Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

K042911

DEC 27 2004

Cementek® LV
510(k) Summary
October 18, 2004

Submitter: Teknimed, S.A.
11 rue Apollo
31240 L'Union
FRANCE

Contact person: J.D. Webb
1001 Oakwood Blvd
Round Rock, TX 78681
512-388-0199

Trade Name: Cementek® LV

Common name: Bone void filler

Classification name: Class II per 21 CFR section 888.3045

Product Code: MQV

Equivalent Device: Cementek ® (K040669)

Device Description
As an injectable bone substitute, Cementek® LV is packaged as a solid phase and a liquid phase. The liquid and solid phases are mixed in the operating room, then introduced with a syringe into the osseous cavity and allowed to set. This reaction is an athermic reaction resulting in an apatitic calcium phosphate cement. Cementek® LV is marketed in a 16cc dosage.

Intended Use
Cementek® LV is intended for use only as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, the calcium phosphate scaffold resorbs and is replaced with bone during the healing process.

Summary of Technological Characteristics Compared to Predicate Device
Cementek® LV is equivalent to Cementek® in terms of physical form, how supplied, compressive strength, porosity, average pore size, composition of final product and indications.

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

Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 27 2004

Teknimed, S.A.
c/o Mr. J.D. Webb
The Orthomedix Group, Inc.
1001 Oakwood Blvd.
Round Rock, TX 78681

Re: K042911
Trade Name: Cementek LV Bone Substitute
Regulation Number: 21 CFR 888.3045
Regulation Name: Resorbable calcium salt bone void filler device
Regulatory Class: Class II
Product Code: MQV
Dated: December 6, 2004
Received: December 8, 2004

Dear Mr. Webb:

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

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

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manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally 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/dsma/dsmamain.html

Sincerely yours,

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

Enclosure

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

Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

Indications for Use

510(k) Number (if known): K042911

Device Name: Cementek® LV

Indications for Use:

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process.

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

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

for Mark N Milhem

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

510(k) Number K042911

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 27 2004

Teknimed, S.A.
c/o Mr. J.D. Webb
The Orthomedix Group, Inc.
1001 Oakwood Blvd.
Round Rock, TX 78681

Re: K042911
Trade Name: Cementek LV Bone Substitute
Regulation Number: 21 CFR 888.3045
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Questions?Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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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

Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

Indications for Use

510(k) Number (if known): K042911

Device Name: Cementek® LV

Indications for Use:

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

for Mark N Melkerson

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

510(k) Number K042911

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 16 2004

Teknimed, S.A.
c/o Mr. J.D. Webb
The Orthomedix Group, Inc.
1001 Oakwood Blvd.
Round Rock, TX 78681

Re: K042911
Trade Name: Cementek LV Bone Substitute
Dated: October 18, 2004
Received: October 21, 2004

Dear Mr. Webb:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require the following additional information.

(b)(4)

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

Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

(b)(4)

The deficiencies identified above 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/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

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The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

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

If you have any questions concerning the contents of the letter, please contact Nadine Y. Sloan at (301)594-1296, ext 205. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (301) 443-6597, or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

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

Enclosure

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

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Teknimed, S.A.
c/o Mr. J.D. Webb
The Orthomedix Group, Inc.
1001 Oakwood Blvd.
Round Rock, TX 78681

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Received: October 21, 2004

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Rockville, Maryland 20850

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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

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FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
240	Sloan	11/15/04						
240	Stevens	11/15/04						

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

Records processed under FOIA Request 2018-697; Released by CDRH on 6/19/2018

cc: HFZ-401 DMC
HFZ-404 510(k) Staff
HFZ- 410 DGRND
D.O.

nyr:11-15-04

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

October 21, 2004

TEKNIMED SA
C/O THE ORTHOMEDIX GROUP, INC.
1001 OAKWOOD BLVD
ROUND ROCK, TX 78681
ATTN: J.D. WEBB

510(k) Number: K042911
Received: 21-OCT-2004
Product: CEMENTEK LV

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

On May 21, 2004, FDA issued a Guidance for Industry and FDA Staff entitled, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. Please review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

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 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 www.fda.gov/cdrh/ode/a02-01.html.

You should be familiar with the regulatory requirements for medical device available at Device Advice http://www.fda.gov/cdrh/devadvice/". If you have other procedural or policy questions, or want information on how to check on the status of your submission, please contact DSMICA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsmamain.html or me at (301)594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
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

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K042911

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

MEDICAL DEVICE USER FEE COVER SHEET

PAYMENT IDENTIFICATION NUMBER (b) (4)

Write the Payment Identification Number on your check.

A completed Cover Sheet must accompany each original application or supplement subject to fees. The following actions must be taken to properly submit your application and fee payment:

1. Electronically submit the completed Cover Sheet to the Food and Drug Administration (FDA) before payment is sent.
2. Include a printed copy of this completed Cover Sheet with a check made payable to the Food and Drug Administration. Remember that the Payment Identification Number must be written on the check.
3. Mail Check and Cover Sheet to the US Bank Lock Box, FDA Account, P.O. Box 956733, St. Louis, MO 63195-6733. (*Note: In no case should payment be submitted with the application.*)
4. If you prefer to send a check by a courier, the courier may deliver the check and Cover Sheet to: US Bank, Attn: Government Lockbox 956733, 1005 Convention Plaza, St. Louis, MO 63101. (Note: This address is for courier delivery only. Contact the US Bank at 314-418-4821 if you have any questions concerning courier delivery.)
5. For Wire Transfer Payment Procedures, please refer to the MDUFMA Fee Payment Instructions at the following URL: http://www.fda.gov/cdrh/mdufma/faqs.html#3a. You are responsible for paying all fees associated with wire transfers.
6. Include a copy of the completed Cover Sheet in volume one of the application when submitting to the FDA at either the CBER or CDRH Document Mail Center.

1. COMPANY NAME AND ADDRESS (Include name, street address, city, state, country, and post office code)

TEKNIMED
11 RUE APOLLO
L'H UNION, 31240
FR

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)

2. CONTACT NAME
JD WEBB

2.1 E-MAIL ADDRESS
ortho.medix@sbcglobal.net

2.2 TELEPHONE NUMBER (Include Area Code)
512-388-0199

2.3 FACSIMILE (FAX) NUMBER (Include Area Code)
512-388-0199

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

Select an application type:

- Premarket notification (510(k)); except for third party
- Biologic License Application (BLA)
- Premarket Approval Application (PMA)
- Modular PMA
- Product Development Protocol (PDP)
- Premarket Report (PMR)

3.1 Select one of the types below:

- Original Application

Supplement Types:

- Efficacy (BLA, PMR)
- Panel Track (PMA, PMR, PDP)
- Real-Time (PMA, PMR, PDP)
- 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status.)

YES, I meet the small business criteria and have submitted the required qualifying documents to FDA

NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number:

5. 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, parents, and partner firms
- This biologic 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

6. 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 THE USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).)

YES NO

7. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS APPLICATION

(b) (4)

SK 32
PM II 30

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

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THE ORTHOMEDIX GROUP, INC.

October 18, 2004

Document Mail Center (HFZ401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

Re: Premarket Notification – Cemetek® LV Bone Substitute
Modification to Cementek® Bone Substitute K041493

Dear Sir/Madam,

Teknimed, S.A. hereby submits this **Special 510(k): Device Modification** to request modifications to our Cementek® Bone Substitute (K041493). We believe the modifications to this product are eligible for the Special 510(k) process since they have the same fundamental scientific technology and intended use as the predicate device.

Applicant	Teknimed, S.A.
Address	11 rue Apollo 31240 L'Union FRANCE
Contact Person	J.D. Webb
Address	1001 Oakwood Blvd Round Rock, TX 78681
Telephone Number	512-388-0199
Fax Number	512-388-0199
E-mail Address	ortho.medix@sbcglobal.net

We consider our intent to market this device as confidential commercial information and request that it be treated as such by FDA. We have taken precautions to protect the confidentiality of the intent to market this device.

Respectfully,

JD Webb

J.D. Webb
Authorized Contact Person

K032

1001 Oakwood Blvd • Round Rock, TX 78681 • (512)388-0199 Tele • (512)388-0199 Fax • ortho.medix@sbcglobal.net

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

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Table of Contents

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PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT

[As required by 21 CFR 807.87(k)]

I certify that, in my capacity as <*M.LEONARD Alain* > of <TEKNIMED> I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

(Signature)

A LEONARD

(Typed name)

04.10.2004

(Dated)

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

* For a new submission, leave the space for the 510(k) number blank.

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Indications for Use

510(k) Number (if known): K042911

Device Name: Cementek® LV

Indications for Use:

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process.

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

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

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Cementek® LV
510(k) Summary
October 18, 2004

Submitter: Teknimed, S.A.
11 rue Apollo
31240 L'Union
FRANCE

Contact person: J.D. Webb
1001 Oakwood Blvd
Round Rock, TX 78681
512-388-0199

Trade Name: Cementek® LV

Common name: Bone void filler

Classification name: Class II per 21 CFR section 888.3045

Product Code: MQV

Equivalent Device: Cementek ® (K040669)

Device Description
As an injectable bone substitute, Cementek® LV is packaged as a solid phase and a liquid phase. The liquid and solid phases are mixed in the operating room, then introduced with a syringe into the osseous cavity and allowed to set. This reaction is an athermic reaction resulting in an apatitic calcium phosphate cement. Cementek® LV is marketed in a 16cc dosage.

Intended Use
Cementek® LV is intended for use only as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, the calcium phosphate scaffold resorbs and is replaced with bone during the healing process.

Summary of Technological Characteristics Compared to Predicate Device
Cementek® LV is equivalent to Cementek® in terms of physical form, how supplied, compressive strength, porosity, average pore size, composition of final product and indications.

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1. Device Name

1.1. Trade Name
Cementek® LV

1.2. Common Name
Bone void filler

1.3. Classification Name
Filler, calcium sulfate, preformed pellets

2. Registration Number
9615788

3. Classification

3.1. Class
Class II per 21 CFR Sec. 888.3045

3.2. Panel
Orthopedic

3.3. Product Code
MQV

4. Performance Standards
There are no performance standards for calcium phosphate cement.

5. Labeling (Exhibit I)
Draft labels and Instructions for Use can be found in Exhibit I.
No changes to the labels or Instructions for Use have occurred.

6. Substantial Equivalence Comparison
Cementek® LV is similar to Cementek® (K041493). A table comparing the various properties is shown in Exhibit II.

7. Device Description
As an injectable bone substitute, Cementek® LV is packaged as a solid phase and a liquid phase. The liquid and solid phases are mixed in the operating room, then injected as a paste into the osseous cavity and allowed to set.

7.1. Indications for Use
Cementek® LV is intended for use only as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated

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for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, the calcium phosphate scaffold resorbs and is replaced with bone during the healing process.

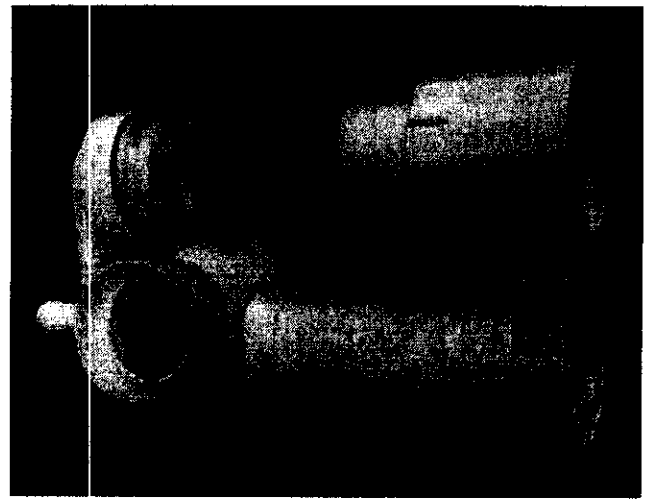
7.2. Chemical Composition

Cementek® LV is manufactured by processing and mixing calcium carbonate and calcium dihydrogenophosphate, creating tetracalcium phosphate(TTCP). In parallel, amorphous tricalcium phosphate(TCP) is processed creating α-tricalcium phosphate. These two components are mixed with sodium glycerophosphate and polydimethyl siloxane with a solvent (cyclohexane) to produce the solid phase of the product. Following mixing the solid phase is dried to remove the solvent.

A schematic of the manufacturing process can be found in Exhibit III.

Calcium hydroxide, orthophosphoric acid and water are mixed and processed to create the liquid phase of Cementek® LV.

The solid and liquid phases are packaged separately in a pouch and flask then boxed together as a kit. A mixing kit comprised of a spatula, a funnel, a mixer and a plunger is provided. (see photo below) The mixed material is introduced to the surgical site with a syringe.



Spatula, funnel, mixer and plunger
for mixing Cementek® LV

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7.2.1. Raw materials

(b) (4)

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7.3.1. Physical form
Injectable paste intended to set *in-vivo*.

7.3.2. Cementek® LV is marketed in 16cc dosage.

(b) (4)

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(b) (4)

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(b) (4)

7.4.6. Animal study

(b) (4)

7.4.7. Cadaveric study

(b) (4)

8. Summary of Design Control Activities

The risk analysis method used to assess the impact of the modifications was a Failure Modes and Effects Analysis (FMEA). Differences between Cementek® LV and Cementek®, and the risk analysis are presented in Exhibit V.

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9. Sterility

(b) (4)

9.5. Packaging

Cementek®LV

The liquid is contained in a 10 ml glass flask.
The solid phase is contained in an aluminum heat sealed pouch.
The both products are packaged in a blister.
This blister is packaged in a tyvek pouch.

Mixing tools

Double packaged in tyvek pouches

9.6. Pyrogens

This material is not tested for the presence of pyrogens.

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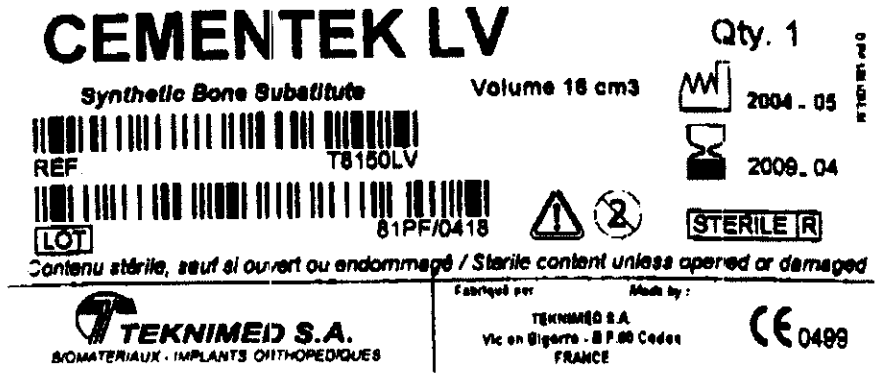
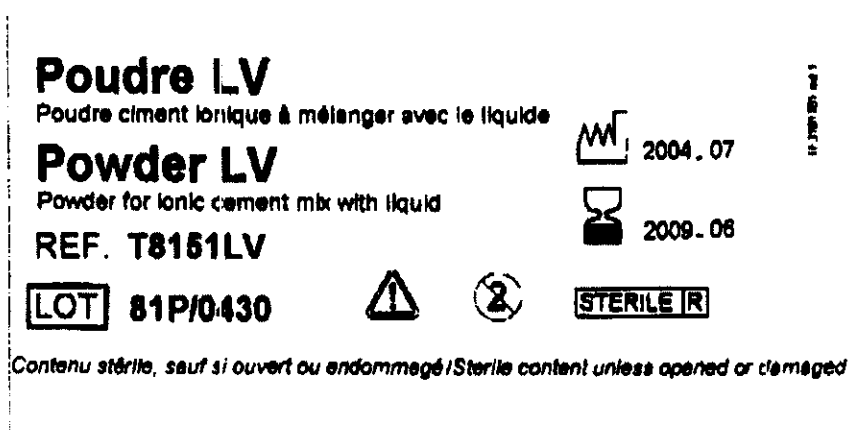
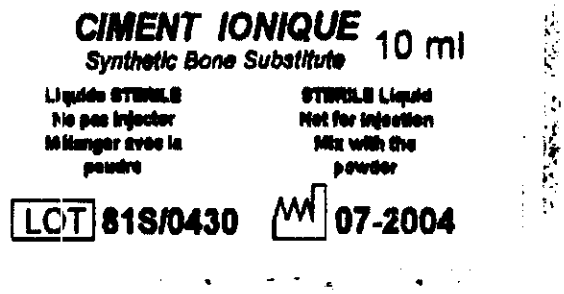
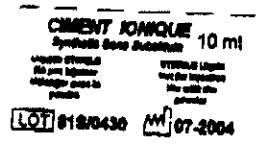
Sample Labels









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CEMENTEK® LV

Synthetic Bone Substitute

The malleable bone substitute

CE0499
Instructions leaflet
Manufactured in France by:
TEKNIMED S.A.
B.P. 60
65502 VIC-EN-BIGORRE Cedex
Tél. 33 (0)5 62 96 88 38
Fax 33 (0)5 62 96 28 72

Caution: U.S. Federal law restricts this device to sale by or on the order of the physician (or properly licensed practitioner)

Before using Teknimed products, the operating surgeon should study thoroughly the safety information specified in these instructions as well as the product-specific information (product description, surgical procedures, brochures etc.). The related documentation is obtainable from the respective national representative. At the same time the operating surgeon must be aware of the residual risks associated with the use of the intended products.

GENERAL INSTRUCTIONS

The implantation of Teknimed products may only be carried out by surgical staff who possess a thorough knowledge of and experience in the area of joint replacement and, in particular, have mastered the product specific surgical techniques relating to Teknimed products. The particular surgical techniques required for Teknimed bone substitute can be learned at Teknimed distributors.
Cementek ® LV bone substitute is in the form of an apatitic paste designed for the osteoconductive replacement of bone.

COMPOSITION

This product of synthesis is controlled during all its manufacture, from raw material to the final product.
Composition:

Powder:	
tetracalcium phosphate	49%
α tricalcium phosphate	38%
Sodium glycerophosphate	12%
Polydimethylsiloxane	1%
Liquid:	
calcium hydroxide	3,4%
phosphoric acid	13,8%
water	82,8%

PREPARATION FOR USE

Mix in a cup the whole of the powder and liquid to achieve a homogeneous mixture. The paste obtained will become less and less malleable, until becoming hard after 10 min.
Full hardening follows in-situ within 48 to 72 hours.
Match the quantity of Cementek® LV to the site of bone defect to obtain the fullest contact with the lost bone.

INSTRUCTIONS FOR USE

1. Open the sachet and pour the powder in the mixer.
2. Pour the liquid on the powder.
3. Mix energetically with the mixer the powder and the liquid during 1 to 2 min.
4. Place mixed paste into syringe.
5. After having dried the cavity, put the paste in the bone defect. It is possible to clean and to dry the cavity with STERILE hydrogen peroxide, unless otherwise exceptions.

PRECAUTIONS FOR USE

The cavity must be carefully irrigated and dried before application of Cementek® LV.
Cementek® LV has stability of shape after 10 minutes. It is recommended to limit the load applied during the first 48 hours, on large bone defects. Cementek® LV is not intended to provide load-bearing structural support during the healing process, therefore, Cementek® LV is contraindicated where the device is intended as load-bearing structural support in the skeletal system.
Manipulations of the paste should be avoided as it may change the mechanical properties.

INDICATIONS

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process

CONTRAINDICATIONS

The same as applying to all bone grafts
- metabolic conditions.
- use in an infected area (osteomyelitis, tuberculosis).
- in an area having no possibility of regeneration or infected bone (risk of sequestration).

POSSIBLE ADVERSE EFFECTS

Possible adverse effects include, but are not limited to:
- Wound complications including hematoma, site drainage, bone fracture, infection, and other complications that are possible with any surgery
- Fracture or extrusion of Cementek® LV with or without generation of particulate debris
- Deformity of the bone at the site
- Incomplete, or lack of, osseous ingrowth into bone void, as is possible with any bone void filler.

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STERILIZATION

Cementek ® LV is sterilized with 25 to 40 kGy (2,5 to 4,0 Mrad) gamma radiation. All sterile implants are to be kept unopened in the original packaging until the time of implantation. Before using the implant, the protective packaging should be checked for damage as this could be detrimental to the sterility. Aseptic procedures should be observed when removing the implant from the protective package.

Cementek® LV is delivered sterile under double wrapping, ready for use in an operating room.

Remarks:

Verify the integrity of the packaging before use, the guarantee of sterilization is 5 years from the date of sterilization.

Use after the peremptory date is not allowed. All re-sterilization of the product is forbidden use only once.

PATIENT INFORMATION

The doctor must draw the patient's attention to the contents of the indications and contraindications paragraph, as well as factors which can impair the results of the operation and to possible complications which can arise as a result of an indication. The patient must also be informed about the measures which the doctor will use to minimize the possible effects of these factors.

PACKAGING AND STORAGE

Individually wrapped in quantities.

Designation	Reference	Volume cm^3
Cementek® LV	T8150LV	$16cm^3$

Store at room temperature

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Equivalence of Cementek® LV with the Predicate Cementek®

Changes are noted in **bold and underlined**

Cementek® LV	*Property*	Cementek®
	Chemical Composition	
(b) (4)		
	Performance Testing - Bench	
(b) (4)		

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Cementek® LV	*Property*	Cementek®
(b) (4)		

(b) (4)

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PROCESS OF CEMENTEK® LV

(b) (4)

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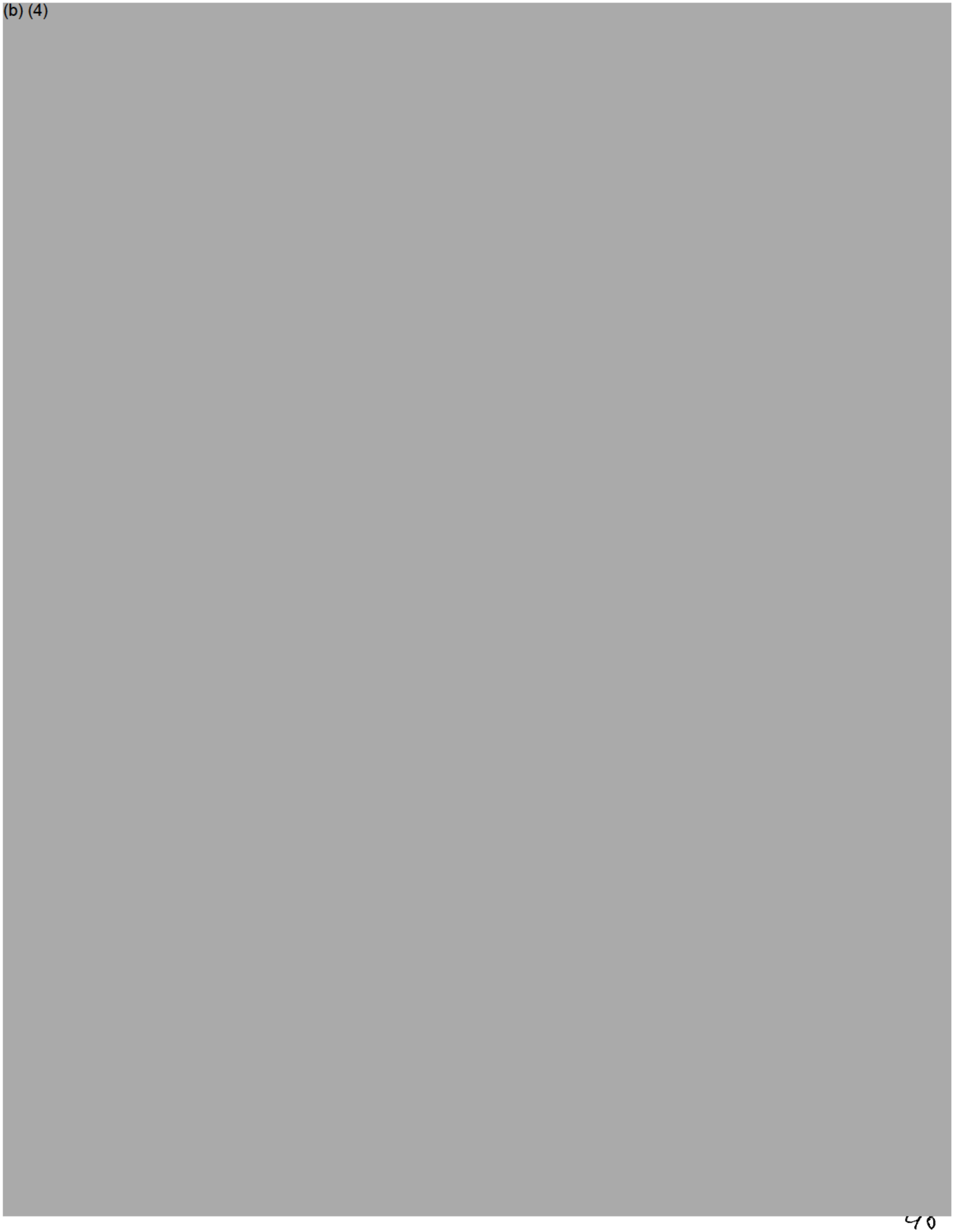

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Key Engineering Materials Vols. 192-195 (2001) pp. 789-792
Proceedings of the 13th Int. Symp. on Ceramics in Medicine, Bologna, Italy, 22-26 Nov. (2000) pp. 789-792

Formulation of an Injectable Phosphocalcium Cement

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Keywords: Bone Ingrowth, Calcium Phosphate Cement, Polyglycol, Silicon

Abstract: In orthopedic surgery, the loss or the reinforcement of osseous substance often requires filling of the defective part. In order to make the surgical operations easier we sought to make an injectable form. This study examined the effect of silicone and polyglycol on the injectability, setting time and mechanical properties of the cement.
The basic solid phase was composed of a mixture of tetracalcium phosphate ($Ca_4(PO_4)_2O$), α-tricalcium phosphate ($Ca_3(PO_4)_2$) and sodium glycerophosphate. The basic liquid phase was made up of lime, orthophosphoric acid and water. Silicone was previously dissolved in cyclohexane and introduced in the solid phase. Polyglycol is a water-soluble compound so it is introduced in the liquid phase.
For the mechanical properties, the strong increase in the percentage of additives decreased the compressive strength. Silicone and polyglycol made it possible to improve viscosity without modifying the basic setting time. The rate of evolution was different with the two different additives. From the data it was possible to optimize the formulation of cements to give predicted properties. Testing the in vivo implantation of the cement has already started. Preliminary results show the perfect osteointegration of the new cements without reactions to the foreign body in spite of the presence of silicone.

Introduction:
Nowadays calcium phosphate cements are being increasingly used in surgery. Their current applications are multiple. However new applications using techniques, such as catheterisation [1,2], are possible but require the use of injectable cement. The osseous catheterisation makes it possible to treat the lesions indirectly decreasing the post operational traumatism and the duration of the periods of convalescence. The aim of this work was to modify the formulation of an already existing calcium phosphate cement Cementek®[3] to modify its viscosity while preserving its main properties. Cementek® is mainly used for osseous fillings: cotyle filling, stabilisation of the implants without PMMA cement and hip arthroplasties. The global chemical reaction is the following :

$$a\ Ca(OH)_2 + b\ Ca_3(PO_4)_2 + c\ Ca_4(PO_4)_2O + d\ H_3PO_4 \longrightarrow Ca_{10}(PO_4)_6(OH)_2$$

with $a + 3b + 4c = 10$ and $d + 2b + 2c = 6$.
The cement results from acido-basic reactions and a dissolution-precipitation process. Its evolution towards apatite, successively passing in the brushite then octocalcium phosphate phases, is now well-known [4,5]. The injection of cement carried out just after the mixing will thus be mainly made up of brushite. The role of the additive will be to improve the rheology of this phase of the cement. The effect of various additives was studied using an experimental plan: silicone and polyglycol seemed to be the best.

Materials and methods:
The basic cement is composed of two phases:
- a liquid phase containing lime, phosphoric acid and water for injectable preparation.
- a solid phase with tetracalcium and tricalcium phosphates and sodium glycerophosphate.

The two additives are not added cement in the same way. Silicone is dissolved beforehand into cyclohexane then introduced into the solid phase. The solvent is completely evaporated

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after 48 hours at ambient temperature. The polyglycol is a water-soluble compound and is therefore introduced in the liquid phase. The cement is presented in a package containing the exact quantities of solid and liquid phases for one dose. The package is sterilized by gamma radiation.

All the different cements were tested for injectability, setting time and mechanical properties. Other tests of standard characterization included infrared spectra (Perkin-Elmer FTIR), X-ray diffraction (CPS 120 INEL), scanning electronic microscopy (S.E.M: LEO 435 VP5). The compression resistance tests were carried out with samples of standard size (diameter and height), using a Hounsfield Serie S device. The setting time, which corresponds to a penetration resistance of 300 g/mm², was assessed with a penetrometer (TAXT2). Injectability was measured using a system developed in the laboratory [6], making it possible to determine an injection pressure. It includes a manometer, a syringe, a catheter and a Tee connector.

The study was undertaken on 10 White New Zealand rabbits (male weighing 4.5 to 5.2 kg), divided into 2 groups of 5 individuals [7,8]. Each group corresponded to a time of given retreat (4 and 12 weeks). Each rabbit remained in an individual cage with free access to water and food. Each received 2 implants: in the femur: cement of reference (A) and injectable cement (B). Both femurs were operated in same operational time by external surgical access of the side condyle under general anaesthesia. A window of 6 mm by 6 was cut from the bone and separated from the spongy subjacent tissue, followed creation of an osseous defect 4.5 mm in diameter and 6 mm length. The osseous cavity was drained and filled manually by cement then closed again by the cortical shutter.

Results and discussion

Two experimental plans were used to optimize the percentage of additive. Thus the ideal percentage for silicone is about 1% (table 1). In the other plan, it is necessary to add 2% polyglycol (table 2). Thereafter, the influence of each additive was studied in larger quantities. Thus the percentage of silicone was varied up to 10% and the percentage of polyglycol up to 5%.

		Levels					Step
Coded variable	X1, X2, X3	-1.682	-1	0	1	1.682	ΔXi
Natural variable	X1= %EL	0	0.406	1	1.594	2	0.594
xi	X2= %HS 15	1	1.406	2	2.594	3	0.594
	X3= %NaGP	8	9.013	10.5	11.986	13	1.486

Table 1: Working range and variation step

		Levels					Step
Coded variable	X1, X2, X3	-1.682	-1	0	1	1.682	ΔXi
Natural variable	X1= %Si V50	0.5	0.906	1.5	2.094	2.5	0.594
xi	X2= %NaGP	7	8.22	10	11.78	13	1.78
	X3= %H_3PO_4	11.5	11.81	12.25	12.69	13	0.44

Table 2: Working range and variation step

Influence of percentage of silicone and polyglycol on the mechanical properties: The influence of silicone on the compressive strength (table 3) is very limited up to 5%. For higher values, the mechanical properties are seriously degraded: in large amounts, the silicone

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decreases the mechanical resistance due to the increase of the porosity of cement. In the cement with 10 % silicone, the porosity increased by 47 % to 55 %. For under 3 % polyglycol, the mechanical properties of the cement (table 4) were not modified because the porosity remained unchanged, equal to 52 %. Over 5 % additive, the compressive strength strongly decreased. So polyglycol and silicone can present an interest for quantities added lower than or equal to 3 %.

% SIL	0	0.5	1	3	5	10
Compressive strength (MPa)	12.1	11.7	11.7	11.7	11.8	8.7
Setting time (min)	26	24	24	26	28	29

Table 3: Compressive strength & setting time for cement with silicone

% PEG	0	1	2	3	5
Compressive strength (MPa)	12.1	14.3	11.6	12.0	7.9
Setting time (min)	26	24	24	25	26

Table 4: Compressive strength & setting time for cement with polyglycol

Fig 1: X-ray diffraction diagrams of cement with 0% to 5% of polyglycol

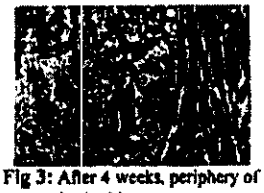

Fig 3: After 4 weeks, periphery of cement colonised by new osseous spans

Fig 4: New osseous spans broadsides by a base of osteoblastic cells (high magnificance of fig 3)

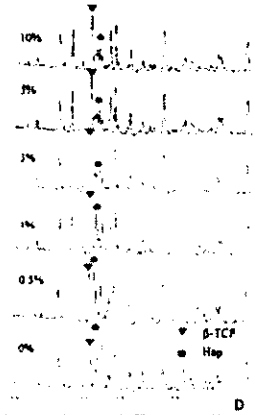

Fig 2 : X-ray diffraction diagrams of cement with 0% to 10 % of silicone

Influence of percentage of silicone and polyglycol on evolution: The figures present the evolution of cements according to the percentages of added additives. The X-ray diffraction diagrams with polyglycol (fig 1) are identical, so the influence on the evolution of cement is limited. However the diagrams (fig 2) with silicone, are different. The rate of evolution of the hydroxyapatite is slower in this case. The major β-TPC phase on the diagrams with 10 % silicone confirms this.

Influence of percentage of silicone and polyglycol on setting time: All the setting times are close to the value of the initial cement (table 3 and 4). The influence of silicone and polyglycol on setting time is limited.

Influence of percentage of silicone and polyglycol on injectability: All cements resulting from the 2 experimental plans were injectable over about thirty centimetres through catheters of 2 or 3 mm internal diameter. These cements have pressures of injection lower than 1 bar and do not surbed in water. The time of injection is related to the percentage of additives but also to the phosphoric acid percentage. All times of injection were lower than 15 minutes.

Animal study:

At 4 weeks : All samples were studied with a scanner; cement appeared homogeneous, with a high density but without any artifacts. The density size of the KING 0,01 cm^2 varied between 1680 and 1790 UH. The contours of the implants were clear and bone/cement contact appeared to be direct. (fig. 3).

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The histology showed that the periphery of the cement was colonized by lately formed osseous spans, bordered by osteoplastic cells, which came to replace the cement gradually. Between the spans, the tissue was richly vascularized. There was no fibrous reaction between the newly formed bone and the mature bone located at the periphery of the cement. No inflammatory reaction was observed. (fig. 4).

At 11 weeks : no significant modification was noted with the scanner compared to the samples at 4 weeks. The cement always appeared dense (the measurements of density carried out in the center of the cement found values close to those of the first time of retreat). The contact with the bone was direct without edging of repair. First osteocondensation areas are present in the seat juxtamedullary cement.

Conclusion

The experimental plans were used to optimize the formulation of two types of injectable cement. In one case, it is necessary to introduce 1 % of silicone in weight into the solid phase (0.7 % in total weight, liquid plus solid phases) and in the other case 2 % of polyglycol in weight in the liquid phase (0.8 % in total weight). The main physical chemical properties (evolution, mechanical properties, setting time) of the cements are preserved. The role of each additive is however slightly different. Silicone improves the rheology of cement, due to its lubricating character, but also slows down the rate of the evolution of the cement. Polyglycol has an effect on the rheology of cement without modifying its rate of the evolution. The first histological observations do not show fibro-inflammatory reactions. A large quantity of new formed bone appeared from the first month and osteointegration continued till the third month.

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Article original

Augmentation expérimentale de la résistance du radius distal ostéoporotique par un ciment phosphocalcique

Experimental increase of osteoporotic distal radius strength using a calcium phosphate cement

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Résumé

Le diagnostic et le traitement de l'ostéoporose sont focalisés sur la lutte contre la déminéralisation. Or, la densité minérale de l'os n'est pas directement corrélée à la résistance mécanique de l'os. Comme tout matériau, la résistance mécanique de l'os dépend de son élasticité et de sa répartition géométrique. En clinique, la résistance mécanique de l'os peut être appréciée de manière non invasive par l'imagerie pQCT (*peripheral quantitative computed tomography*) en calculant un index de résistance. Dans ce travail, nous avons cherché à augmenter le seuil fracturaire du radius distal en améliorant directement la résistance de l'os plutôt que sa densité. Les vingt poignets de dix sujets anatomiques ont été remplis en percutané avec un ciment phosphocalcique. Des images fluoroscopiques et de pQCT ont été réalisées avant radioplastie et 24 heures après cristallisation du ciment en hydroxyapatite. On obtint ainsi la mesure des densités osseuses trabéculaire et totale, mais aussi le calcul d'un indice de résistance osseuse appelé SSI (*stress strain index*). Les résultats ont montré que la densité osseuse trabéculaire avait été augmentée d'un facteur 2,85 alors que la densité totale l'a été de 1,61 et l'indice de résistance osseuse SSI de 1,99. Les images fluoroscopiques ont montré deux fuites minimes de ciment par l'orifice d'entrée du trocart d'injection. Cette étude montre que la radioplastie percutanée avec un ciment phosphocalcique a augmenté la résistance du radius distal, et donc d'autant son seuil fracturaire. Cette méthode pourrait être employée dans l'avenir pour prévenir l'apparition de fractures chez les patients ostéoporotiques.

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Abstract

Diagnosis and treatment of osteoporosis are focused on demineralisation but bone mineral density is not directly correlated with bone strength. As with every material, the mechanical strength of bone depends upon its Young's modulus and its cross-sectional moment of inertia. In the clinical situation, bone strength can be quantified using peripheral quantitative computed tomography imaging (pQCT), a non-invasive imaging method, which allows calculation of a strength index. In this study, we tried to increase the fracture threshold of the distal radius by directly increasing bone strength rather than density. Twenty wrists in 10 cadavers were filled percutaneously with a calcium phosphate cement. Fluoroscopy and pQCT were performed twice, once before cementing and again 24 h after cement crystallisation to hydroxyapatite. We obtained measurements of trabecular and total bone density, and also stress strain index (SSI). Our results showed that trabecular bone density increased by a factor of 2.85, whereas total bone density increased by 1.61 and SSI by 1.99. Fluoroscopy showed two small leaks of cement at the point of injection. This study demonstrated that percutaneous injection of calcium phosphate cement increased distal radius strength, and consequently its fracture threshold. This technique could be employed in the future to prevent the occurrence of fractures in osteoporotic patients.

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Mots clés : Ciment phosphocalcique ; Densité osseuse ; Ostéoporose ; pQCT ; Résistance osseuse

Keywords: pQCT; Bone density; Bone strength; Calcium phosphate cement; Osteoporosis

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1. Introduction

L'ostéoporose est une maladie systémique du squelette caractérisée par une augmentation de la résorption par rapport à la formation osseuse qui se traduit par une diminution de la masse minérale et une détérioration microarchitecturale du tissu osseux. Les conséquences qui en résultent sont une augmentation de la fragilité osseuse et une susceptibilité aux fractures dans certaines zones préférentielles comme le col du fémur, le rachis et le poignet [1]. Du fait de l'augmentation de la durée de vie, notamment dans les régions occidentale et asiatique, l'incidence de l'ostéoporose s'accroît à la manière d'une pandémie. Ce fléau a un coût économique estimé à dix milliards de dollars par an aux États-Unis, et un coût sanitaire telle que l'incidence des fractures du poignet y est estimé à deux cent quarante mille cas par an [2].

La mise en œuvre d'un diagnostic précoce et d'un traitement préventif de l'ostéoporose devrait donc diminuer l'incidence de ces fractures.

Le diagnostic précoce de l'ostéoporose est habituellement envisagé sous l'angle de la déminéralisation du tissu osseux [3]. Il est souvent avancé que la diminution de la densité minérale osseuse est le facteur prédictif le plus important de survenue des fractures [4] et que l'objectif final du traitement médicamenteux de l'ostéoporose postménopausique est d'augmenter la densité minérale de l'os [5]. Cette vision purement minérale de l'ostéoporose est probablement liée au fait que les moyens de diagnostiques non invasifs disponibles en routine (absorptiométrie biphotonique) se limitent à n'observer qu'une densité minérale de surface. Certains auteurs, conscients que la valeur des résultats donnés par les appareils conventionnels n'est pas infaillible, cherchent à la conforter par d'autres critères. Ils utilisent volontiers la présence de fractures vertébrales [6] ou d'autres facteurs de risques [7] comme facteur prédictif de fractures ultérieures sur d'autres sites du squelette ostéoporotique. De plus, la densité osseuse n'est pas directement corrélée aux propriétés mécaniques de l'os [8]. C'est la résistance de l'os qu'il faudrait plutôt prendre en compte, car c'est le seul paramètre permettant de déterminer un seuil fracturaire avec acuité, mais les méthodes densitométriques conventionnelles ne permettent pas de mesurer les propriétés mécaniques de l'os [9].

Avec la nouvelle génération de densitomètres, les pQCT (*peripheral quantitative computed tomography*), de nouveaux algorithmes et techniques ont été développés pour estimer de manière non invasive la résistance osseuse [8]. La résistance de l'os, comme celle de tout matériau, dépend de deux facteurs, élasticité et géométrie [10]. La qualité ou élasticité du matériau osseux est estimée par le module élastique de Young qui ne peut pas être calculé directement par la technologie pQCT, mais qui est fortement lié à la densité corticale volumétrique qui, elle, peut être calculée par pQCT [11]. La distribution spatiale ou géométrie du matériau osseux est mesurée par le moment d'inertie de la section, qui représente la résistance en flexion et en torsion de l'os [12]. Avec la technologie pQCT, il est possible de calculer le moment d'inertie polaire et axial directement à partir des coupes transversales d'images tridimensionnelles [8]. Plusieurs études expérimentales ont déjà mis en pratique ces mesures de résistance osseuse. Une forte corrélation entre le produit de la densité corticale volumétrique et le moment d'inertie de la section d'une part et le seuil fracturaire d'autre part a ainsi été montrée chez le rat [12]. Par ailleurs, le moment d'inertie de la section du radius humain est fortement corrélé avec le seuil fracturaire du col du fémur [13]. En fait, l'apport diagnostique majeur vient de la description d'index biomécaniques qui permettent de calculer précisément et de manière non invasive les propriétés mécaniques de l'os : *stress strain index* ou SSI [8] et *bone stress index* ou BSI [9]. SSI et BSI qui sont obtenus directement par la technologie pQCT devraient permettre d'améliorer le diagnostic précoce de l'ostéoporose. Certaines études physiologiques ont déjà mis en évidence l'intérêt du calcul du SSI par rapport à la mesure de la densité minérale osseuse. Ainsi, alors que la densité osseuse corticale du radius proximal était similaire chez un groupe d'adolescents quel que soit le sexe, le SSI était plus élevé chez les garçons que chez les filles [11], avec comme corollaire une répartition différente de la masse minérale à l'intérieur de l'os. Par ailleurs, le BSI a significativement augmenté au niveau du radius distal après traitement par alendronate [14].

Le traitement préventif de l'ostéoporose se focalise actuellement sur la conservation voire l'augmentation du composant minéral de l'ensemble du squelette [5,15] et n'agit donc que secondairement sur la résistance osseuse. Quelles que soient les médications utilisées : apport vitaminocalcique, hormonothérapie, et récemment bisphosphonates [5,14,16], trois écueils ne peuvent être évités : efficacité partielle, action non ciblée sur les zones squelettiques à risque, complications et contre-indications fréquentes [17]. Quant aux thérapeutiques chirurgicales classiques, si elles agissent sur la résistance mécanique de l'os, ce n'est que de manière indirecte et secondaire, par l'intermédiaire d'un matériel d'ostéosynthèse, une fois les fractures apparues.

Dans le cas des fractures du radius distal, ces dernières décennies ont vu l'apparition puis le développement des biomatériaux. Le méthylmétacrylate a été proposé [18,19] chez des patients très âgés, puis abandonné au profit des substituts osseux phosphocalciques seuls [20], ou associés à d'autres techniques d'ostéosynthèse [21]. Parmi les biomatériaux à base d'hydroxyapatite, le Cémentek LV® (Teknimed™) possède des propriétés physicochimiques intéressantes [22,23] qui l'ont fait choisir pour cette étude. C'est le substitut osseux dont la structure minérale, avec un rapport calcium/phosphore de 1,63, est la plus proche de l'os naturel. L'hydroxyapatite qui le compose, totalement synthétique, est chimiquement non stoechiométrique, ce qui signifie que les échanges ioniques entre la surface des cristaux et le milieu extracellulaire sont importants. Il est microporeux, avec des pores inférieurs au micron, ce qui explique la lenteur de sa biodégradation qui se mesure en années en fonction du volume implanté [24]. Il n'est pas macroporeux, ce qui procure

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une bonne contrainte à la rupture en compression, de l'ordre de 20 MPa, le situant entre l'os trabéculaire et l'os cortical.

Nous pensons qu'il existe une place pour une thérapeutique préventive d'action prolongée des fractures de l'os poreux par une technique chirurgicale percutanée pauci-invasive, ciblée sur les zones squelettiques à risque, avec pour objectif l'amélioration des propriétés mécaniques de l'os. Dans cette optique, le but de notre travail est d'augmenter la résistance osseuse du radius distal par l'injection percutanée d'un ciment phosphocalcique lentement résorbable, et d'en mesurer précisément les effets minéral et mécanique par l'utilisation de la technologie pQCT.

2. Méthodes

2.1. Sujets

Dix sujets anatomiques adultes, cinq hommes et cinq femmes, tous de type caucasien, ont été préparés à l'École de chirurgie de l'assistance publique–hôpitaux de Paris. L'âge moyen au décès était de 83,2 ans (52–100). Les deux poignets de chaque sujet ont été utilisés. Parmi les vingt poignets, cinq présentaient des antécédents lésionnels de fractures consolidées du radius distal (Tableau 1).

2.2. Technique

La procédure anatomique des vingt poignets a été conduite par l'auteur. Un orifice percutané a été réalisé à travers la pointe de la styloïde radiale par un trocart de 11 de 10 cm de long poussé le long de sa bissectrice jusqu'à atteindre la corticale médiale du radius sans la perforer. Une dose de 20 mg de Cémentek LV® a été préparée par gâchage à la main, permettant d'obtenir une pâte malléable homogène introduite dans une seringue d'injection (Cook osteo-force™) sur laquelle a été adapté le trocart. L'injection a ensuite été réalisée sous fluoroscope (GE-OEC 7700™) pour contrôler le déroulement de la radioplastie qui a été arrêté en cas de fuite de produit ou lorsque le remplissage a été jugé satisfaisant par l'opérateur. La résistance de la seringue d'injection à un couple de torsion était de 1000 psi, valeur au-delà de laquelle la seringue se cassait automatiquement.

2.3. Méthode de mesure

Nous avons utilisé un appareillage pQCT (Stratec XCT2000™) pour mesurer différents indices de densité (densité osseuse totale DOT et densité osseuse trabéculaire DOTr) et de résistance (*stress strain index* SSI) osseuses [8]. Les mesures ont été réalisées avant radioplastie puis répétées 24 heures après, lorsque le processus de cristallisation du substitut osseux avait conduit à la formation d'hydroxyapatite stable [22].

2.4. Analyse des données

Les valeurs moyennes et les écarts-types des mesures des trois variables DOT, DOTr et SSI ont été calculés pour les deux situations « avant » et « après » radioplastie. Pour

Tableau 1
Caractéristiques minérales et mécaniques des 20 poignets de dix sujets anatomiques avant et après injection de ciment phosphocalcique dans le radius distal

Sujets			Avant injection				Après injection			
Nombre (n = 20)	Sexe	Âge (ans)	Fracture	DOT (mg/mm³)	DOTr (mg/mm³)	SSI (mm³)	DOT (mg/mm³)	DOTr (mg/mm³)	SSI (mm³)	Fuite
I_R	H	52	–	336,8	198	310,4	519,3	384,54	479,6	–
I_L	H	52	–	442	190,3	474,7	507,5	369,3	490	–
II_R	F	90	+	256,2	154,9	103,2	542,8	616,9	328,8	–
II_L	F	90	–	326,6	155,9	245	510,4	530,1	278,2	–
III_R	H	75	+	180,8	104,8	108	404,3	593,1	344,5	–
III_L	H	75	+	212,4	125,2	76,7	387,4	386,1	313,2	–
IV_R	H	73	–	279,7	219,6	86,4	520,8	634,9	451,9	–
IV_L	H	73	–	271,4	212,8	103,3	317,3	332,8	154,5	–
V_R	F	82	–	167,7	102,6	6,7	311,6	214,7	135,7	–
V_L	F	82	–	194,4	122,7	51,1	292,3	300,6	66,3	–
VI_R	F	92	–	125,9	76,3	0,1	134,8	81,4	2,3	–
VI_L	F	92	–	164,5	90,4	29,7	580,4	812,9	599,2	–
VII_R	F	100	+	175,3	105,5	57,9	520,4	716	438,8	+
VII_L	F	100	+	196,6	125,4	76,9	274,7	260,4	95,5	–
$VIII_R$	H	95	–	294,8	193,3	204	381,1	353,6	364,7	–
$VIII_L$	H	95	–	348,2	245,9	232,1	353,5	371,3	195,3	–
IX_R	F	88	–	228,5	92,8	123,5	518,8	641	354	–
IX_L	F	88	–	287,3	168,3	161,7	397,5	401	194,3	+
X_R	H	85	–	275,6	158,3	242,3	418,6	323,6	77,1	
X_L	H	85	–	270,6	143,9	178,3	245,9	184,3	368,5	–
Moyenne		83,2		251,77	149,345	143,6	406,97	425,427	286,62	

DOT : densité osseuse totale ; DOTr : densité osseuse trabéculaire ; SSI : stress strain index

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chacune de ces trois variables, un test de Shapiro-Wilk a testé la normalité de la répartition de la différence des résultats entre les deux situations à tester. Si la normalité était rejetée, on testait la différence par un test de Wilcoxon apparié, et à défaut on réalisait un test de Student apparié. Une valeur de $p < 0,05$ a été considérée comme significative.

Par ailleurs, nous avons cherché une corrélation entre la préexistence ou non d'une fracture et les valeurs de densité minérale ou de résistance mécanique osseuses. Un test de Student (non apparié) a été réalisé pour tester la différence entre ces deux situations. Une valeur de $p < 0,05$ a été considérée comme significative.

3. Résultats

Les caractéristiques d'âge et de sexe de la série des dix sujets figurent dans le Tableau 1, ainsi que l'ensemble des résultats de densité et de résistance des vingt poignets avant et après radioplastie. L'existence d'une fracture consolidée préexistant au décès a été indiquée. L'analyse statistique de ces résultats figure au Tableau 2.

Les mesures obtenues par pQCT ont mis en évidence une augmentation moyenne significative de la DOTr d'un facteur 2,85 alors que la DOT a été augmentée en moyenne significativement d'un facteur 1,61 et que le SSI s'est accru en moyenne significativement d'un facteur 1,99 (Tableau 2). Avant injection, la DOT était supérieure à la DOTr dans les vingt poignets (Tableau 1). Il est à noter certaines discordances apparentes dans les résultats. La DOTr a toujours augmenté après injection dans les vingt cas. En revanche, dans un cas (X_L), la DOT a discrètement diminué après injection, alors que les autres paramètres (DOTr et SSI) ont augmenté (Tableau 1). Dans ce cas, la coupe de pQCT passait par l'orifice de pénétration du trocart. Par ailleurs, dans deux autres cas différents ($VIII_L$, X_R), le SSI avait diminué après injection, alors que les autres paramètres (DOTr et DOT) avaient augmenté (Tableau 1). La répartition du substitut osseux semblait dans ces deux cas plutôt centrale, alors qu'elle était plutôt périphérique contre la corticale antérieure du radius dans tous les autres cas (Fig. 1).

Les images obtenues par fluoroscopie ont mis en évidence une fracture consolidée antérieure au décès du sujet anatomique dans cinq cas (Tableau 1). L'augmentation de la DOTr après injection n'était pas différente en présence ou non d'une fracture consolidée, alors que la DOT avant injection était significativement supérieure d'un facteur 1,28 et que le SSI avant injection était significativement inférieur d'un facteur 1,93 en présence d'une fracture consolidée (Tableau 2). Les images fluoroscopiques ont aussi permis de mettre en évidence des fuites minimes par l'orifice d'entrée du trocart dans deux cas. Enfin, neuf remplissages ont été jugés importants (Fig. 2) et onze faibles. C'est dans ces derniers cas que la seringue a cassé sous la pression de remplissage.

4. Discussion

L'injection de biomatériaux dans le radius distal n'est pas nouvelle [25] et de nombreux auteurs les ont utilisés soit en association pour renforcer des ostéosynthèses [21,26], soit seuls comme moyen unique de contention des fractures [27,28]. Dans le premier cas, la stabilité du montage était due principalement à l'ostéosynthèse et le biomatériau n'avait

Tableau 2
Résultats de l'analyse statistique des comparaisons de moyennes des caractéristiques minérales et mécaniques des 20 poignets de dix sujets anatomiques avant et après injection de ciment phosphocalcique dans le radius distal

Variable	n	moyenne	p	facteur
		mg/mm³		
DOTr avant injection	10	149,345	0,00000191 ᵃ	2,85
DOTr après injection	10	425,427		
		mg/mm³		
DOT avant injection	10	251,77	0,0000119 ᵃ	1,61
DOT après injection	10	406,97		
		mm³		
SSI avant injection	10	143,6	0,00134 ᵃ	1,99
SSI après injection	10	286,62		
		mg/mm³		
Gain DOTr après injection avec fracture préexistante	5	391,34	0,164ᶜ	1,47
Gain DOTr après injection sans fracture préexistante	15	265,35		
		mg/mm³		
DOT avant injection avec fracture préexistante	5	123,16	0,02446 ᵇ	1,28
DOT avant injection sans fracture préexistante	15	158,07		
		mm³		
SSI avant injection avec fracture préexistante	5	84,556	0,03621 ᵇ	1,93
SSI avant injection sans fracture préexistante	15	163,286		

DOT : densité osseuse totale ; DOTr : densité osseuse trabéculaire ; SSI : *stress strain index*
ᵃ si $p < 0,005$
ᵇ si $p < 0,05$
ᶜ si $p > 0,05$

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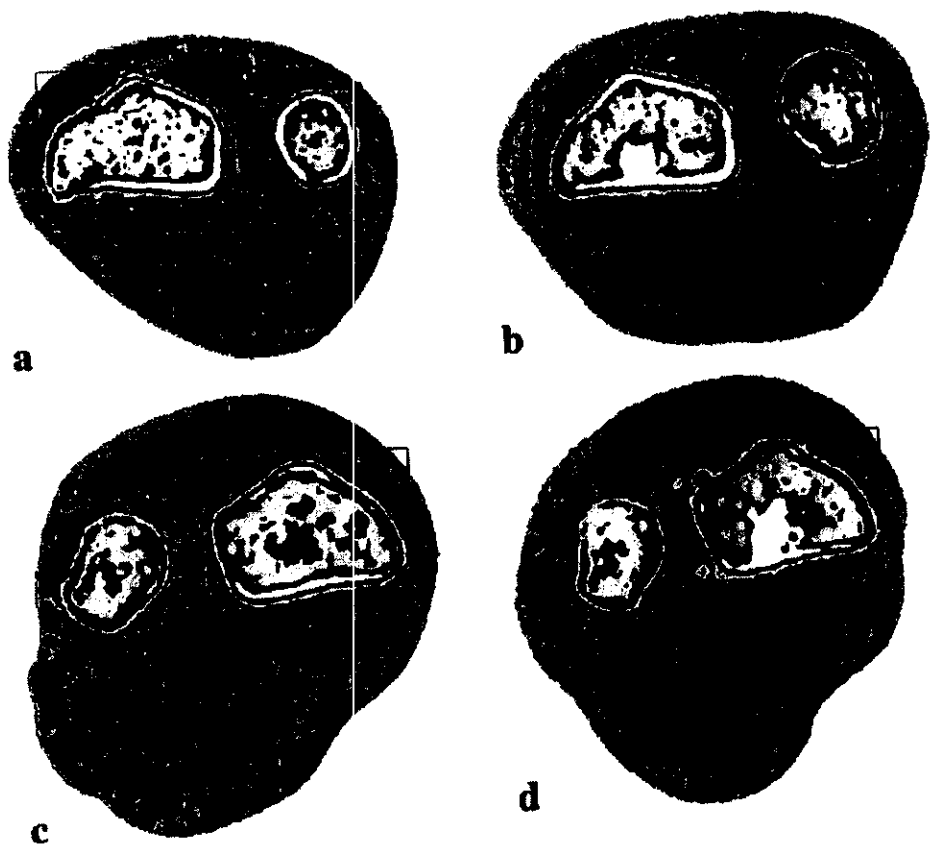

Fig. 1. Images de coupes transversales du poignet obtenues par pQCT.
a. Sujet III_R avant injection
b. Sujet III_R après injection du radius distal par un ciment phosphocalcique On note une répartition plutôt périphérique du ciment phosphocalcique.
c. Sujet X_R avant injection
d. Sujet X_R après injection du radius distal par un ciment phosphocalcique On note une répartition plutôt centrale du ciment phosphocalcique.

qu'un rôle de comblement d'une perte de substance osseuse [29]. Dans le second cas, les propriétés mécaniques des biomatériaux n'ont pas empêché les déplacements secondaires [26]. Dans ce travail, nous avons utilisé les propriétés d'un biomatériau injectable dans le but de mettre au point une méthode d'amélioration des propriétés mécaniques du radius distal ostéoporotique au stade préfracturaire. Il s'agissait du Cémentek LV®, substitut osseux dont la composition en hydroxyapatite a permis d'augmenter le composant minéral de l'épiphyse radiale. Mais la minéralisation n'est pas le facteur fondamental à améliorer dans l'ostéoporose car elle n'est pas directement proportionnelle aux propriétés mécaniques [3]. C'est la résistance de l'os qui doit être augmentée en priorité. Dans notre étude, la radioplastie du radius distal a certes augmenté les densités osseuses totale et trabéculaire, mais c'est surtout la résistance osseuse qui a presque doublé (Tableau 1). Le SSI étant proportionnel au carré de la distance maximum du centre de gravité [11], il apparaît possible d'accroître encore le gain de résistance en améliorant la répartition géométrique du substitut osseux. Pour ce faire, il faudrait diminuer la densité du substitut osseux au centre et l'augmenter à la périphérie de la section du radius distal. Quoiqu'il en soit, si le ciment phosphocalcique utilisé a permis de doubler la résistance osseuse, il faut se rappeler que le composant minéral de l'os, l'hydroxyapatite, n'est responsable que de la résistance à la compression de l'os, alors que c'est le composant organique, le collagène, qui est responsable de sa résistance à la traction [10]. De plus, si la radioplastie a amélioré la résistance de l'os en compression, elle provoque de fait un gap de résistance à la jonction zone injectée – zone non injectée susceptible de produire une fracture plus proximale. La technique actuelle doit donc être améliorée non seulement pour augmenter la résistance osseuse en traction, mais aussi en optimisant la répartition du ciment dans la cavité médullaire.

Lors de cette étude expérimentale nous avons mis au point une technique originale d'injection percutanée et centromédullaire de ciment phosphocalcique dans le radius distal par la pointe de la styloïde radiale. Les techniques d'injection de substituts osseux dans le radius distal décrites précédemment dans la littérature ont toutes été réalisées par voie d'abord dorsale en regard du foyer [21,26–28,30] dans le cadre de fractures récentes du poignet. Mais alors que l'injection de substitut osseux a en général pour objectif de renforcer une ostéosynthèse fragile sur un os porotique, notamment en regard de la comminution postérieure, la manipulation d'un

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Fig. 2. Images fluoroscopiques d'un radius distal avant injection de face (2a) et de profil (2b), et après injection percutanée du radius distal par un ciment phosphocalcique de face (2c) et de profil (2d). Noter une fuite minime de ciment phosphocalcique sur l'image de face (2c).

trocart introduit par le foyer de fracture peut théoriquement aggraver cette comminution postérieure. En effet, le trocart introduit par voie postérieure par le trait de fracture est dirigé nécessairement en avant et en bas du trait de fracture avec comme conséquence l'accès à un espace centromédullaire réduit. Cet espace peut certes être agrandi en retournant le trocart en haut et en avant. Mais dans ces conditions, le trocart s'appuie alors sur la corticale postérieure distale qu'il menace de fragiliser sans pour autant améliorer le remplissage postérieur.

Nous pensons qu'il faut préserver en l'évitant la corticale postérieure du radius distal car c'est une zone particulièrement fragile chez l'ostéoporotique. Nous préconisons le remplissage du radius distal par la pointe de la styloïde radiale car le trocart peut y être mobilisé selon un cône virtuel mobile en fonction de la profondeur d'introduction du trocart jusqu'à la corticale médiale du radius, en amont du foyer de fracture potentielle. Cette voie d'abord possède l'avantage d'être réalisée en percutané, sans risque de lésion de l'appareil tendineux extenseur ni des branches terminales du nerf radial, qui sont à distance. Une fois (cas X_L), le point de pénétration du trocart était trop proximal et passait par la coupe transversale de mesure d'imagerie pQCT, pouvant expliquer l'apparente contradiction des résultats obtenus. Dans ce cas, la DOT a diminué après injection du ciment phosphocalcique, alors que les autres paramètres (DOTr et

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SSI) ont augmenté (Tableau 1). On aurait pu invoquer une erreur de repérage de coupe pour la mesure des paramètres après injection, mais cela n'expliquerait pas plus la discordance. En fait, la coupe de mesure passant dans ce cas par l'orifice d'entrée du trocart qui perfore la corticale, il est logique après injection de perdre en densité osseuse corticale, donc en DOT, mais pas en DOTr ni en SSI puisque la répartition du biomatériau était relativement périphérique.

La discordance dans les résultats des cas $VIII_L$ et X_R ne peut pas être expliquée de la même manière. Le SSI a diminué après injection du ciment phosphocalcique dans ces deux cas, alors que le remplissage semble avoir été correct (Tableau 1). La minéralisation du radius distal s'est améliorée mais sa résistance a diminué. La raison en est probablement la répartition du substitut osseux qui semblait dans ces deux cas plutôt centrale, alors qu'elle était plus périphérique dans tous les dix-huit autres cas (Fig. 1). Le SSI étant proportionnel au carré de la distance du centre de gravité par rapport au point le plus éloigné de la tranche de section osseuse [3], ces deux exemples illustrent la supériorité de la mesure des indices biomécaniques par rapport à celle de la minéralisation osseuse pour connaître la fragilité d'un os porotique. Il est également démontré l'importance de la technique d'injection du biomatériau pour optimiser le résultat en termes de résistance mécanique. Une injection périphérique du substitut osseux, proche des corticales, est mécaniquement meilleure qu'une injection centrale.

Sur le plan diagnostique de l'ostéoporose, la mesure de la densité de surface de l'os par absorptiométrie biphotonique conventionnelle n'est pas toujours pertinente [11]. Ainsi, nous avons trouvé une discordance entre la densité minérale et la résistance du radius distal. Il est apparu en effet que la DOT avant radioplastie était significativement supérieure en cas d'antécédent de fracture consolidée, et on pouvait penser si la densité était proportionnelle à la résistance, que dans ce cas l'os serait plus solide. Or, le SSI avant radioplastie était nettement plus faible en cas de fracture.

5. Conclusion

En conclusion, il apparaît utile de remettre en question l'utilisation des méthodes conventionnelles de diagnostic précoce de l'ostéoporose au profit de mesures non invasives d'indices de résistance osseuse. Par ailleurs, il semble prometteur de poursuivre la recherche de mise au point de méthodes de traitement préventif des fractures de l'os porotique par l'utilisation des substituts osseux phosphocalciques selon les lois de la biomécanique.

Remerciements

Les remerciements pour l'aide technique à la réalisation :

L'analyse statistique a été réalisée par Nicolas Molinari, laboratoire de biostatistiques, IURC, 641, avenue Gaston-Giraud, 34093 Montpellier, France.

Laboratoire d'anatomie de l'école de chirurgie du Fer-à-Moulin, Paris, France.

Société Teknimed, Vic-en-Bigorre, France.

Société Stratec Medizintechnik, Pforzheim, Allemagne.

Société General Electrics, Buc, France.

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Special 510(k)

Declaration of Conformity with Design Controls

To the best of my knowledge, the verification activities, as required by the risk analysis, for the modification were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met.

	Date	Name
<Title> Ph. D		GONCALVES Stéphane
<Company> TEKNIMED	04.10.04	

The manufacturing facility, [Company Name] is in conformance with the design control requirements as specified in 21 CFR 820. 30 and the records are available for review.

	Date	Name
<Title> Ph. D		GONCALVES Stéphane
<Company> TEKNIMED	04.10.04	

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

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Differences Between Cementek® and Cementek® LV
Effect on Risk

Characteristic	Cementek®	Cementek® LV		Risk	Is Risk Increased?
Material(s), including all additives	(b) (4)				
Physical form					

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

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Characteristic	Cementek®	Cementek® LV	Risk	Is Risk Increased?
	(b) (4)			
Mass, volume and density				
Liquid: solid ratio				

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

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Characteristic	Cementek®	Cementek® LV	Risk	Is Risk Increased?
Introduction to surgical site			(b) (4)	

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

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K042911/S1 DUPLICATE

THE ORTHOMEDIX GROUP, INC.

December 6, 2004

Document Mail Center (HFZ401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

Re: Premarket Notification – Cemetek® LV Bone Substitute – K042911
Supplement 1

Dear Sir/Madam,

This supplement is in response to the deficiency letter received November 15, 2004.

1. A revised Design Control Activities Summary table is attached. In it all possible risks associated with each modification have been identified along with the verifications activities, the acceptance criteria and results.

2. A revised Information for Use leaflet is attached. It addresses the concerns regarding adding additional substances, excess material, contraindication for vertebral compression fractures and over-pressurizing the material.

I trust that these deficiencies have beer. adequately addressed.

Respectfully,

JD Webb

J.D. Webb
Authorized Contact Person

1001 Oakwood Blvd • Round Rock, TX 78681 • (512)388-0199 Tele • (512)388-0199 Fax • ortho.medix@sbcglobal.net

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

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Design Control Activities Summary
Cementek® LV

Modification	Risk	Verification Activity	Acceptance Criteria	Results of Verification
(b) (4)	(b) (4)			

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

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CEMENTEK® LV

Synthetic Bone Substitute

The malleable bone substitute

CE0499
Instructions leaflet
Manufactured in France by:
TEKNIMED S.A.
B.P. 60
65502 VIC-EN-BIGORRE Cedex
Tél. 33 (0)5 62 96 88 38
Fax 33 (0)5 62 96 28 72

Caution: U.S. Federal law restricts this device to sale by or on the order of the physician (or properly licensed practitioner)

Before using Teknimed products, the operating surgeon should study thoroughly the safety information specified in these instructions as well as the product-specific information (product description, surgical procedures, brochures etc.). The related documentation is obtainable from the respective national representative. At the same time the operating surgeon must be aware of the residual risks associated with the use of the intended products.

GENERAL INSTRUCTIONS

The implantation of Teknimed products may only be carried out by surgical staff who possess a thorough knowledge of and experience in the area of joint replacement and, in particular, have mastered the product specific surgical techniques relating to Teknimed products. The particular surgical techniques required for Teknimed bone substitute can be learned at Teknimed distributors.
Cementek ® LV bone substitute is in the form of an apatitic paste designed for the osteoconductive replacement of bone.

COMPOSITION

This product of synthesis is controlled during all its manufacture, from raw material to the final product.
Composition:

Powder:	
tetracalcium phosphate	49%
α tricalcium phosphate	38%
Sodium glycerophosphate	12%
Polydimethylsiloxane	1%
Liquid:	
calcium hydroxide	3,4%
phosphoric acid	13,8%
water	82,8%

PREPARATION FOR USE

Mix in a cup the whole of the powder and liquid to achieve a homogeneous mixture. The paste obtained will become less and less malleable, until becoming hard after 10 min.
Full hardening follows in-situ within 48 to 72 hours.
Match the quantity of Cementek® LV to the site of bone defect to obtain the fullest contact with the lost bone.

INSTRUCTIONS FOR USE

1. Open the sachet and pour the powder in the mixer.
2. Pour the liquid on the powder.
3. Mix energetically with the mixer the powder and the liquid during 1 to 2 min.
4. Place mixed paste into syringe.
5. After having dried the cavity, put the paste in the bone defect. It is possible to clean and to dry the cavity with STERILE hydrogen peroxide, unless otherwise exceptions.

PRECAUTIONS FOR USE

The cavity must be carefully irrigated and dried before application of Cementek® LV.
Cementek® LV has stability of shape after 10 minutes. It is recommended to limit the load applied during the first 48 hours, on large bone defects. Cementek® LV is not intended to provide load-bearing structural support during the healing process, therefore, Cementek® LV is contraindicated where the device is intended as load-bearing structural support in the skeletal system.
Cementek LV® is contraindicated for treating vertebral compression fractures.
Manipulations of the paste should be avoided as it may change the mechanical properties.
Do not add any additional substances other than those provided in this package.
Avoid over-pressurizing Cementek LV® as this may lead to extrusion of the device beyond the site of its intended applications and damage the surrounding tissues.
Over pressurizing may also lead to fat embolization or embolization of the material into the bloodstream.

INDICATIONS

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process.

CONTRAINDICATIONS

The same as applying to all bone grafts

- metabolic conditions.
- use in an infected area (osteomyelitis, tuberculosis).
- in an area having no possibility of regeneration or infected bone (risk of sequestration).

POSSIBLE ADVERSE EFFECTS

A successful result is not achieved in every surgical case. Re-operation to remove or replace the implant may be required

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at any time due to medical reasons or device failure. One or more of the following complications may occur and corrective action should be taken:

- Wound complications including hematoma, site drainage, bone fracture, infection, and other complications that are possible with any surgery
- Fracture or extrusion of Cementek® LV with or without generation of particulate debris
- Deformity of the bone at the site
- Incomplete, or lack of, osseous ingrowth into bone void, as is possible with any bone void filler.

STERILIZATION

Cementek ® LV is sterilized with 25 to 40 kGy (2,5 to 4,0 Mrad) gamma radiation. All sterile implants are to be kept unopened in the original packaging until the time of implantation. Before using the implant, the protective packaging should be checked for damage as this could be detrimental to the sterility. Aseptic procedures should be observed when removing the implant from the protective package.

Cementek® LV is delivered sterile under double wrapping, ready for use in an operating room.

Remarks:

Verify the integrity of the packaging before use, the guarantee of sterilization is 5 years from the date of sterilization.

Use after the peremptory date is not allowed. All re-sterilization of the product is forbidden use only once.

PATIENT INFORMATION

The doctor must draw the patient's attention to the contents of the indications and contraindications paragraph, as well as factors which can impair the results of the operation and to possible complications which can arise as a result of an indication. The patient must also be informed about the measures which the doctor will use to minimize the possible effects of these factors.

PACKAGING AND STORAGE

Individually wrapped in quantities.

Designation	Reference	Volume cm^3
Cementek® LV	T8150LV	$16cm^3$

Store at room temperature

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Memorandum

From: Reviewer(s) - Name(s) Nadine Y. Haan

Subject: 510(k) Number K042911/S1

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☐ Requires additional information (other than refuse to accept).
- ☒ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.).

Is this device subject to Section 522 Postmarket Surveillance?	☐ YES	☒ NO
Is this device subject to the Tracking Regulation?	☐ YES	☒ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☒ NO
Is this a prescription device?	☒ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☒ NO
Special 510(k)?	☒ YES	☐ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☒ NO

Truthful and Accurate Statement ☐ Requested ☒ Enclosed

☒ A 510(k) summary OR ☐ A 510(k) statement

☐ The required certification and summary for class III devices NA

☒ The indication for use form

Combination Product Category (Please see algorithm on H drive 510k/Boilers) N

Animal Tissue Source ☐ YES ☒ NO Material of Biological Origin ☐ YES ☒

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90

Predicate Product Code with class: MAV class II

Additional Product Code(s) with panel (optional):

Review: (Branch Chief) KEDB (Branch Code) 12/23/04 (Date)

Final Review: (Division Director) Mark N. Melkerson 12/27/04 (Date)

Revised 4/2/03

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Memorandum

From: Reviewer(s) - Name(s) Nadine Sloan

Subject: 510(k) Number K042911

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☒ Requires additional information (other than refuse to accept). 11/15/04
- ☐ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Section 522 Postmarket Surveillance?	☐ YES	☐ NO
Is this device subject to the Tracking Regulation?	☐ YES	☐ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☐ NO
Is this a prescription device?	☐ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☐ NO
Special 510(k)?	☐ YES	☐ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☐ NO

Truthful and Accurate Statement ☐ Requested ☐ Enclosed

☐ A 510(k) summary OR ☐ A 510(k) statement

☐ The required certification and summary for class III devices

☐ The indication for use form

Combination Product Category (Please see algorithm on H drive 510k/Boilers) N

Animal Tissue Source ☐ YES ☐ NO Material of Biological Origin ☐ YES ☐ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

Review: [signature] (Branch Chief) REOB (Branch Code) 11/15/04 (Date)

Final Review: _____ (Division Director) (Date)

Revised:4/2/03

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

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REVIEW MEMORANDUM

DATE: 11/15/04

FROM: Nadine Y. Sloan
DGRND/REDB

SUBJECT: K042911; Teknimed; Cementek LV Bone Substitute – Special 510(k)

TO: File

Contact: J.D. Webb 512-338-0199

This 510(k) is submitted as a special 510(k) requesting changes to the company's previously cleared bone void filler (Cementek Bone Substitute; K041493).

(b) (4)

Recommended Deficiencies:

(b) (4)

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

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(b) (4)

Nadine Y. Sloan
cementek.Special.AI.rev

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

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Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		
2. Did we grant expedited review?		
3. Have you verified that the Document is labeled Class III for GMP purposes?	NA	
4. If, not, has POS been notified?		
5. Is the product a device?	✓	
6. Is the device exempt from 510(k) by regulation or policy?		✓
7. Is the device subject to review by CDRH?	✓	
8. Are you aware that this device has been the subject of a previous NSE decision?		✓
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		
10. Are you aware of the submitter being the subject of an integrity investigation?		✓
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		

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

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The deficiencies identified above 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/cdrh/modact/leastburdensome.html

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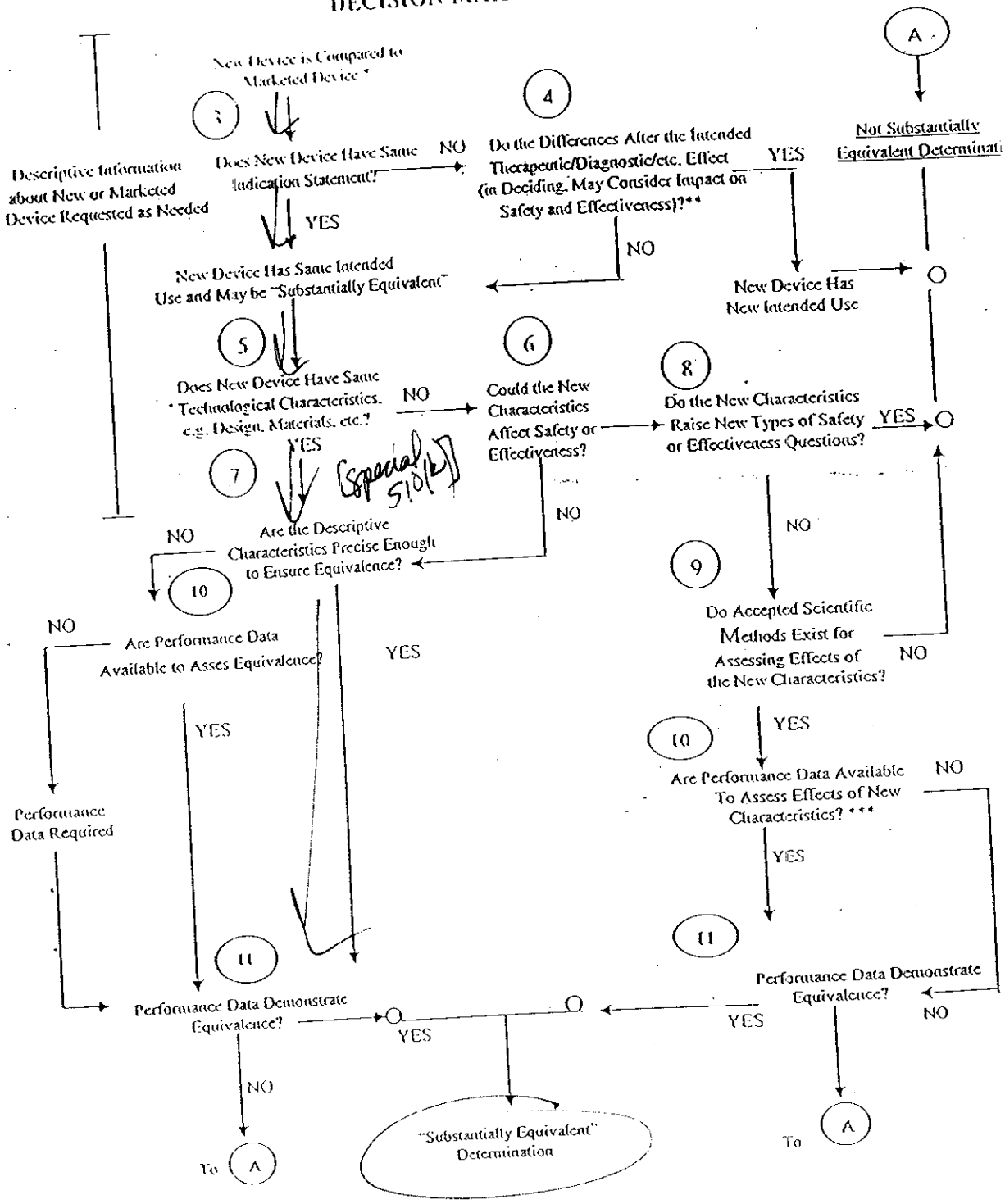
510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



* 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.

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Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?	special ✓	
2. Did we grant expedited review?	✓	
3. Have you verified that the Document is labeled Class III for GMP purposes?	NA	
4. If, not, has POS been notified?		
5. Is the product a device?	✓	✓
6. Is the device exempt from 510(k) by regulation or policy?	✓	
7. Is the device subject to review by CDRH?		✓
8. Are you aware that this device has been the subject of a previous NSE decision?		
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		✓
10. Are you aware of the submitter being the subject of an integrity investigation?		
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		

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SPECIAL 510(k): Device Modification

ODE Review Memorandum (Decision Making Document is Attached)

To: THE FILE

RE: DOCUMENT NUMBER K042911
Cementek LV (Teknimed, S.A.)

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary):

(b) (4)

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

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(b) (4)

[redacted]

(Reviewer's Signature) (Date)

revised:8/1/03

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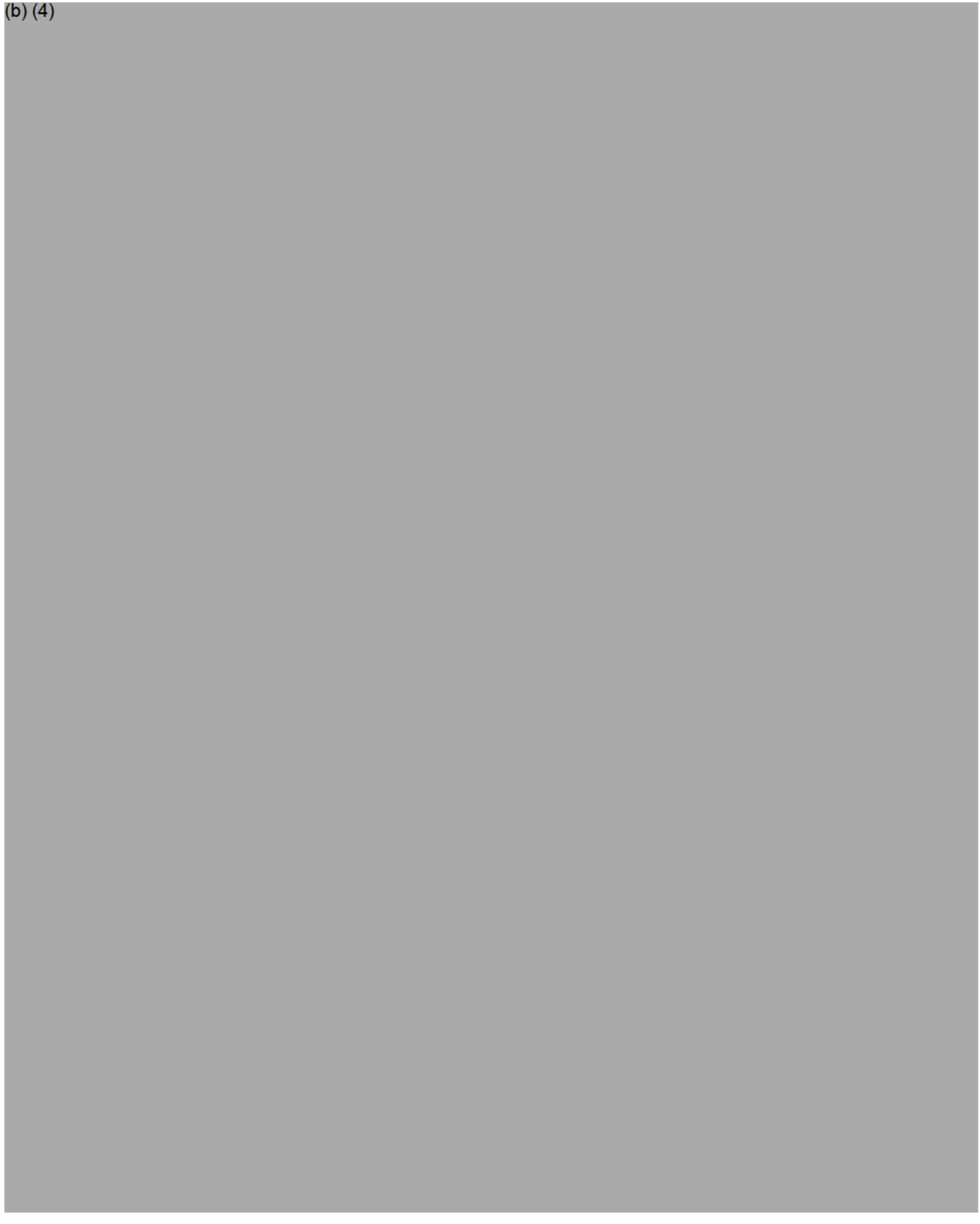
(b) (4)



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(b) (4)

Nadine Y. Sloan
teknimed.Cementek LV.special.rev

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

December 08, 2004

TEKNIMED SA
C/O THE ORTHOMEDIX GROUP, INC.
1001 OAKWOOD BLVD
ROUND ROCK, TX 78681
ATTN: J.D. WEBB

510(k) Number: K042911
Product: CEMENTEK LV

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (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 www.fda.gov/cdrh/ode/a02-01.html.

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 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 or policy questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301) 443-6597 or at their toll-free number (800) 638-2041, or contact me at (301) 594-1190.

Sincerely yours,

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

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

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THE ORTHOMEDIX GROUP, INC.

December 6, 2004

Document Mail Center (HFZ401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

Re: Premarket Notification – Cemetek® LV Bone Substitute – K042911
Supplement 1

Dear Sir/Madam,

This supplement is in response to the deficiency letter received November 15, 2004.

1. A revised Design Control Activities Summary table is attached. In it all possible risks associated with each modification have been identified along with the verifications activities, the acceptance criteria and results.

2. A revised Information for Use leaflet is attached. It addresses the concerns regarding adding additional substances, excess material, contraindication for vertebral compression fractures and over-pressurizing the material.

I trust that these deficiencies have been adequately addressed.

Respectfully,

JD Webb

J.D. Webb
Authorized Contact Person

S11 32

1001 Oakwood Blvd • Round Rock, TX 78681 • (512)388-0199 Tele • (512)388-0199 Fax • ortho.medix@sbcglobal.net

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

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Design Control Activities Summary
Cementek® LV

Modification	Risk	Verification Activity	Acceptance Criteria	Results of Verification
(b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)

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

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CEMENTEK® LV

Synthetic Bone Substitute

The malleable bone substitute

CE0499
Instructions leaflet
Manufactured in France by:
TEKNIMED S.A.
B.P. 60
65502 VIC-EN-BIGORRE Cedex
Tél. 33 (0)5 62 96 88 38
Fax 33 (0)5 62 96 28 72

Caution: U.S. Federal law restricts this device to sale by or on the order of the physician (or properly licensed practitioner)

Before using Teknimed products, the operating surgeon should study thoroughly the safety information specified in these instructions as well as the product-specific information (product description, surgical procedures, brochures etc.). The related documentation is obtainable from the respective national representative. At the same time the operating surgeon must be aware of the residual risks associated with the use of the intended products.

GENERAL INSTRUCTIONS

The implantation of Teknimed products may only be carried out by surgical staff who possess a thorough knowledge of and experience in the area of joint replacement and, in particular, have mastered the product specific surgical techniques relating to Teknimed products. The particular surgical techniques required for Teknimed bone substitute can be learned at Teknimed distributors.
Cementek ® LV bone substitute is in the form of an apatitic paste designed for the osteoconductive replacement of bone.

COMPOSITION

This product of synthesis is controlled during all its manufacture, from raw material to the final product.
Composition:

Powder:	
tetracalcium phosphate	49%
α tricalcium phosphate	38%
Sodium glycerophosphate	12%
Polydimethylsiloxane	1%
Liquid:	
calcium hydroxide	3,4%
phosphoric acid	13,8%
water	82,8%

PREPARATION FOR USE

Mix in a cup the whole of the powder and liquid to achieve a homogeneous mixture. The paste obtained will become less and less malleable, until becoming hard after 10 min.
Full hardening follows in-situ within 48 to 72 hours.
Match the quantity of Cementek® LV to the site of bone defect to obtain the fullest contact with the lost bone.

INSTRUCTIONS FOR USE

1. Open the sachet and pour the powder in the mixer.
2. Pour the liquid on the powder.
3. Mix energetically with the mixer the powder and the liquid during 1 to 2 min.
4. Place mixed paste into syringe.
5. After having dried the cavity, put the paste in the bone defect. It is possible to clean and to dry the cavity with STERILE hydrogen peroxide, unless otherwise exceptions.

PRECAUTIONS FOR USE

The cavity must be carefully irrigated and dried before application of Cementek® LV.
Cementek® LV has stability of shape after 10 minutes. It is recommended to limit the load applied during the first 48 hours, on large bone defects. Cementek® LV is not intended to provide load-bearing structural support during the healing process, therefore, Cementek® LV is contraindicated where the device is intended as load-bearing structural support in the skeletal system.
Cementek LV® is contraindicated for treating vertebral compression fractures.
Manipulations of the paste should be avoided as it may change the mechanical properties.
Do not add any additional substances other than those provided in this package.
Avoid over-pressurizing Cementek LV® as this may lead to extrusion of the device beyond the site of its intended applications and damage the surrounding tissues.
Over pressurizing may also lead to fat embolization or embolization of the material into the bloodstream.

INDICATIONS

Cementek® LV is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. Cementek® LV is indicated for use in the treatment of surgically created osseous defects or osseous defects created from traumatic injury to bone. The putty can be injected into the bony voids or gaps in the skeletal system (i.e. extremities, spine, and pelvis). Following placement in the bony voids or gap, Cementek® LV resorbs and is replaced with bone during the healing process.

CONTRAINDICATIONS

The same as applying to all bone grafts

- metabolic conditions.
- use in an infected area (osteomyelitis, tuberculosis).
- in an area having no possibility of regeneration or infected bone (risk of sequestration).

POSSIBLE ADVERSE EFFECTS

A successful result is not achieved in every surgical case. Re-operation to remove or replace the implant may be required

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at any time due to medical reasons or device failure. One or more of the following complications may occur and corrective action should be taken:

- Wound complications including hematoma, site drainage, bone fracture, infection, and other complications that are possible with any surgery
- Fracture or extrusion of Cementek® LV with or without generation of particulate debris
- Deformity of the bone at the site
- Incomplete, or lack of, osseous ingrowth into bone void, as is possible with any bone void filler.

STERILIZATION

Cementek ® LV is sterilized with 25 to 40 kGy (2,5 to 4,0 Mrad) gamma radiation. All sterile implants are to be kept unopened in the original packaging until the time of implantation. Before using the implant, the protective packaging should be checked for damage as this could be detrimental to the sterility. Aseptic procedures should be observed when removing the implant from the protective package.

Cementek® LV is delivered sterile under double wrapping, ready for use in an operating room.

Remarks:

Verify the integrity of the packaging before use, the guarantee of sterilization is 5 years from the date of sterilization.

Use after the peremptory date is not allowed. All re-sterilization of the product is forbidden use only once.

PATIENT INFORMATION

The doctor must draw the patient's attention to the contents of the indications and contraindications paragraph, as well as factors which can impair the results of the operation and to possible complications which can arise as a result of an indication. The patient must also be informed about the measures which the doctor will use to minimize the possible effects of these factors.

PACKAGING AND STORAGE

Individually wrapped in quantities.

Designation	Reference	Volume cm^3
Cementek® LV	T8150LV	$16cm^3$

Store at room temperature

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Generic "Design Control Activities Summary"

Device Modification	Risk	Verification Activity	Acceptance Criteria	Results of Verification
(b) (4)				

Sample "Design Control Activities Summary"

Modification	Risk	Verification Actvity	Acceptance Criteria	Results of Verification
(b) (4)				

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