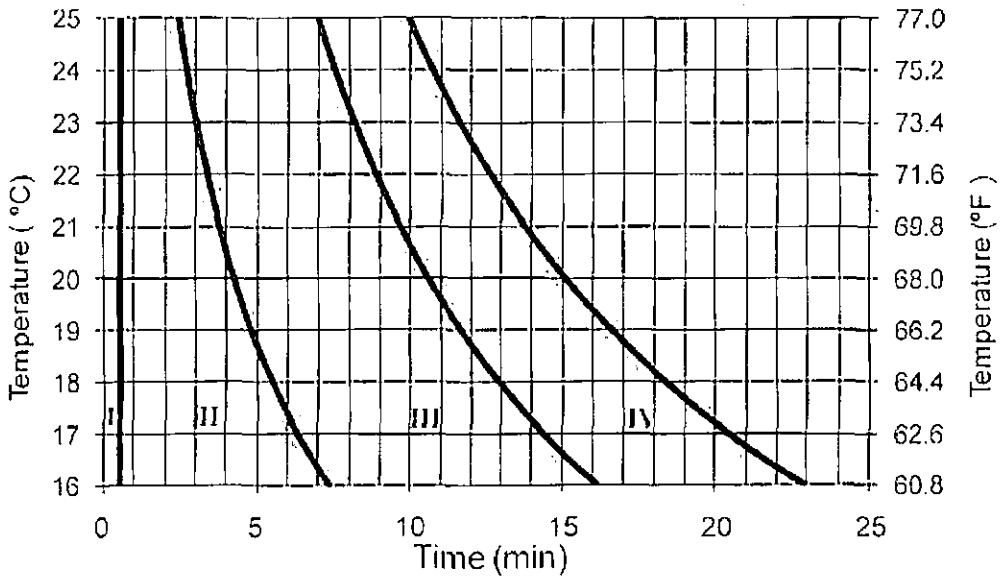
Vacuum Mixing at Ambient Temperatures

Ambient and component temperature	18° C	20° C	23° C
Mixing time	0'30"	0'30"	0'30"
Start of dough phase	3'25"	2'45"	2'10"
End of application phase	10'00"	8'15"	6'30"
Hardening	14'15"	11'45"	9'15"

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

DJA x00054

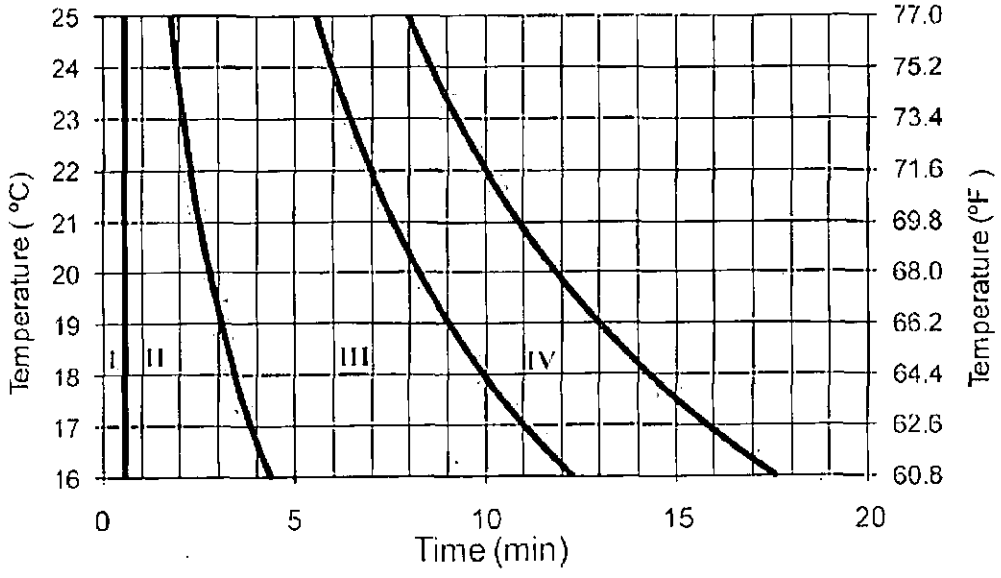
Handling and Setting Times vs. Temperature for
Open Bowl Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

Handling and Setting Times vs. Temperature for
Vacuum Mixing of Cobalt™ MV with Gentamicin Bone Cement



I – Mixing phase III – Post-dough phase

II – Pre-dough phase IV – Final hardening phase

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

DJA x00055

Reviewer's Comments:

The sponsor has provided adequate labeling including indications, contraindications, warnings, precautions, adverse events, important information to the user and handling times based on temperatures encountered in the operating room. This labeling was previously cleared for G-HV Bone (K051532) cement for another Biomet Bone Cement containing the same amount of gentamicin bone cement for a 2 stage revision.

Sterilization/Shelf Life/Packaging

Shelf Life

Cobalt™ G-MV Bone Cement has a one-year shelf life. The packaging material and level of BPO support a 1 year shelf life. This is a conservative estimate considering the decomposition rate of BPO, the storage conditions and packaging material.

Sterility Information

Cobalt™ G-MV powder and the packet containing the powder are provided sterile by gas sterilization methods as follows:

Gas Type:	Ethylene Oxide (EtO)
Residuals:	meet the AMMI/ANSI/ISO 10993-7:1995 and AAMI TIR No. 19-1998
Sterility Assurance Level:	10^{-6}
Sterility Validation Method:	AMMI/ANSI/ISO 11135:1994
Pyrogen-Free:	No claims will be made
Labeling:	All packages will display a black/dark brown to green chemical indication dot along with a statement that the device has been sterilized by Ethylene Oxide (EtO).
Contract Sterilization Site:	Centurion Sterilization Services A Division of Tri-State Hospital Supply Corp. 301 Catrell Drive Howell, Michigan 48843 Registration Number: 1824619

The Cobalt™ G-MV liquid component is sterile filtered and aseptically filled. The interior of the pouch is sterilized by exposure to gamma irradiation prior to monomer fill. The exterior of the pouch containing the liquid is sterilized by exposure to vaporous hydrogen peroxide, as well as the outside of the liquid packet and inside of the overwrap. The filtration and vaporous hydrogen peroxide sterilization methods are as follows:

Filtration

Filter Size: membranes of porosity not greater than 0.22μm
Sterility Validation Method: U.S.P. test methods
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, IN 46582

Vaporous Hydrogen Peroxide

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: EN 550, revised protocol
Sterilization Site:
Biomet Manufacturing Corp.

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

DJA x00056

56 East Bell Drive
Warsaw, In 46582

These are the same sterilization methods used for the predicate Cobalt™ HV cleared in K051496.

Packaging

Packaging

Cobalt™ G-MV is double packaged. The packaged powder and liquid components are placed into a fiberboard outer box after the individual components are packaged as discussed below.

Powder

The powder component's inner gas permeable pouch is made of Tyvek®/Mylar® and enclosed in a foil-lined protective overwrap pouch, also made of foil. The packaging of Cobalt™ G-MV powder is similar to that of the predicate Cobalt™ G-HV Bone Cement's powder component (K051532). Since FDA's clearance of Cobalt™ G-HV in 2005, Biomet has changed the exterior packaging for its bone cements from a paper/foil/polymer laminated pouch to a foil/polymer laminated pouch comprised of TPC-0814B. This change utilized internal documentation pursuant to FDA's guidance document, *"Deciding when to Submit a 510(k) for a Change to an Existing Device (K97-1)*. The exterior foil packaging has been validated and poses no new risks. A copy of the validation for TPC-0814B is on file at Biomet and can be accessed at any future FDA inspection. The inside packaging for Cobalt™ G-MV is the same as the predicate Cobalt™ G-HV's inside packaging, which has not changed since it was cleared.

Liquid (Monomer)

The liquid monomer's inner container is a Cryovac T6050B co-extruded film pouch (LLDPE sealant layer, polypropylene skin, and barrier of EVOH sandwiched between nylon layers). The outer container is a Tyvek® pouch. The packaging for the liquid monomer is the same as that of its predicate, Cobalt™ G-HV (K051532).

Sterilization

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The exterior surfaces of the cement liquid packages are sterilized by exposure to vaporous hydrogen peroxide that takes place at Biomet Manufacturing Corp. The label will include an EtO sterility identifier.

The sterilization of the liquid component of Cobalt™ G-MV Bone Cement is identical to that of the predicate Cobalt™ G-HV Bone Cement's liquid component (K051532). Please refer to the following table for a comparison of the packaging and sterilization of Cobalt™ G-MV Bone Cement to its predicates.

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

DJA x00057

Sterility Information
Cobalt™ G-MV powder and the packet containing the powder are provided sterile by gas sterilization methods as follows:

Gas Type:	Ethylene Oxide (EtO)
Residuals:	meet the AMMI/ANSI/ISO 10993-7:1995 and AAMI TIR No. 19-1998
Sterility Assurance Level:	10^{-6}
Sterility Validation Method:	AMMI/ANSI/ISO 11135:1994
Pyrogen-Free:	No claims will be made
Labeling:	All packages will display a black/dark brown to green chemical indication dot along with a statement that the device has been sterilized by Ethylene Oxide (EtO).
Contract Sterilization Site:	Centurion Sterilization Services A Division of Tri-State Hospital Supply Corp. 301 Catrell Drive Howell, Michigan 48843 Registration Number: 1824619

The Cobalt™ G-MV liquid component is sterile filtered and aseptically filled. The interior of the Softpac pouch is Gamma sterilized prior to the asceptic fill. The exterior of the pouch containing the liquid is sterilized by exposure to vaporous hydrogen peroxide, as well as the outside of the liquid packet and inside of the overwrap. The filtration and vaporous hydrogen peroxide sterilization methods are as follows:

Gamma

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: *Gamma Irradiation Product Adaption, File #229*
Sterilization Site:
STERIS Isomedix
1880 Industrial Drive
Libertyville, Illinois 60048

Filtration

Filter Size: membranes of porosity not greater than 0.22µm
Sterility Validation Method: U.S.P. test methods
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, IN 46582

Vaporous Hydrogen Peroxide

Sterility Assurance Level: 10^{-6}
Sterility Validation Method: EN 550, revised protocol
Sterilization Site:
Biomet Manufacturing Corp.
56 East Bell Drive
Warsaw, In 46582

These are the same sterilization methods used for the predicate Cobalt™ G-HV cleared in K051532.

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

Cobalt™ G-MV's powder component is EtO-sterilized by Centurion Sterilization Services. The liquid component is sterile filtered and aseptically filled by Biomet Manufacturing Corp. The exterior surfaces of the cement liquid packages are sterilized by exposure to vaporous hydrogen peroxide that takes place at Biomet Manufacturing Corp. The label will include an EtO sterility identifier.

The sterilization of the liquid component of Cobalt™ MV Bone Cement is identical to that of the predicate Cobalt™ MV (K091608).

Powder Component Packaging and Sterilization				
		Cobalt™ G-MV (New)	**Cobalt™ G-HV (K051532)**	**Simplex® P w/ Tobramycin (K014199)**
Innermost Pouch	**Material**	Tyvek®/Mylar	Tyvek®/Mylar	Multi-layer clear plastic barrier film
	Sterility	Contents & exterior sterile (EtO)	Contents & exterior sterile (EtO)	Contents & exterior sterile (Gamma)
Overwrap	**Material**	Foil	Foil	Plastic pouch with breathable header
	Sterility	Contents sterile	Contents sterile	Contents sterile
Liquid Component Packaging and Sterilization				
Inner Container	**Material**	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Cryovac T6050B coextruded film pouch (LLDPE sealant layer, polypropylene skin, & barrier of EVOH sandwiched between nylon layers)	Glass ampoule
	Sterility	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & e-beam or Gamma of pouch prior to aseptic fill)	Contents sterile (filtration of liquid, & sterilization of ampoule prior to aseptic fill)
	Comment	Very good barrier. Durable package.	Very good barrier. Durable package.	Impermeable barrier, but fragile. Hazardous to open; glass shards may fall into monomer upon opening.
Outer Container	**Material**	Tyvek® pouch	Tyvek® pouch	Rigid plastic blister with breathable lid
	Sterility	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (vaporous hydrogen peroxide)	Contents sterile (EtO)
	Comment	Vaporous hydrogen peroxide permeable	Vaporous hydrogen peroxide permeable	EtO permeable lid stock

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

DJA x00059

STORAGE

Store package in a dry, ventilated place between 6° and 23°C (43° to 74°F). Improper exposure to high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties, and clinical result.

Sufficient units should be removed from stocks and stored at about 23°C (73°F), or at the temperature appropriate to give desired cement handling and setting properties, for 24 hours before use.

Reviewer's Comments:

The packaging and sterilization information is considered adequate based on the sponsor's identification of the packaging material, sterilization method to be used by the end user.

Biocompatibility

Materials and Biocompatibility

Changes made to the concentrations of the powder and monomer components might adversely affect monomer elution. Due to this possibility, cytotoxicity testing was conducted in accordance with USP Elution Test (MEM Extract) to ensure that the formulation change did not adversely affect the monomer elution. According to USP Specifications, the sample meets the test requirements if the cell culture treated with the sample is less than or equal to grade 2 (mild reactivity). The sample of Cobalt™ G-MV Bone Cement met the USP requirements for this test. The testing demonstrated that the formulation change did not affect monomer elution. The test report is included in the **Mechanical Testing** section of this submission.

Testing Laboratory:

Pacific BioLabs (formerly Northview Pacific Laboratories)
551 Linus Pauling Drive
Hercules, CA 94547
FDA Registration No. 29-14117

Biocompatibility

Component	Material	Applicable Standard
Powder (copolymer)	• Methyl methacrylate-styrene copolymer • Poly(methyl methacrylate) • Zirconium dioxide • Benzoyl peroxide • Gentamicin Sulfate • FD&C Blue No.2 Aluminum Lake	ASTM F 451-99a ISO 5833:2002
Liquid (monomer)	• Methyl methacrylate (stabilized with hydroquinone) • N,N-dimethyl-p-toluidine	ASTM F 451-99a ISO 5833:2002

Reviewer's Comments:

The sponsor has provided adequate rationale why additional biocompatibility is not needed for this

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

DJA x00060

formulation that has a long history of being biocompatible.

IV. Software

N/A

V. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

N/A

Performance Testing – Animal

None provide and none required for this PMMA Bone Cement.

Performance Testing – Clinical

None provide and is not needed because the materials and similar formulations have a long history of clinical success.

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

DJA x00061

Substantial Equivalence Discussion

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
510(k) No.	New	K051532	K014199
Cement Design	Cobalt™ G-MV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Cobalt™ HV Bone Cement provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.	Surgical Simplex® P provides two separate, pre-measured sterilized components which when mixed form radiopaque fast-setting bone cement.
Cement Materials	Powder component/ liquid monomer	Powder component/ liquid monomer	Powder component/ liquid monomer
Powder Component	Methyl methacrylate-styrene copolymer 29.83g Poly(methyl methacrylate) 6.00g Zirconium dioxide 4.00g FD&C Blue No. 2 Aluminum Lake 0.05g Residual benzoyl peroxide (0.44g) Benzoyl peroxide (hydrous 75%) 0.12g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methylmethacrylate-methacrylate copolymer with FD&C Blue No. 2 Aluminum Lake 33.86 – 33.42g --- Zirconium dioxide 5.94g --- --- Benzoyl peroxide, (hydrous 75%) 0.20 – 0.64g Gentamicin sulfate (equivalent to 0.50g Gentamicin) 0.84g	Methyl methacrylate-styrene-copolymer 30.00g Polymethyl methacrylate 6.00g Barium Sulfate, U.S.P. 4.00g --- Residual benzoyl peroxide (0.51g) Tobramycin Sulfate 1.0g active
Liquid Monomer Component	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 18.424g N,N-dimethyl-p-toluidine 0.376g Hydroquinone 60 ± 20ppm	Methylmethacrylate (monomer) 97.4% v/v N, N-dimethyl-p-toluidine 2.6% v/v Hydroquinone 75 ± 15ppm

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

DJA x00062

	Cobalt™ G-MV	Cobalt™ G-HV	Simplex® P w/ Tobramycin
Sterilization	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Ethylene Oxide (EtO) Liquid Monomer Component Sterile Membrane Filtered	Powder Component Gamma Irradiation Liquid Monomer Component Membrane Filtration
Packaging	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in a gas permeable sterile packet, enclosed in a sterile paper-foil protective overwrap Liquid Monomer Component Sterile Flexible film packet	Powder Component Packaged in sterile packet, enclosed in a sterile protective package Liquid Monomer Component Pre-sterilized ampoule, enclosed in a pre-sterilized ampoule package
Anatomical Sites	Osseous tissue	Osseous tissue	Osseous tissue

Reviewer's Comments:

The sponsor has provided a comparison to a predicate bone cement. However, additional information is needed regarding the fatigue testing. See the deficiency list at the end of the memo.

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

X. **Recommendation**

Regulation Number: 21 CFR 888.3027
Regulation Name: PMMA Bone Cement;
Regulatory Class: Class II
Product Code: LOD, MBB

Reviewer — Date: 9-25-09

CONCUR

Branch Chief — Date: 09/25/09

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

DJA x00063

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

I am placing this document on hold until the sponsor adequately addresses the following deficiencies:

1. In your device description and package insert you state you have a range of benzoyl peroxide was 0.35-1.0 grams. You state the your bone cement formulation contains 1.38% w/w of benzoyl peroxide but you have not provide the range of benzoyl peroxide in your release criteria for benzoyl peroxide levels for the product. Please provide the lowest and highest level of benzoyl peroxide in your release criteria and what level tested in all the pre-clinical testing that you have provided in your submission. This information is needed to help determine the handling characteristics and physical and mechanical properties for your bone cement formulation. See the PMMA guidance document for a discussion for benzoyl peroxide levels in bone cement formulations.

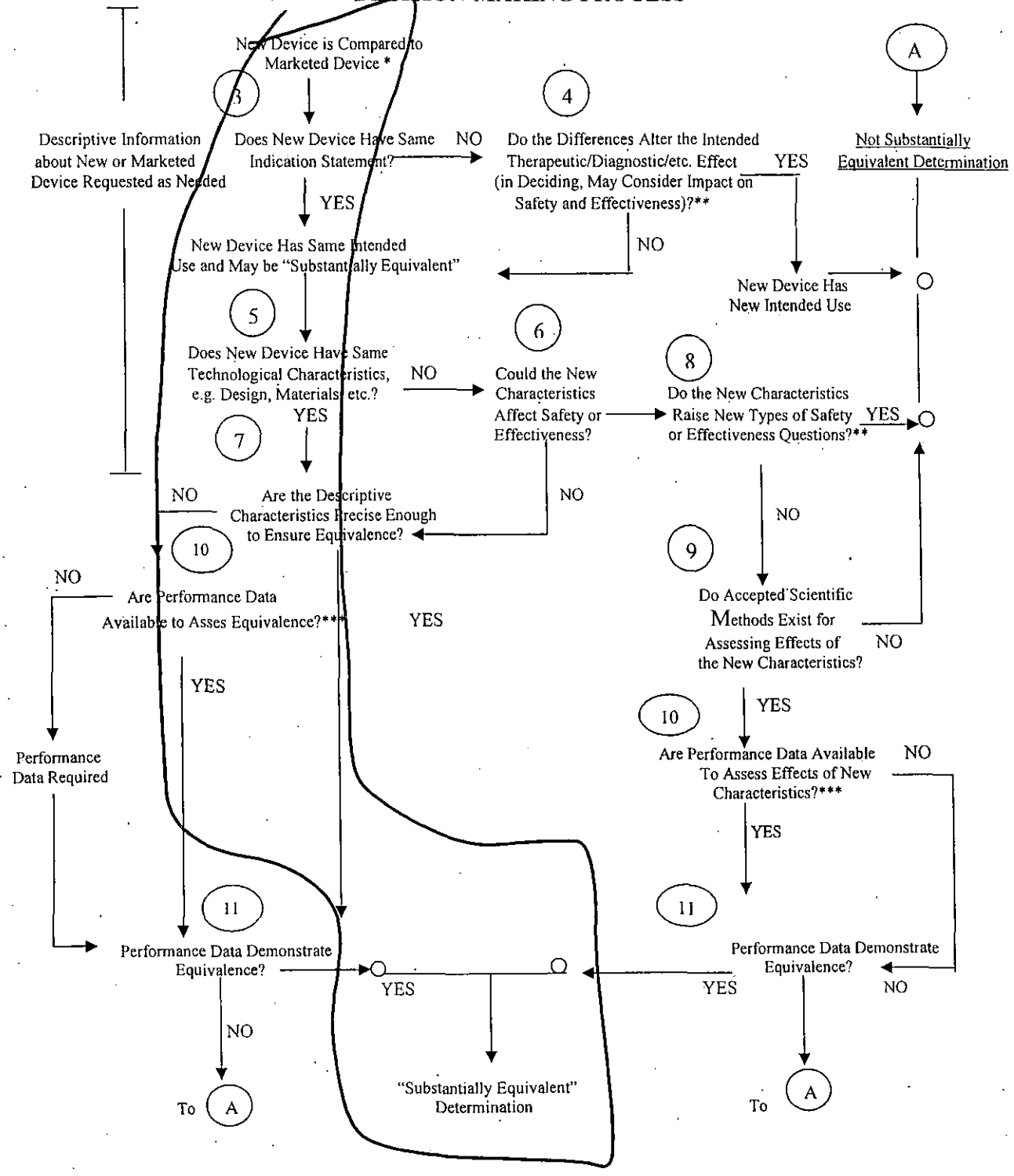
2. You have provided limit fatigue testing at 15 MPa and 10 MPa. At 10 MPa you have only performed testing to a run out of 1 million cycles. Please perform fatigue testing in accordance with ASTM F2118 where run-out is considered 5 million cycles.

3. You have stated the gentamicin sulfate will be added to the powder component. However you have not provided the particle size distribution of the gentamicin sulfate. In addition, please identify the supplier for the gentamicin sulfate.

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

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



❖ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

❖❖ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

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

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

K092150/S1

BIOMET
MANUFACTURING CORP.

October 7, 2009

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

OCT - 8 2009

ATTN: Mr. Hany Demian

RE: K092150
Cobalt™ MV with Gentamicin Bone Cement

Dear Mr. Demian:

The following is Biomet's response to FDA's e-mail of September 25, 2009 requesting additional information regarding Biomet's 510(k) submission for Cobalt™ MV Bone Cement (K092150).

1. **In your device description and package insert you state you have a range of benzoyl peroxide of 0.35-1.0 grams. You state that your bone cement formulation contains 1.38% w/w of benzoyl peroxide but you have not provided the range of benzoyl peroxide in your release criteria for benzoyl peroxide levels for the product. Please provide the lowest and highest level of benzoyl peroxide in your release criteria and what level tested in all the pre-clinical testing that you have provided in your submission. This information is needed to help determine the handling characteristics and physical and mechanical properties for your bone cement formulation. See the PMMA guidance document for a discussion for benzoyl peroxide levels in bone cement formulations.**

(b) (4)
[redacted]

2. **You have provided limited fatigue testing at** (b) (4) [redacted] **you have only performed testing to a run-out of 1** (b) (4) [redacted] **Please perform fatigue testing in accordance with ASTM F2118 where run-out is considered** (b) (4) [redacted]**.**

(b)(4) Testing
[redacted]

Mailing Address:
P.O. Box 587
Warsaw, IN. 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574-267-8137

Shipping Address:
56 e Bell Drive
Warsaw, IN 46582

K23

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

3. **You have stated the gentamicin sulfate will be added to the powder component. However, you have not provided the particle size distribution of the gentamicin sulfate. In addition, please identify the supplier for the gentamicin sulfate.**

(b) (4)

[redacted]

Please contact me at (574) 267-6639, or at sue.alexander@biomet.com or tracy.johnson@biomet.com, if you have additional questions or require further information.

Sincerely,

Susan Alexander

Susan Alexander
Regulatory Affairs Specialist
Biomet Orthopedics

Attachments

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

BIOMET
MANUFACTURING CORP.

October 7, 2009

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

ATTN: Mr. Hany Demian

RE: K092150
Cobalt™ MV with Gentamicin Bone Cement

Dear Mr. Demian:

The following is Biomet's response to FDA's e-mail of September 25, 2009 requesting additional information regarding Biomet's 510(k) submission for Cobalt™ MV Bone Cement (K092150).

1. **In your device description and package insert you state you have a range of benzoyl peroxide of 0.35-1.0 grams. You state that your bone cement formulation contains 1.38% w/w of benzoyl peroxide but you have not provided the range of benzoyl peroxide in your release criteria for benzoyl peroxide levels for the product. Please provide the lowest and highest level of benzoyl peroxide in your release criteria and what level tested in all the pre-clinical testing that you have provided in your submission. This information is needed to help determine the handling characteristics and physical and mechanical properties for your bone cement formulation. See the PMMA guidance document for a discussion for benzoyl peroxide levels in bone cement formulations.**

(b) (4) [redacted]

2. **You have provided limited fatigue testing at 1** (b) (4) [redacted] **you have only performed testing to a run-out of** (b) (4) [redacted] **Please perform fatigue testing in accordance with ASTM F2118 where run-out is considered** (b) (4) [redacted]

(b) (4) [redacted]

Mailing Address:
P.O. Box 587
Warsaw, IN. 46581-0587
Toll Free: 800.348.9500
Office: 574.267.6639
Main Fax: 574-267-8137

Shipping Address:
56 e Bell Drive
Warsaw, IN 46582

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

3. **You have stated the gentamicin sulfate will be added to the powder component. However, you have not provided the particle size distribution of the gentamicin sulfate. In addition, please identify the supplier for the gentamicin sulfate.**

(b) (4)

[redacted]

Please contact me at (574) 267-6639, or at sue.alexander@biomet.com or tracy.johnson@biomet.com, if you have additional questions or require further information.

Sincerely,

Susan Alexander

Susan Alexander
Regulatory Affairs Specialist
Biomet Orthopedics

Attachments

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

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

Cobalt G-MV Bone Cement vs. Simplex® P w/tobramycin

Summary of Chemical, Physical, Handling & Mechanical Testing

(b)(4) Testing

[redacted]

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

(b)(4) Testing

[redacted]

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

(b)(4) Testing

[redacted]

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

Records processed under FOIA Request #2014-8120; Released by CDRH on 12-8-2015

(b)(4) Testing

[redacted]