Pathology of Alloplastic Interpositional Implants in the Temporomandibular Joint

Weit Yulg, DDS, MS, * and Ralph G. Merritt, DDS, MSedD

Prior to arthroscopy, the surgical management of bone destruction by the temporomandibular joint (TMJ) involved disk repair or disk replacement, even without replacement or with replacement by either alloplastic implants or amniotic tissue. The insertion of biologically acceptable alloplastic material into the TMJ had the objectives of preventing recurrence and preventing adhesion between the mandible and temporal bone. Early alloplastic materials are silastic sheeting and a lacerate of proplast with porous Teflon. Proplast is used permanently, whereas silastic rubber has been used both temporarily and permanently. Initial reports of Silastic and Proplast implants in joints experimentally and clinically indicated that these materials were successful, but malunion of sites since then have demonstrated the probability of failure, whether due to form of reactive synovitis, destructive arthritis, heterotopic bone growth, or fibrous pseudosubstitute reactions. These TMJ implants can cause serious problems, and even open bite deformities.

Despite the discouraging results of implantation in the TMJ, these studies were not associated with the benefit of the implants. The results of this present investigation are: (1) to give additional evidence of the destruction potential of these implants; (2) to show that the damage is not short term but lasts for beyond the removal of the retained implant; (3) to illustrate the destructive effect of these implants on subsequent tissue growth; and (4) to give practitioners insight into the removal of symptomatic implants even though they appear intact at the time of surgery.

LITERATURE REVIEW

Silastic implants have been extensively studied and utilized clinically as implants for a wide range of purposes in various anatomic locations. **1,2,3** Success in 1955 introduced silastic rubber to replace ridge joints. **4** The use of silastic to retain and to relieve pain to improve or control by disease or trauma was not entirely successful. **5,6,7** Silastic rubber has been used by other researchers for replacement of a proplast or replacement of a disk that has not been well healing. **8** The above conclusions are based on the present author's experience.

Despite the discouraging results of implantation in the TMJ, these studies were not associated with the benefit of the implants. The results of this present investigation are: (1) to give additional evidence of the destruction potential of these implants; (2) to show that the damage is not short term but lasts for beyond the removal of the retained implant; (3) to illustrate the destructive effect of these implants on subsequent tissue growth; and (4) to give practitioners insight into the removal of symptomatic implants even though they appear intact at the time of surgery.
implant and bone interface, resulting in implant failure. Previous and recent studies noted an increase in bone loss and implant failure at the PTFE-bone interface, varying results of bone resorption and implant failure at these sites over time after implantation. However, a thorough analysis of bone resorption over time has not been reported.

The failure of PTFE implants is attributed to several factors: wear debris, stress shielding, and bone resorption. The wear debris generated by the implant can lead to a foreign body reaction, which can cause bone resorption and implant failure. Stress shielding is another factor contributing to implant failure, as the implant can reduce bone density and strength, leading to bone resorption and implant failure.

RESULTS
Silicone Implants
Short-duration Implants
Grundy, the silicone implants were inserted and were usually covered by fibrous tissue. Microscopically, fragmentation of silicone with chronic inflammation, foreign body giant cell reaction, and various degrees of fibrosis were observed in the connective tissues, capsulitis, and surrounding tissue.

Long-duration Implants
Grundy, the integrity of the implants ranged from a thinning of the articular surface to severe bone destruction. The surrounding bone showed evidence of fibrous tissue to form fibrous synovial-like tissue. The articular surface of both the implant and the bone showed marked bone loss and severe bone destruction. The implants were retrieved at various time points ranging from 3 to 48 months postoperatively. In some cases, the silicone implants were found within the metaphysis and bone cells in the metaphyseal bone.

Fracture Followed by Dorsal Craft Placement
Grundy, the fracture was followed by a dorsal craft placement. The articular surface of both the implant and the bone showed marked bone loss and severe bone destruction. The implants were retrieved at various time points ranging from 3 to 48 months postoperatively. In some cases, the silicone implants were found within the metaphysis and bone cells in the metaphyseal bone.

Fracture Followed by Prolonged Temporal Multiple Flaps
Grundy, the fracture was followed by a temporary multiple flap. The articular surface of both the implant and the bone showed marked bone loss and severe bone destruction. The implants were retrieved at various time points ranging from 3 to 48 months postoperatively. In some cases, the silicone implants were found within the metaphysis and bone cells in the metaphyseal bone.
Implants Followed by Dead Graft Placement

Gently, dead grafts bleached with tissue and granulation tissue. A proliferation of the osteoid-stalked surface and glial tissue was seen. Osteometabolites had occurred. Microscopically, marked Proplast foreign-body reaction with chronic inflammation was present. LGGRH was marked by necrosis, degeneration, and regeneration. In addition, proliferative or amorphous transformation often occurred.

Implants Followed by Dead Grafts

Gently, significant Bruns and granulation tissue resulted in fibrosis and bone injury. An anti-invasive halides reaction and the glial tissue was often present. Microscopically, a marked Proplast foreign-body reaction with chronic inflammation was noted in connective or regeneration of dead tissue. In one case, an area of osteoid-stalked surfaces was surrounded by Langhans' giant cells (Fig. 8). The foreign-body reaction was marked by foreign-body necrosis and foreign-body granulation tissue. The chronic inflammation caused by the foreign-body reaction was evident. The foreign-body reaction was marked by foreign-body necrosis and foreign-body granulation tissue. The chronic inflammation was evident.

Implants Followed by Partially Temporized Replaced Fibers

Gently, granulation tissue and fibrosis were present. Microscopically, bud of Proplast foreign-body granules and adjacent muscle fiber degeneration were observed.

Discussion

Early studies with alloplastic implants indicated that they were biodegradable, and oxygen showed high thyroid hormone rate in the TM. **Although some degenerative changes in the joint were observed microscopically, it was thought that these were an expected and necessary result of joint surgery. Biochemically, giant-cell reactions were composed of inflammatory cells and foreign-body granulation tissue. The foreign-body reaction was marked by foreign-body necrosis and foreign-body granulation tissue. The chronic inflammation was evident.**

The foreign-body reaction will be necessary because of frequent joint pain, swelling, or acute arthritic changes and has shown a physical breakdown of the alloplastic material associated with a foreign-body granulation tissue. Although the cause of the foreign-body reaction is not clear, foreign-body granulation tissue has been observed microscopically in connective or regeneration of dead tissue. The chronic inflammation caused by the foreign-body reaction was evident. The foreign-body reaction was marked by foreign-body necrosis and foreign-body granulation tissue. The chronic inflammation was evident.

The foreign-body reaction will be necessary because of frequent joint pain, swelling, or acute arthritic changes and has shown a physical breakdown of the alloplastic material. The chronic inflammation caused by the foreign-body reaction was evident. The foreign-body reaction was marked by foreign-body necrosis and foreign-body granulation tissue. The chronic inflammation was evident.
Neat® studied the tissue response to three types of synthetic implant materials—Gore-Tex (polytetrafluoroethylene), Proplast (polypropylene-coated silicone), and porcine polyethylene—in New Zealand white rabbits. The implants were the peripheral space of the platysma, the succenturiate lobe of the liver, and the retroperitoneal region. Gore-Tex seemed to be better than Proplast. Gore-Tex is hypersensitive to the surrounding tissues when it is removed, whereas a prosthesis of these cells was not seen around the Proplast. Moreover, Proplast causes more inflammation than Gore-Tex. It is believed that under the same experimental conditions, the biomechanical or biocompatible characters of implants will greatly influence host tissue reactions.

Excessive functional overloading probably is an important factor that will enhance particulate formation by implants. An implant must be completely encapsulated by connective tissue if it is to be successful, probably because encapsulated implants will be isolated from the rest of the host tissues, restricting the destruction of tissue.

Dendro arboriformes® have described cellular-mediated immunity in the forming graft present in a foreign-body reaction. Immunopathological inflammation with foreign-body giant cells usually originates as an immune reaction to an offending agent that is washable or difficult to remove and destroy. Thymus and adrenals have also been associated with foreign-body reactions. Foreign-body reactions, absorbing tissue or plasma protein to form an antigen complex, immunopathology in...
Silicone implant in the experimental TMJ. The
other bones (thigh, fibula, and seven parietal
plates in mimics in the length order follow-
ing each implant in the TMJ) (Fig. 1). These
water dispersed microscopic and macroscopic observations are very
difficult to remove from the joint and
adjacent tissues and may be part of the reason
for the development of infection and en-
trapment of the implant. Numerous workers have
emphasized the destructive actions of foreign-
body reactions to interimplanted, but no
recently have been made about the influence
of residual interposed material after the
implant has been removed. This study has pro-
duced a new in which residual material has
presented and contributed to the disease of
the joint. Thus the implant must be en-
terprise after the removal of the original alloplastic
material.

We also observed allogenic postimplantational
implants in 1985 and bone and several organs and
allegedly to repair the damage caused by the alloplastic foreign-body reaction. Grafts
had been used in 1985 and showed. Lympho-
1. The same study was used for a short time in
1988 and also used because of binding of foreign-body reaction and achyllosis. Also the
response to interimplanted, but no recently have been made about the influence
of residual interposed material after the
implant has been removed. This study has pro-
duced in which residual material has
presented and contributed to the disease of the joint. Thus the implant must be en-
terprise after the removal of the original alloplastic
material.

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of residual interposed material after the
implant has been removed. This study has pro-
duced in which residual material has
presented and contributed to the disease of the joint. Thus the implant must be en-
terprise after the removal of the original alloplastic
material.
6. Lumsden RH, Dvorak AM, Guaducci D. Foreign body
reaction in different biological configurations of the
stratification of the papillary dermis. The authors also studied the histological changes in the papillary dermis and the dermis proper in the toad skin. They found that the papillary dermis and the dermis proper were composed of a dense, collagenous network. The authors suggested that the dermis proper might be involved in the mechanoreception of the skin, as it is densely innervated by sensory nerve fibers. The study was supported by a grant from the National Institute of Arthritis and Metabolic Diseases.
APPENDIX 3—FDA WARNING LETTERS TO MANUFACTURERS OF JAW IMPLANTS AND FDA SAFETY ALERT TO DENTISTS

JUN 12 1992

WARNING LETTER

CERTIFIED MAIL - RETURN RECEIPT REQUESTED

Dr. Andrew Tose
President
Ceramed Corporation
1290 West Cedar Drive
Lakewood, Colorado 80226

Re: Paramec Ridge Alveolar Ridge Hydroxyapatite Matrix
OsteoGraft® Alveolar Ridge Hydroxyapatite

Dear Dr. Tose:

It has come to our attention that Ceramed Corporation has been promoting and commercially distributing Paramec Ridge and OsteoGraft® Alveolar Ridge Hydroxyapatite implants. These products are devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(o) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act.

Should your Alveolar Ridge Hydroxyapatite implant devices be found to be not substantially equivalent to existing Class I or Class II devices, then they are classified by statute in Class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the devices. Failure to submit a PMA application prior to marketing a Class III device adulterates the devices under Section 501(f)(1)(B) of the Act.

Continuous distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Denver District Office. We request that the action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch (HFD–232), 1990 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latich.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance and Surveillance
Center for Devices and Radiological Health
MAY 29 1982

CERTIFIED MAIL
POSTAGE RECEIPT REQUESTED

Douglas Morgan, D.D.S.
President
TUJ Research Foundation
2043 Foothill, Suite #2
La Crescenta, California 91214

Re: TUJ Implants for Partial or Total Joint Prostheses

Dear Mr. Morgan:

It has come to our attention that you have been promoting and commercially distributing temporomandibular joint (TMJ) implants, intended as partial or total joint prostheses. These products are medical devices as that term is defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(jj) of the Act, and results in the device being misbranded within the meaning of Section 502(f) of the Act. Additionally, your firm has not submitted an establishment registration nor listed any devices with the FDA, as required by 21 CFR Part 807. Failure to do this also misbrands your device within the meaning of Section 502(f).

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, accelerates your device under Section 520(h)(4)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Los Angeles District Office, we request that action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch, (W-201), 1290 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latifi.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and Radiological Health
WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Richard A. Buss
President
Osteomed Corporation
2057 San Fernando Road
Glendale, California 91202

Re: TMA Implants for Partial or Total Joint Prostheses

Dear Mr. Buss:

It has come to our attention that Osteomed Corporation has been promoting and commercially distributing temporary modular joint (TMA) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 505(a) of the Act, and results in the device being misbranded within the meaning of Section 502(a) of the Act.

Should your TMA devices be found to be not substantially equivalent to existing Class I or Class II devices, then they are classified by statute in Class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a Class III device endangers your device under Section 515(i)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the device, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Los Angeles District Office. We request that action be taken to remove the products from the market also to be reported.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and Radiological Health
May 29, 1992

Mr. Roger Ammann
President
Technetica, Inc.
1201 Flynn Road
Camarillo, California 93012

Re: TKU Implants for Partial Joint Prostheses

Dear Mr. Ammann:

It has come to our attention that Technetica, Incorporated has been promoting and commercially distributing temporary modular joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices at that time as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibition act under Section 505(e) of the Act, and results in the device being misbranded within the meaning of Section 502(a) of the Act.

Should your TKU devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 515(f)(1)(C) of the Act.

Continuous distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

Sincerely yours,

Ronald P. Johnson
Director
Office of Compliance and Surveillance
Center for Devices and Radiological Health
CERTIFIED MAIL -
RECEIPT REQUESTED

Ms. Mary P. Pongan
President
Timesh, Inc.
76 Spectrum Road
Las Vegas, Nevada 89101

RE: TMJ Implants for Partial or Total Joint Prostheses

Dear Ms. Pongan:

It has come to our attention that Timesh, Incorporated has been promoting and commercially distributing Temporomandibular Joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (FDCA).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 505(a) of the Act, and results in the device being misbranded within the meaning of Section 502(a) of the Act.

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute as class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 506(f)(1)(B) of the Act.

Continuous distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days,
DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Bldg. 32, Denver Federal Center
Post Office Box 8009
Denver, CO 80201-8009
303-245-3000 (FAX: 776-1000)

January 27, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Robert V. Christensen, President
TMI Implants, Inc.
17351 West Colfax Avenue, Suite 275
Golden, Colorado 80401

WARNING LETTER

Dear Mr. Christensen:

During an inspection of your firm TMI Implants, Inc., located at
17351 West Colfax Avenue, Suite 275, Golden, Colorado, between
December 14, 1991 and January 7, 1992, Investigator Jose R.
Berenguer at my request, reviewed all NDI, premarket submittals,
and premarket submissions (section 510(k) of the Federal Food, Drug,
and Cosmetic Act) for certain implantable devices. Our inspection revealed that the manufacturing process was significantly altered by TMI Implants, Inc. for the purpose of rendering the device sterile. You were informed by
Investigator Berenguer at the time of the inspection that a
premarket submission is required for such a change in the device
manufacturing process.

In your January 10, 1992 letter to Mr. Richard Alman, Director
of Investigations, Denver District, you cite pages 229 of the ISO
Publication, "Sterile Medical Devices: A QM Workshop Manual" as
justification for not having to submit a 510(k) premarket
notification. However, per that document, a manufacturer must have
"... provided adequate assurance through change control procedures,
... process validation, personal training, and development of routine sterilization procedures... that these changes could not affect the safety and effectiveness of the device...". Our inspection of your firm revealed that you did not properly validate this change in order to assure that
radiation sterilization has not in fact affected the safety and
effectiveness of your device.

The continued marketing of medical devices without complying with
the premarket notification requirements of section 510(k) causes the
articles to be adulterated under section 502(a) of the act.
The continued marketing of these devices may result in regulatory
action without further notice. These actions include seizure
and/or injunction.

Several deviations from the Good Manufacturing Practice
Regulations (Title 21, Code of Federal Regulations, part 820)
were noted during this inspection. These deviations include:

1. Inadequate quality assurance and audit procedures (21 CFR
820.20(a) 1(b))
2. Incomplete device master records (21 CFR 820.101)
3. Inadequate finished device inspection procedures (21 CFR
820.160)
4. Failure to perform adequate complaint investigations (21
CFR 820.198(b))

The above identification of violations is not intended to be an
all-inclusive list of deficiencies at your facility. It is your
responsibility to assure adherence with each of the regulations.
Until these violations are corrected, Federal agencies will be
instructed to forward a notification of non-compliance to the
appropriate parties.

You should notify this office in writing, within 15 working days of
receipt of this letter, of the specific steps you have taken
to correct the noted violations, including an explanation of each
corrective action being taken to prevent the recurrence of similar
violations. If corrective action cannot be completed within 15 working
days, state the reason for the delay and the time within which
the correction will be completed.
Your reply should be sent to the Food and Drug Administration, Denver District Office, Attention: Regine A. Barrett, Compliance Officer at the above address.

Sincerely,

[Signature]

District Director

Enclosure: FDA 483

Dear Dr. Christiansen,

This letter is in response to your correspondence dated March 16, 1993 and April 17, 1992, and as a follow-up to our meeting of March 10, 1992. As you will recall during our March 10 meeting, we discussed the need for your firm to have validated the sterilization procedures used on the Peace and Concord Prostheses. We informed you that without such validation data, a premarket notification application (510K) was required to be submitted.

The documentation you submitted indicates that you have utilized a biocidal of 4.2 cpm/g as the sludge for the 200°F, 2 dose setting determinations. Examination of the biocidal data shows that none of the inoculum concentrations exceeded (five times the average of 4.2) this contamination level. The utilization of 4.2 cpm/g and a verification dose of 4.0 cpm/g may not be valid as it appears that your firm has not reliably determined the true biocidal levels present on your devices. In order to support your use of these levels, the results of several tests for which biocidal levels were determined would need to be studied.

The package integrity testing performed by your firm is not adequate in validating the sealing operations. Your firm has not documented sealing equipment operational settings, in order to demonstrate the process is under control and that the settings are traceable. The test method used is not well defined in the FDA 483. Furthermore, you have failed to submit standard operating procedures that reflect the operating settings for the packaging equipment.

The inadequacy of these and other responses noted to the FDA 483 list of observations regarding sterilization and/or OSE issues will be determined at the next inspection of your facility. However, we
have determined that the changes made to your devices are indeed significant ones which may, in fact, require the submission of a premarket notification application.

Aside from the issue of sterilization, it has come to our attention that in a symposium held in B
erkeley, New Jersey, March 1982, MRI Implants I was informed that they had made "great improvements" to their devices. These improvements include a change in the sterilization process and a change in the composition of the device. The changes may have significant effects on the safety of the device.

We are concerned that these changes may have implications for the use of the devices and may require additional testing or changes in the labeling.

Sincerely,

Regina A. Barrett
Compliance Officer

Department of Health & Human Services

[Signature]
These devices are misbranded under Section 502(a) in that you have either failed to file a premarket notification submission as required by Section 510(k) of the Act or these devices have undergone significant changes in labeling or material composition, which warranted the submission of a new premarket notification 510(k).

Furthermore, we note that labeling for your Proplast products contain claims which have not been included in any previous 510(k)s. These claims include references which describe the properties of the Proplast material, such as "chemically inert; its porosity promotes stabilization enabling as much as 80% of implant volume to become tissue without widening the implanting site; and prevents sagging or migration." Labeling also describes Proplast II and HA as being "inert, biocompatible, free from observable systemic or allergic effects, and aids in the migration of cells; and Proplast HA as osteoconductive."

We are not aware of preclinical or clinical evidence to support these claims. Therefore, if you have any information supported by preclinical or clinical evidence from scientifically valid studies that you wish us to consider you must provide the information in new 510(k) submissions filed in accordance with 21 CFR 807.81, as outlined in the described format in 21 CFR 807.90.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory action without further notice. These actions include, but are not limited to, seizure, injunction, civil penalties, and/or automatic detention and refusal to permit entry of products offered for entry into the United States.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. A copy of this letter has been provided to the Dallas District Office. We request that the action being taken to remove these violative products from the market be reported to them.
FDA SAFETY ALERT
SERIOUS PROBLEMS WITH PROPLAST\textsuperscript{\textregistered}-COATED TMJ IMPLANT

To Oral and Maxillofacial Surgeons:
December 28, 1990

This is to urge you to re-examine all of your patients who have received temporomandibular joint (TMJ) interpositional implants which were manufactured or marketed by older Viva Inc., or Oral Surgery Marketing, Inc. (both of Sanrussa, Texas). These implants were distributed between February 1981 and June 1983 and were the subject of Viva’s March 23, 1990 safety alert. The patient for this medical device is currently held by Brahms, Ltd. (Williams, Virgin Islands). Any remaining implant should be returned and a decision should be made on:

- Removal
- Retention

PRODUCT:
Three implants, all of which are made of Proplast\textsuperscript{\textregistered} (Prolene, nylon, or Teflon\textsuperscript{\textregistered}) interpositional implants contain the composite, a drug polymer and a drug delivery system. In a few cases, patients have reported progressive bone degeneration of the mandibular ramus against the bone (2). If bone degeneration continues unabated, it could result in severe pain and movement based dysfunction. The many hundreds of patients with Proplast\textsuperscript{\textregistered} coated TMJ interpositional implants who experienced complications demonstrates progressive bone degeneration is as likely as one in two years (2). In a second study, implant failure and bone degeneration occurred in both symptomatic and asymptomatic patients (3).

RECOMMENDATIONS:
Because asymptomatic patients may experience bone degeneration, FDA recommends that all patients with these implants who have not had a radiograph taken in the past six months undergo orthodontic and orthopedic examinations. The physician ordering the examination should determine if bone implant injury has occurred or if progressive bone degeneration is occurring.

- If bone injury is present or progressive bone degeneration is not occurring, regular radiographic examinations of the implant should be performed every six months for as long as knowledge remains in the jaw.
- If either bone injury or progressive bone degeneration is found, explantation may be appropriate. The patient and the implant should be explanted when active bone grafting or an arthrodectomy (sympathectomy management) are performed.

APPLIQUE 4—DOCS PROV BY MANUFACTURERS ABOUT SAFETY OF THEIR JAW IMPLANTS

June 2, 1992

The Honorable Ted Weiss
Chairman, Subcommittee on Human Resources
and Intergovernmental Relations
U. S. Government Operations Committee
3-792 Rayburn House Office Building
Washington, D.C. 20515-5148

Dear Chairman Weiss:

Thank you for your letter of May 26th offering Dow Corning the opportunity to provide information for your June 4 Subcommittee hearing.

As indicated in the attached product brochure and package insert, Dow Corning developed a temporary implant specifically designed for treating internal derangements in the temporomandibular joint or TMJ. Available since 1985, the Silastic Temporary Mandibular Joint Implant (Silastic) differs from other TMJ implants in the following ways:

- It is a temporary implant which should be removed one to two months after surgery. This modality was specifically selected to minimize the potential problems occasionally noted with long-term TMJ implants.
- This device is a disk used as a temporary spacer rather than a permanent total joint replacement implant. This approach was selected because it was known in the medical community that a permanent device could have complications in load bearing joints. For additional information, please refer to the medical paper from the American Association of Oral and Maxillofacial Surgeons.
- The device is fully fabricated from silicone elastomer rather than other materials like carbon fiber or teflon.

Dow Corning’s TMJ implant became commercially available in 1985 after receiving FDA 510K approval in 1984. This special purpose implant was specifically designed solely for the treatment of TMJ dysfunctions in accordance with the package insert and is our preferred product for those specific situations.

DOW CORNING CORPORATION, MIDLAND, MICHIGAN 48655-9995 TELEPHONE 517-468-4600
EVALUATION

This summary of non-clinical safety studies of silicone elastomer is directed to dimethylsiloxane elastomers, peroxide and platinum-catalyzed, that are relevant to metals used in ortho/periodontal and joint/bone applications. Safety studies of closely related dimethyl elastomers are also included in the non-clinical review.

ACUTE TOXICITY - These silicone elastomers are not toxic with regard to cytotoxicity, U.S.P. Class V, pyrogenicity, skin sensitization, hemolysis or thrombogenicity.

TERATOLOGY/REPRODUCTIVE - Silicone elastomers are without teratogenic activity nor do they alter normal reproduction.

IMMUNOTOXICITY - Silicone elastomers and elastomer extracts are genetically inactive in the Ames bacterial reverse mutation assay.

IMMUNOSUPPRESSION - Platinum system elastomer does not have immunosuppression or immunosuppression activity in validated animal models.

CHRONIC/CHRONIC TOXICITY - Peroxide and platinum system silicone elastomers are associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroelastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersion of macrophages and giant cells is characteristic throughout the entire period although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intraosseous and subcutaneous implantation sites.

The results of elastomer implantation studies ranging in duration from a few days to 2 years demonstrate that reinforced silicone elastomers induce no consistent systemic adverse effects on any organ system.

Elastomer samples measuring 0.32 cm (0.26 cm²) and total surface area up to 2 cm² per rat do not induce implantation site tumors (solid-state tumorigenesis) nor an excess of tumors remote...
from the implantation site.

ACKNOWLEDGMENTS: The fused amorphous silica used as a reinforcing silica maintains a stable distribution within silicone elastomers. In addition, the surface morphology of the elastomer is not influenced by up to 6 month subcutaneous implantation.

SUMMARY OF BIOCOMPATIBILITY TESTING

Silicone sheeting is known to have been used as an intra-articular spacing material to correct TKJ defects. In addition, a fabricated spacer known as the Wilkes design is manufactured by Dow Corning Corporation and distributed by Dow Corning Wright. Sheet catalog numbers 508, 501 and 507 are polydimethylsiloxane elastomers that are peroxide catalyzed using 1,1-dichlorobenzoyl peroxide. The basic materials in this category include MDH-372 (also known as MDX-4511) and MDH-373 (also known as MDX-4518). These peroxide-catalyzed elastomers are compositionally closely related. Safety studies supporting the use of another elastomer sheeting and the Wilkes design TKJ device are both both of the platinum-catalyzed high performance (PJP). Toxicity data supporting these materials is summarized following the peroxide systems.

PEROXIDE-CATALYZED ELASTOMERS

These peroxide-catalyzed elastomers encompass a small number of products by material number including MDH-372 (also known as MDX-4511) and MDH-373 (also known as MDX-4518).

ROUTE TOXICITY:

Route toxicity testing of peroxide elastomers includes cytotoxicity, s.c., i.p., i.v., intrinsic, sensitization and hemolysis/thrombogenicity testing.

1. IN VITRO CYTOXICITY:

Tissue cell culture biocompatibility testing usually employs WI-38 human embryonic lung cells. The tabulated results indicate that peroxide system elastomers are not cytotoxic in culture.
2. U.S.P. CLASS V -
U.S.P. Class V tests have been done for both of the peroxide elastomers. Each elastomer was tested for systemic toxicity in the mouse and intradermal toxicity in the rabbit using U.S.P. protocols. No adverse effects were seen.

3. PYROPHOBICITY -
Both peroxide elastomers pass U.S.P. pyrophenidity testing.

4. SENSITIZATION -
Both peroxide elastomers have been tested for skin sensitization in the guinea pig using topical contact and intradermal PPD injected between the insult and challenge application of silicone gel. There was no evidence of sensitization for any of the silicone gel formulations.

5. HEMOLYSIS AND THERMOHOMOBICITY -
MDX4-4515 has been tested directly and as saline extracts for hemolytic activity using rabbit blood. This elastomer is not hemolytic.

MDX4-4515 has been assayed for thrombogenicity in a clotted cell kinetic blood coagulation test using dog blood. This elastomer was found to be more thrombogenic than a reference elastomer.

* NCE - no Cytotoxic effect.

4 rods I.M. and 3 rods S.Q. per animal.
$ FBR = Foreign Body Reaction.
These subchronic studies indicate that peroxide system silicone elastomers are associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the T.E.P. polyethylene employed as the control material in these studies. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibromastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersal of macrophages and giant cells was present long-term although this is not characteristic in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

CHRONIC TOXICITY:

Three chronic peroxide-catalyzed elastomer studies are available as summarized in the following table.

<table>
<thead>
<tr>
<th>MATERIAL</th>
<th>SPECIES</th>
<th>DOSE</th>
<th>DURATION</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDX4-4515</td>
<td>Dog</td>
<td>5 dogs, Wafees, 3 Year</td>
<td>FBR #</td>
<td>FBR with Particle Generation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDX4-4515</td>
<td>rat</td>
<td>3.6ml on Rod 2 Year</td>
<td>NAE **</td>
<td>NAE **</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDX4-4515</td>
<td>Dog</td>
<td>2 Dogs, 10 Year</td>
<td>FBR with</td>
<td>FBR with</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amputation Stumps</td>
<td>Particle Generation</td>
</tr>
</tbody>
</table>

# FBR = Foreign Body Reaction.
** NAE = No Adverse Effect.

PLATINUM-CATALYZED ELASTOMERS

These dimethyl elastomers are of the tear resistant high performance type and are classified as system D elastomers; i.e., platinum catalyzed. Safety studies are also available for several other elastomer products that contribute to an understanding of the safety of system D elastomers. The product designations are Q7-2423, Q7-2222, Q7-3383, Q7-2412, Q7-2414, Q7-2416, Q7-2712, Q7-2743, Q7-2744 and QDR-0077 and NDR-0081. All of these elastomers are closely related using the same elastomer base, amorphous silicone filler, silicone plasticizer, catalyst, cross-linker and processing technique to achieve the desired physical properties. In addition, some of these products contain additives such as water and barium sulfate to impart radiopacity.

ACUTE TOXICITY:

Acute toxicity testing of system D elastomers includes eye/skin/oral, cytotoxicity, O.D.P., Class V, pyrogenicity, sensitization and hemolysis/chromogenicity testing.

1. IN VITRO CYTOTOXICITY -

Tissue cell culture biocompatibility testing usually employed WI-38 human embryonic lung cells. The tabulated results indicate that system D elastomers are not pyrogenic in culture.

<table>
<thead>
<tr>
<th>MATERIAL</th>
<th>DIRECT CONTACT</th>
<th>MATERIAL EXTRACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q7-2222</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2352</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2412</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2433</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2424</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2566</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2643</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>MATERIAL</td>
<td>DIRECT CONTACT</td>
<td>MATERIAL EXTRACTS</td>
</tr>
<tr>
<td>----------</td>
<td>----------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Q7-2712</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2741</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>Q7-2744</td>
<td>NCE</td>
<td>NCE</td>
</tr>
<tr>
<td>MDF-0077</td>
<td>NCE</td>
<td>-</td>
</tr>
<tr>
<td>MDF-0081</td>
<td>NCE</td>
<td>NCE</td>
</tr>
</tbody>
</table>

* NCE = No Cytotoxic effect.

2. U.S.P. CLASS V -
U.S.P. Class V tests have been done for 11 of the 12 elastomers listed in the preceding table. Each elastomer was tested for systemic toxicity in the mouse and intradermal toxicity in the rabbit using D.S.P. protocols. No adverse effects were seen.

3. PYROGENICITY -
Ten of the 12 system D elastomers have passed U.S.P. pyrogenicity testing.

4. SENSITIZATION -
Ten of the 12 system D elastomers have been tested for skin sensitization in the guinea pig using topical contact and intradermal PCA injected between the incised and challenged applications of silicone gel. There was no evidence of sensitization for any of the silicone gel formulations.

5. HEMOLYSIS AND THROMBOGENICITY -
Q7-2766, Q7-2843 and Q7-2743 have been tested directly and as saline extracts for hemolytic activity using rabbit blood. Neither elastomer was found to induce hemolysis.

Q7-2833, Q7-2843-Q7-2865 and Q7-2843 have been assayed for thrombogenicity in a clotted cell kinetic blood coagulation test using dog blood. These elastomers were found to be less thrombogenic than a reference elastomer.

6. TERATOLOGY/REPRODUCTION -
Elastomer Q7-2473/Q7-251 was tested for teratogenic potential in the rabbit. U.S.P. polyethylene and a viscous solution of carboxymethylcellulose served as the control materials. All materials were implanted subcutaneously in 4 weeks prior to mating. There were no significant treatment-related effects on adult female appearance, behavior, body weight change or necropsy findings for any of the silicone elastomer group. No developmental effects including teratogenecity were observed in the litters in the treatment group implanted with Q7-2473/Q7-251.

Elastomer Q7-2159A/Q7-251 has been the subject of study regarding reproductive effects and teratogenicity in a non-generation rat reproduction study. No adverse effects were reported.

7. GENOTOXICITY -
MDF-0077 has been evaluated for mutagenic activity in the Ames bacterial reverse mutation assay using Salmonella typhimurium. There was no evidence of genetic activity for DMH, ethanol or saline extracts of MDF-0077.

8. IMMUNOLOGY -
1. NONSPECIFIC IMMUNE SYSTEM EFFECTS -
An imbalance in the regulatory network of the immune system may result in immune enhancement; e.g., hyperresponsivity, or suppression; e.g., decreased resistance to infection. Silicone elastomer Q7-2423 was tested in rats for a nonspecific (constitutive) modulation of the immune system using a lalitiria hemolysis assay which primarily assesses immune enhancement. This assay has been validated by the National Toxicology Program. Female rats received 0.1 cm x 0.1 cm rod of elastomer subcutaneously at 1 rod per mouse (surface area = 0.245 cm²). This is equivalent to 683 cm² elastomer surface area normalized to a 50 kg human. The surface area of one Dow Corning teardrop mammary implant is 401 cm².

Immunosuppression was demonstrated using cyclophosphamide and immunosuppression using Cimetidine. Resistance to Listeria infection was evaluated in terms of life-span and
mortality 10, 45 and 90 days after elastomer implantation. No treatment-related effects were observed in the data that were evaluated separately or collapsed over the 3 exposure periods. Therefore, it was concluded that elastomer Q7-2423 under the conditions of the assay has no effect on immune competence.

2. SPECIFIC IMMUNE SYSTEM EFFECTS -

Silicone elastomer Q7-2423 was tested for immunologic sensitization potential in a granuloma model utilizing immunodeficient nude/mu) and their immunologically normal heterozygous littermates (nu/nu). In this model the change in granulomatus reaction at the site of material implantation in mice previously exposed to the same material can be distinguished as being immune regulated or a classic foreign body reaction that is not immune dependent. While a granulomatus reaction in that is a simple foreign body reaction is not distinguishable from an immunologically regulated reaction, the immune reaction can be distinguished from a non-immune reaction by a change in the immune response. The immune response is the only known mechanism by which a non-immune reaction can be amplified. That is, the granulomatus response in a sensitized host is accelerated and/or amplified.

Q7-2423 was implanted subcutaneously as described above in nu/nu and nu/nu mice followed with a challenge implantation of Q7-2423 at the same dose at 28 days. At 2, 4 and 13 weeks thereafter the challenge implantation sites were evaluated with regard to capsule thickness, cellular composition, and changes in the ability to stimulate a granulomatus reaction in combination with 0.1% DMSO. These results are shown in Table 1 and the differences between the two groups of animals was statistically significant at all times. All rats were made for each dose level and exposure period using a series of statistical approaches that is, chi-square, Mantel-Haenszel and Fisher's exact test. No PEMS treatment-related effects were observed for any of the 4 histological parameters measured.

Based on these findings it was concluded that the granulomatus response to Q7-2423 is of the classic foreign body reaction type and not an immunologically active inflammatory response.

These studies of effects on the immune system demonstrate that silicone elastomer Q7-2423 is not inherently an immune adjuvant but does Q7-2423 at a relatively large subcutaneous dose cause immune enhancement or immunosuppression in appropriate animal models.

<table>
<thead>
<tr>
<th>GEL</th>
<th>SPECIES</th>
<th>DOSE</th>
<th>DURATION</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q7-2222</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>3,10,30,90 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>3,10,30,90 Days</td>
</tr>
<tr>
<td>Q7-2352</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>10,30,90 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>10,30,90 Days</td>
</tr>
<tr>
<td>Q7-2412</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>7,28,91 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>7,28,91 Days</td>
</tr>
<tr>
<td>Q7-2423</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>10,29,90 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>10,29,90 Days</td>
</tr>
<tr>
<td>Q7-2546</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>3,10,20,60 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>3,10,20,60 Days</td>
</tr>
<tr>
<td>Q7-2743</td>
<td>Rabbit</td>
<td>4:0.1x1 cm</td>
<td>I.M.</td>
<td>10,30,90 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2:0.1x1 cm</td>
<td>S.O.</td>
<td>10,30,90 Days</td>
</tr>
</tbody>
</table>
the degree of response and generally to a greater extent than observed for micropilared silicone elastomer.

**CHRONIC TOXICITY:**
Several chronic elastomer studies are available as summarized in the following table.

<table>
<thead>
<tr>
<th>MATERIAL</th>
<th>SPECIES</th>
<th>DOSE</th>
<th>DURATION</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q7-2556</td>
<td>Rabbit</td>
<td>25 mg/Animal</td>
<td>1 Year</td>
<td>FBR #</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 mg/Animal</td>
<td>1 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>Q7-2383</td>
<td>Rabbit</td>
<td>25 mg/Animal</td>
<td>1 Year</td>
<td>FBR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 mg/Animal</td>
<td>1 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>MD-0077</td>
<td>Rat</td>
<td>&quot;0.1ml cm Rod 2 Year</td>
<td>NAE++</td>
<td>S.O.</td>
</tr>
<tr>
<td>Q7-4750</td>
<td>Rat</td>
<td>&quot;6:0.1ml cm Rods 2 Year</td>
<td>NAE</td>
<td>S.O.</td>
</tr>
<tr>
<td>Q7-2423</td>
<td>Rat</td>
<td>0.1ml cm Rods 2 Year</td>
<td>In-Process</td>
<td>S.O.</td>
</tr>
<tr>
<td>MD-0002</td>
<td>Dog</td>
<td>6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>MD-0003</td>
<td>Dog</td>
<td>6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>MD-0004</td>
<td>Dog</td>
<td>6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>MD-0005</td>
<td>Dog</td>
<td>6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
</tr>
<tr>
<td>MD-0006</td>
<td>Dog</td>
<td>6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
</tr>
</tbody>
</table>

* A rod I.M. and 2 rods S.O. per animal.

# FBR = Foreign Body Reaction.

These subchronic studies reviewed here indicate that silicone system B elastomers are all associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the U.S.P. polyethylene employed as the control material in these studies. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltration of polymorphonuclear leukocytes) that transitions to fibroplastic activity and fibrosis comprising a collagenous matrix. In addition, the presence of granulomas containing collections of macrophages and giant cells may persist long-term although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

Another subchronic study in rabbits was designed to compare the local tissue response of the smooth silicone elastomer with the micro-pilared silicone elastomer.

Groups of 4 rabbits were implanted subcutaneously with one cm disks of elastomers as well as disks of material from competitive products: i.e., Biomar and the Nene polyurethane coated shell. Groups were sacrificed at 7, 28, 56 and 84 days after implantation for histopathologic evaluation of the local tissue response.

There was a continuum of local foreign body response with the Nene polyurethane eliciting the greatest degree of acute and chronic inflammation, capsule formation, misaligned fibroblast organization, disruption of capsule collagen, and the highest incidence of implant material particulates. The smooth silicone elastomer elicited the least response for all measured
CHEMICAL ELASTOMER IMPLANTATION (Cont)

<table>
<thead>
<tr>
<th>MATERIAL</th>
<th>SPECIES</th>
<th>DOSE</th>
<th>DURATION</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDF-0087</td>
<td>Dog 6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
<td></td>
</tr>
<tr>
<td>NDF-0088</td>
<td>Dog 6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
<td></td>
</tr>
<tr>
<td>NDF-0089</td>
<td>Dog 6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
<td></td>
</tr>
<tr>
<td>NDF-0099</td>
<td>Dog 6: Rectangles</td>
<td>2 Year</td>
<td>FBR</td>
<td></td>
</tr>
<tr>
<td>QT-2383</td>
<td>Rabbit 25 mg Particles</td>
<td>1 Year</td>
<td>Granulomas</td>
<td></td>
</tr>
</tbody>
</table>

Joint Injection

* Number of elastomer rods/animal.
$ FBR = $ Foreign Body Reaction.
** 8 AE = No Adverse Effect.

1. ONE-YEAR RABBIT IMPLANTATION STUDY OF QT-2566 AND QT-2383 -

Groups of 15 rabbits were implanted as outlined in the above table using elastomer spallation particles. There was a sham control group. Groups were sacrificed at 2, 4, 12, 24 and 36 weeks after implantation for histopathologic evaluation of the implanted perivertebral muscle and bone synovium and periapical connective tissue. Inguinal lymph nodes were also examined. The contralateral knee was examined as well. The contralateral knee was examined as described previously. At the synovial and periapical sites the reaction varied from essentially none to a (relatively mild inflammatory reaction) i.e., a granulomatous reaction. There was no evidence of pathologic change in the contralateral knee suggestive of an absence of a systemic immunologic reaction. There was no pathology observed in the inguinal lymph nodes.

2. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF NDF-0077 -

Goups of 50 male and 50 female rats were implanted subcutaneously with NDF-0077 in a study conducted to industrial Bio-Test. The precisely dimensions and number of elastomer samples were prepared as stated in the study report, but was most probably a single rod per animal measuring 0.1 cm. A control group was not included. The occurrence of adverse material-related effects were observed with regard to mortality. No histopathologic or the types and incidence of tumors. This study does not conform to GMP regulations.

3. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF QT-4750 -

QT-4750 is a system D (that is, platinum catalyzed) elastomers that differs from QT-2423 only in that QT-4750 is formulated with hexamethyldisilazane (HMDSO) while QT-2423 is formulated. In final composition these elastomers are virtually identical in that HMDSO does not survive cure conditions.

A 2-year rat implantation study of QT-4750 was recently completed and conformed to GMP regulations throughout.

Groups of 50 rats per sex were implanted with 6 implants measuring 0.1 cm. Control groups of 60 rats per sex received an equal number of U.S.P. polyethylene rods as a material control. Two rods were placed I.M., I.P. and S.Q. There were no treatment-related adverse effects in terms of body weights, food consumption, mortality, clinical chemistry, hematology, organ weights, gross pathology or histopathology, excluding tumor types or incidence. The absence of all associated serum demonstrated that the size and total number of implants falls below the threshold for solid-state tumors to be a detectable event.

4. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF QT-2423 AND QT-2561 -

The in-life phase of a 2-year rat implantation study of QT-2423 and QT-2561 was completed in January, 1991, and conformed to GMP regulations throughout. Groups of 60 rats per sex were implanted subcutaneously with 6 implants measuring 0.1 cm. Control groups of 60 rats per sex received an equal number of U.S.P. polyethylene rods as a material control. At the present stage of data analysis there are no known treatment-related adverse effects in terms of body weights, food consumption, mortality, clinical chemistry, hematology or organ weights. Histopathology is in-process.

5. TWO-YEAR IMPLANT STUDIES WITH SILICATED MATERIALS IN DOGS -

Groups of 3 male and 3 female bitches were implanted S.O. I.P. and I.M. with various combinations of a series of 3 system D elastomers. The elastomer samples were prepared as rectangles varying in size from 5/8 x 1 1/4 inches to 1/2 x 1/4 inches. The control group was not included. The occurrence of adverse material-related effects were observed with regard to mortality. No histopathologic or the types and incidence of tumors. This study does not conform to GMP regulations.
changes in organ weights were noted. The reaction at the implantation sites was a typical foreign body reaction with fibrous encapsulation and chronic inflammation. Chronic inflammation was generally more evident at 6 months than at 2 years.

On the basis of these subchronic and chronic studies of closely related dinethyl system 2 elastomers it is concluded that:

1. Silicone elastomers are all associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the U.S.P. polyethylene employed as the control material in these studies. That is, an acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroplastic activity and fibrous connective tissue encapsulation of the foreign body. Sharp dispersal of elastomer material is not seen as observed in the control material though this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

2. The results of elastomer implantation studies ranging in duration from a few days to 1 year demonstrate that reinforced silicone elastomers induce no detectable systemic adverse effects on any organ system.

3. Elastomer samples measuring 0.1 x 1 cm (0.243 cm³) and total surface area up to 3 cm² per rat do not induce implantation site tumors (solid-state tumorigenesis) nor an excess of tumors remote from the implantation site.

ASSIMILATION/DISTRIBUTION/METABOLISM/EXCRETION (ADME)

Silicone elastomers are not subject to possible systemic distribution as might occur with some silicone gel. However, there has been speculation that the fused amorphous silica used as a reinforcing filler in silicone elastomers is succintly available for distribution. This hypothesis has been evaluated by examining elastomer samples implanted subcutaneously in mice for up to 6 months for evidence of filler redistribution within the elastomer and for signs of change in the surface topography of the elastomer.

There was no degradation or surface modification of the elastomer observed using transmission electron microscopy at 1, 3 or 6 months after subcutaneous implantation. No alterations in silica distribution within the body of the elastomer or at the surface were observed at any time point.
Diana Bucknerman
June 2, 1992

Dear Ms. Bucknerman:

Techmed has designed and produced a limited number of patient-specific custom THA prostheses over the past 15 years for patients with severe degenerative THA joint disease.

These implants employ biomaterials that have a long clinical history of successful use in orthopedics for reconstructing joints such as the hip and knee.

As in orthopedics, the goal of THA joint replacement is to reduce pain while improving mobility, function, and alignment of the affected limb or part.

It has been Techmed’s perception that the clinical problems associated with previous alloplastic (artificial) THA prostheses were a result of poor implant material selection as well as use outside of the proper clinical indications. In future years, a more conservative treatment may have been preferable.

These implants have been available to a limited clientele group so as to facilitate getting with follow-up at predetermined intervals for complete clinical evaluation. Patients who have had these implants have been monitored with thorough follow-up care and inclusionary those patients that will evolve into this program. Fortunately, data has and is currently being collected for the vast majority of these patients enabling us to evolve this product in a controlled and scientific way.

Sincerely,

Dave Sacco
Regulatory Affairs Manager

Enclosures
There are a total of 95 patients in the data set of this closely monitored limited clinical study. The average age of the patients is 42.02 (22 - 64) years. There are 5 males and 90 females with a total of 159 joints treated. These patients have averaged 10.3 (0 - 30) years of TMJ problems and undergone a mean of 5.32 (0 - 22) prior unsuccessful surgeries.

There has been 24 months of pre and post operative data that has been collected to date using a standardized data collection format. Subjective data: pain, function of the mandible, and diet, are collected using a visual analogue scale (VAS) to objectify this data. Objective measures of mandibular range of motion read as interincisal opening and left and right lateral excursion were directly measured from the patient pre and post operatively.

Preliminary analysis of this data reveals a statistically significant decrease in pain (p<0.004), increase in function (p<0.002), and increase in diet (p<0.007). There was improvement in mandibular range of motion recorded as well.

Tissue removed from the articular surfaces of a prosthesis functioning in a patient 2 years post CAD/CAM placement during the revision of scar tissue from around the joint revealed no evidence of a tissue reaction, or the fragments of metal or polyethylene when this tissue was examined histologically.

There have been 9 (5.6%) joints in which complications have been reported. One post operative wound infection requiring removal and replacement of the prosthesis; 3 early prostheses that did not fit properly and had to be remade; 3 prostheses in which the ramal component screws loosened necessitating replacement; and 2 early cases of condylar dislocation from the prosthetic fossa. This problem has been resolved with a design change which added a lip to the anterior of the fossa. There have been no cases of breakage, material or mechanical failure.
Component wear of total knee prostheses using Ti-6Al-4V, titanium nitride coated Ti-6Al-4V, and cobalt-chromium-molybdenum femoral components

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A knee simulator was used to study the wear of carbon fiber reinforced UHMWPE (Poly Tec) (Poly Tec is a registered trademark of Synthes, USA) knee and patellar components with respect to the cobalt-chromium-molybdenum femoral component fretting wear. The prostheses were tested in a multiaxial knee simulator containing simulated knee flexion and extension, internal and external rotation, and anteroposterior translation. The test conditions were a load of 400 N, 100 cycles per second, and a sliding of 12.5 mm per cycle. The samples were tested using a confocal scanning laser microscope to observe the surface morphology. The results showed that the wear of the femoral component was significantly less than the wear of the patellar component. The wear of the femoral component was less than 0.01 mm, while the wear of the patellar component was greater than 0.1 mm. The wear of the carbon fiber reinforced UHMWPE was significantly less than the wear of the metal-on-metal bearings. The wear of the metal-on-metal bearings was greater than 0.5 mm, while the wear of the carbon fiber reinforced UHMWPE was less than 0.2 mm. The wear of the metal-on-metal bearings was also affected by the presence of debris, which was observed on the wear tracks. The wear of the carbon fiber reinforced UHMWPE was not affected by the presence of debris.

INTRODUCTION

There has been considerable interest in the use of titanium, and especially the Ti-6Al-4V alloy, for orthopedic implants because of its biocompatibility, fatigue strength, and corrosion resistance. However, there has been some question of the wear resistance of Ti-6Al-4V against ultrahigh molecular weight polyethylene (UHMWPE). A number of studies have been conducted which evaluate the wear of Ti-6Al-4V and UHMWPE combinations under clean conditions and with acrylic contaminants. Within these studies a number of wear-resistant surface treatments have been evaluated, including nitriding, ion implantation, and special passivation techniques. These...
Studies have been run under sliding conditions, either pin-on-flat or hip simulator studies. Studies of the wear of Ti-6Al-4V against UHMWPE have had conflicting results. Rostoker and Galante found that Ti-6Al-4V specimens exhibited scratches, black deposits, and abnormal wear in two studies of Ti-6Al-4V wearing against UHMWPE using a disk-on-flat geometry. These reports disagree with the results of Miller et al., who found the wear characteristics of Ti-6Al-4V similar to those of stainless steel. In further tests, McKellop et al. found that Ti-6Al-4V is especially susceptible to abrasive wear from acrylic cement particles.

Several studies have been conducted using hip simulator models. McKellop et al. studied the wear of hip prostheses with cobalt-chromium-molybdenum (Co-Cr-Mo) alloy and Ti-6Al-4V alloy femoral components using bovine serum lubrication. The tests were conducted under both clean and contaminant conditions and with several approximately 2 mm-diameter fragments of PMMA cement placed in the acetabular cup. Under the clean conditions the Co-Cr-Mo ball had only light scratching and the titanium ball exhibited slightly more scratching. With acryllic chips present, the Co-Cr-Mo ball had only light surface scratches, whereas the Ti-6Al-4V ball was severely scored and smeared with black residue. Greer, however, found that acrylic cement contaminants caused no change in the appearance of the Ti-6Al-4V femoral heads on the acetabulum.

Rostoker and Galante found that special polishing techniques eliminated the abnormal wear of Ti-6Al-4V that they had previously reported. McKellop et al. reported that nitrified Ti-6Al-4V was virtually undamaged in a pin-on-flat study that included acrylic contamination. Lucas et al. concluded that the corrosion characteristics of Ti-29R coated and nitrogen ion implanted Ti-6Al-4V were very similar to those exhibited by the Ti-6Al-4V control samples, however there have been no studies published on the wear of these coatings against UHMWPE.

There have been two studies of UHMWPE wear of tibial components using knee simulators. Shostrom et al. used a computer controlled simulator which controls the flexion angle and the joint load. Bovine serum lubrication at 37°C was used and wear was determined as weight loss from the tibia component using the method developed by McKellop et al. Wear debris, which consisted of fibrous and, in some cases, granular or globular debris was recovered by Rostoker et al. The prosthesis with higher wear rates had regular periodic cracking. No correlation was found with molecular weight, but rather, it was concluded that the wear rate of UHMWPE tibial components was dominated by high contact stress.

Rostoker et al. examined the UHMWPE wear mechanisms of eight failed tibial and 16 failed knee prostheses and found large cracks in regions where there was no evidence of abrasion. Craters were found forming at the edges of UHMWPE fusion defects. Hoed et al. in a retrieval study, found pits in 90% of recovered tibial components. Much of the pitting appeared to be caused by acrylic debris; however, pits were also found in areas where...
connected to a cable which passes over a fixture holding the test machine and attaches to the "tibia." The simulator is operated at 800 cycles per minute, with loading cycles continuing until failure or after the seventh damage mode was observed, then the data was recorded as existing for that prosthesis. Those components which clearly illustrated one or more of the damage categories were then examined using a scanning electron microscope (SEM). The number of components examined with the SEM was limited because the required carbon coating contaminates subsequent observations.

Test protocol

A total of 10 tests were run during this testing program. The femoral component consisted of two parts, a metal plate and a carbon fiber reinforced unidirectional polyethylene (Poly Two) tibia articulating end. The patellar buttons were also made of Poly Two. The tibia used for the femoral articulating surfaces:

(1) Ti-6Al-4V titanium alloy (regular production—sterilized)
(2) Titanium nitride coated Ti-6Al-4V (experiments)
(3) Co-Cr-Mo alloy (regular production—sterilized)

Three prostheses of each type of femoral component were tested.

One supplemental test was run using an uncoated component and conventional UHMWPE patella and tibial components. This test was run only to make visual comparisons with the femoral components being tested. The polyethylene tibial component was not tested.

Each test consisted of 100,000 cycles (500 K) of simulated 82 kg (180 lb) subject. Each test was divided into 20 blocks of 5000 cycles each. Each block was divided into 204 level walking steps, 8 steps ascending stairs, and 964 descent stairs. This approximates the ratio of level walking to stair climbing for normal activity. The third TiN coated prosthesis (7) underwent an extended period for a total of 500,000 cycles of only 82 kg (180 lb) subject. The TiN coated prosthesis maintained a level walking step, 8 steps ascending stairs, and 964 descent stairs. This approximates the ratio of level walking to stair climbing for normal activity. The third TiN coated prosthesis (7) underwent an extended period for a total of 500,000 cycles of only 82 kg (180 lb) subject.

Visual, microscopic, and SEM evaluations

After testing, all femoral and tibial components were visually and manually inspected for surface damage. Following visual inspection, the tibial and femoral surfaces were then inspected under a stereo-microscope at x20 and x200. Tibial component surface damage was categorized as small, medium, or large.

Stability test

The 100,000 cycle tests were interrupted at steps 1, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100,000 cycles to conduct stability tests. The stability test procedure was also conducted at the end of the 500,000 cycle test. In each stability test, the machine is moved through five activities which study flexion performance as well as adduction/abduction (ad-ab) and tibial rotation stability. The vertical force applied at the "hip" for each assessment is 32 kg (70 lb). This is the peak load used to avoid possible excessive loading during the stability test. The flexion performance routine holds the ad-ab force and tibial torque at zero while the knee is flexed from 10° to 40° and the quadriceps and hamstrings are both non-linear. The adduction/abduction stability routine holds the knee at 30° of flexion and tibial torque at zero, while the adduction/abduction displacement is measured. The tibial rotation stability routine holds the knee at 30° of flexion and ad-ab force at zero while the tibial torque is varied and tibial rotation is measured. The ad-ab and tibial rotation tests are repeated at 40° of flexion. Changes in stability are associated with the change in surface conformity. This is a function of the wear and deformation which occurs with cyclic loading.

Wear measurement

Wear of the tibial components was characterized by the weight of material removed. The tibial and patellar components were pre-toasted in bovine

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*Performed by Dr. T. M. Wright, Hospital for Special Surgery.*
serum at room temperature for a minimum of 14 days prior to the start of the test in order to minimize fluid absorption during the presoaking, the parts were cleaned, vacuum desiccated and a Mettler H2O analytical balance. Following testing, the parts were cleaned, desiccated and weighed. The amount of wear was determined between the weights before and after the test. Fluid absorbed to the test was corrected for by using a soak control similar to that used by Trehan et al.8

RESULTS

Visual, microscopic, and SEM examination

On an unused Poly Two component, the surface has a glassy and a layer of carbon fibers can clearly be seen in the surface in Figure 2. After testing in the simulator, the most common modes found were scratching and carbon-fiber-associated damage. This fiber-associated damage was defined as any surface damage associated exclusively with the presence of carbon fibers. Two different types of carbon-fiber-associated damage: fiber removal, UHMWPE matrix, fiber breakage, and UHMWPE removal. Figure 3 shows the three modes of carbon-fiber-associated

Figure 2. SEM micrograph of unworn carbon fiber matrix.

Figure 3. SEM micrographs of carbon fiber associated damage: (a) UHMWPE removal from carbon fiber, (b) trough from surface carbon fiber removal, (c) carbon fiber breakage.
areas of carbon-fiber-associated damage also exhibited evidence of wear. Scratches, such as those seen in Figures 309, were found in the anteroposterior direction and were possibly due to the presence of the broken fibers or removed particles of UHMWPE. The tibial component from the 500,000 cycle test showed associated wear and a rough surface layer of carbon fiber (Figure 4a). The UHMWPE removal and carbon fiber associated damage on the plateau can be seen along scratches on the surface. The scratches shown were on the anteroposterior tibial plateau wear zone, while the carbon fiber associated damage was also present on the surface fibers and relatively little UHMWPE damage occurred. The scratches are still present.

Surface deformation was noted in eight of the nine tests, with one test exhibiting excessive surface deformation. The deformation on the tibial components took place in the areas of each tibial plateau. Also, the areas of wear were seen to the medial edge of the medial plateau in five of the tests. This implies that, during a step, some portion of the polyethylene is not being supported by the tibial plateau. This tibial component constrains the femoral component and is extended. However, the gap between the femur and the tibial plateau allows for medial/lateral translation for the joint to be partially unsupported when the knee is flexed.

Figure 3. SEM micrograph of 500,000 cycle test tibial component: (a) anterior edge of wear area. (b) center of wear area.
Pitting was found on seven tibial components. In several others, however, there was no apparent abrasion or gaging from which the pit began. Figure 5 shows a portion of a pit, as shown in Figure 6, which is the posterior edge of the lateral condylar wear component. The carbon fiber is visible at the bottom of the pit. On the surface of the pit, there were no signs of carbon fiber ends, as if the pit were pulled away from the carbon fiber that now posed a surface. Figure 6 shows a pit that is in the process of being pulled away from the surface. The material being pulled away by what appears to be a crack.

Two tibial components exhibited minor abrasion. These were what appeared to be wide shallow scratches, but under magnification, there were areas where tufts of polyethylene extended away from the material. Table 1 lists the incidence of the tibial surface damage and carbon fiber associated damage were found together on some components. Surface deformation was found on eight and mechanism on six of the tibial components. Minor abrasion and two of the tibial components. Embedded PMMA and burs were observed on any of the tibial components. From the information in Table 1, no correlation could be found between the incidence and the femoral material.

The results from the contact area measurements are shown in Table 1. During the course of the study, contact area measurements were made and after each test for a total of 28 different tests and flexion angle combinations. Of these combinations, 16 had an increase in contact area and a decrease in contact area. The variation in these results was caused by multiple stable assembly positions for a given flexion angle due to the polyethylene unconstrained tibial component and multi-radius geometry of the femoral component.

<table>
<thead>
<tr>
<th>TABLE 1 Observed Damage Modes</th>
<th>Damage Mode</th>
<th>Polyethylene Material and Lot Number</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total 4V 1 2 3</td>
<td>Total 4V 1 2 3</td>
</tr>
<tr>
<td>Surface deformation</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
</tr>
<tr>
<td>Pitting</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
</tr>
<tr>
<td>Embedded PMMA</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
</tr>
<tr>
<td>Grooving</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
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<tr>
<td>Fracturing</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
</tr>
<tr>
<td>Debulking</td>
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</tr>
<tr>
<td>Carbon fiber damage</td>
<td>x x x x x x</td>
<td>x x x x x x</td>
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</tbody>
</table>
TABLE II
Tibial Surface Contact Areas at Beginning and End of 100,000 Cycle Tests using Co-Cr-Mo and Ti-6Al-4V femoral components. The titanium nitride coated Ti-6Al-4V femoral components, like cobalt-chromium-molybdenum, showed no scratches and retained a polished surface. The uncoated Ti-6Al-4V femoral components, however, exhibited a large number of shallow scratches oriented in the anteroposterior direction. These shallow surface scratches were not observed in the supplementary test of an uncoated Ti-6Al-4V femoral component run with a conventional UHMWPE tibial component which indicated the scratches were not necessarily due to the presence of carbon fiber.

<table>
<thead>
<tr>
<th>Test</th>
<th>10 deg</th>
<th>20 deg</th>
<th>40 deg</th>
<th>60 deg</th>
<th>80 deg</th>
<th>10 deg</th>
<th>20 deg</th>
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</thead>
<tbody>
<tr>
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<td>89</td>
<td>66</td>
<td>60</td>
<td>80</td>
<td>84</td>
<td>54</td>
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<tr>
<td>Co-Cr-Mo</td>
<td>83</td>
<td>67</td>
<td>63</td>
<td>80</td>
<td>70</td>
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<tr>
<td>Co-Cr-Mo</td>
<td>93</td>
<td>61</td>
<td>63</td>
<td>80</td>
<td>81</td>
<td>67</td>
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<tr>
<td>Ti-6Al-4V 1</td>
<td>93</td>
<td>69</td>
<td>122</td>
<td>101</td>
<td>86</td>
<td>71</td>
<td></td>
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<tr>
<td>Ti-6Al-4V 2</td>
<td>84</td>
<td>64</td>
<td>79</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ti-6Al-4V 3</td>
<td>82</td>
<td>66</td>
<td>59</td>
<td>79</td>
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<td>43</td>
<td>69</td>
<td>86</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Titanium nitride 2</td>
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<td>94</td>
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<td></td>
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<td>96</td>
<td>62</td>
<td>63</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Observations of femoral components

Figure 7 is a composite photograph of the lateral condyle of Ti-6Al-4V, and TiN-coated Ti-6Al-4V components after 100,000 cycles. The component photographs have marks oriented in the medial and lateral directions. These marks and lines form a "Y" shape. These marks and lines were formed by the camera opening and photographer's eyepiece, respec-
table scratching or other damage was found on the component surfaces. The results of the knee stability tests showed that the range of rotational excursion gradually decreased from a range of 7°-10° to a range of 2°-6° as the tibial component came to a "stop" on the tibial component. The rotational stiffness (torque per degree rotation) showed a significant increase during the 100,000 step test as illustrated in Figure 8. In the extended test the rotation increased and the stiffness decreased between 100,000 steps and 1000 steps indicating that the "stop" was gradually reduced by wear and/or deformation. No significant correlation was found between the component material and the wear and/or deformation observed with the stability tests.

Figure 7. Lateral condyles of (a) Co-Cr-Mo, (b) Ti-6Al-4V, and TiN-coated Ti-6Al-4V femoral components.

Figure 8. Rotational stiffness over the 100,000 cycle test as measured with the rotational stability test.