K980518

SECTION 1: REGULATORY INFORMATION
SUMMARY OF SAFETY AND EFFECTIVENESS

MAR - 6 1998

Osteomark® is a urinary assay that provides a quantitative measure of the excretion of cross-linked N-telopeptides of type I collagen (NTx) as an indicator of human bone resorption. Elevated levels of urinary NTx indicate elevated human bone resorption. Measurement of NTx is intended for use in:

A. Predicting skeletal response (bone mineral density) to hormonal antiresorptive therapy in postmenopausal women.

B. Therapeutic monitoring of:

1. antiresorptive therapies in postmenopausal women
2. antiresorptive therapies in individuals diagnosed with osteoporosis
3. antiresorptive therapies in individuals diagnosed with Paget's disease of bone
4. estrogen-suppressing therapies

C. Assessing the relative risk for loss of spinal bone mass after one year if not treated with hormonal antiresorptive therapy

Osteomark is a competitive enzyme-linked immunosorbent assay (ELISA) which utilizes a horseradish peroxidase labeled monoclonal antibody directed against the cross-linked N-telopeptides (NTx) present in urine specimens. An Osteomark® kit is comprised of the following reagents:

Antigen Coated 96-Well Plate
Calibrators:
- 1 nM BCE
- 30 nM BCE
- 100 nM BCE
- 300 nM BCE
- 1000 nM BCE
- 3000 nM BCE

Antibody Conjugate Concentrate
Antibody Conjugate Diluent
Level I and Level II Urine Controls

30X Wash Concentrate
Buffered Substrate
Chromogen Reagent
Stopping Reagent

The solid phase utilizes microwells onto which NTx has been adsorbed. NTx in the specimen or Calibrator competes with the solid phase NTx for antibody binding sites. The resulting amount of Antibody Conjugate bound to the solid phase is indirectly proportional to the amount of NTx in the specimen or Calibrator. The quantity of NTx in the specimen is determined from a standard calibration curve using reagents supplied in the kit. Assay values are standardized to an equivalent amount of bone collagen, and are expressed in nanomole bone collagen equivalents per liter (nM BCE). BCE reflects the amount of immunoreactive NTx, as measured by Osteomark, liberated from human bone collagen following digestion with bacterial collagenase, as measured by hydroxyproline by high performance liquid chromatography (HPLC).

Expected Values

Urine Collection:

A multi-center, cross-sectional study was conducted in order to compare the results obtained with either a second morning void (SMV) spot urine collection or a 24 hour urine collection in Osteomark®. The population tested represented 186 normal premenopausal women without diseases, disorders, or currently taking medications which may affect bone metabolism or creatinine excretion.

The SMV mean was 35 (+/- 15) nanomoles BCE/millimole creatinine. The 24 hour urine specimens, normalized for urinary creatinine, had a mean of 26 (+/- 13) nanomoles BCE/millimole creatinine.

Reference Range Data:

In the same study discussed above, the expected values for premenopausal women with the Osteomark® assay were determined. An additional multi-center, cross-sectional

study involving subjects without diseases, disorders, or currently taking medications known to affect bone metabolism or creatinine excretion was conducted to establish the expected values for postmenopausal women. The comparative results are presented in Table 1 below.

Table 1 - Expected Osteomark® Values (nM BCE/millimole creatinine)

Study Group	Mean*	Std Dev	Range*	N
Premenopausal Women (mean 36 years, range 25-49)	35	15	9-84	186
Postmenopausal Women (< 3 years postmenopause, mean 51 years, range 40-58)	65	33	23-188	91

Limitations of the Procedure

Lower Limit of Detection

The lower limit of detection of the Osteomark® assay is 20 nM BCE. This value represents a concentration which is greater than the value which can be distinguished from zero, and was calculated by subtracting 3 standard deviations optical density (A450-A630) from established variability of the 1nM BCE Calibrator. Assay precision below this value is insufficient for accurate results.

Interfering Substances

Common urine components and contaminants, as well as microbiological contaminants, that are known to interfere with many laboratory urine analyses were evaluated for an interfering effect with Osteomark®. The evaluations were performed by adding normal and excessive quantities of each potential inhibitor to normal urine specimens and analyzing for an effect on the final results. Results show that specimens obviously

contaminated with whole blood or that have extensive hemolysis may show interference in the assay. These specimens should be avoided, and the specimen recollected.

Performance Characteristics

Reproducibility

Assay reproducibility was evaluated for intra-assay and inter-assay variability of normal urine specimens across the range of the calibration curve.

Intra-assay variability, or within assay precision, was assessed using eight urine specimens tested in replicates of 10 by each of four operators. Results demonstrate an average intra-assay variability estimate of 8% CV, with a range of 5-19% CV along the calibration curve.

Inter-assay variability, or assay to assay precision, was assessed using three urine specimens tested in duplicate by one operator over 20 separate assay runs. Results demonstrate an average interassay variability estimate of 4% CV, with a range of 3-5% CV along the calibration curve.

Antigen Recovery

Antigen recovery was evaluated by adding known amounts of NTx to each of three normal urine specimens. Recovery represented the observed assay value of the "spiked" specimens, calculated as a percent of the expected urine value (baseline urine value plus added antigen value). Results demonstrate an average antigen recovery of 105%, over an assay value range of 200-2500 nM BCE.

Dilutional Linearity

Dilutional linearity was evaluated by performing serial dilutions of four urine specimens with high nM BCE values into a urine specimen with a low nM BCE value. Results

demonstrated correlation coefficients of r=0.999 to r=1.000 across an assay range of 44-2940 nM BCE.

Osteomark® (PN 9006) Quick Reference

1. Thoroughly read the Assay Procedure before you begin.
2. Bring kit components and specimens to room temperature.
3. Dilute the Antibody Conjugate Concentrate into the Antibody Conjugate Diluent, using a 1:101 ratio.
4. Pipette 25 µL samples of each Calibrator, Control, and specimen into duplicate microwells.
5. Pipette 200 µL of diluted conjugate solution into each microwell. Gently swirl to mix. Incubate the plate at room temperature for 90± 5 minutes.
6. Wash microwells five (5) times with the diluted wash solution, and blot dry.
7. Dilute the Chromogen Reagent into the Buffered Substrate using a 1:101 ratio. Mix gently by inversion only. Do not mix with a stir bar or vortex. Use the Chromogen/Buffered Substrate within 30 minutes of preparation. Add 200 µL of Chromogen/Buffered Substrate to each microwell, and incubate at room temperature for 15 ± 1 minutes.
8. Add 100 µL of Stopping Reagent to each microwell. Then gently swirl the plate for 5 -10 seconds.
9. After five minutes, read the absorbance of each microwell at 450 nm - 630 nm. Calculate the results using the standard curve.

SECTION 1: REGULATORY INFORMATION
TRUTHFUL AND ACCURACY STATEMENT

The information contained herein is to the best of my knowledge truthful and accurate.

Nancy J.S. Mallinak
Vice President, Regulatory and Clinical Affairs
Ostex International, Inc.

January 14, 1998
Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR - 6 1998

Nancy J.S. Mallinak
Vice President, Regulatory and Clinical Affairs
Ostex International, Inc.
2203 Airport Way South, Suite 400
Seattle, Washington 98134

Re: K980518
Osteomark®
Regulatory Class: I
Product Code: JMM
Dated: January 14, 1998
Received: January 16, 1998

Dear Ms. Mallinak:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to 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). 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 (Premarket Approval), 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 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): _____

Device Name: Osteomark

Indications For Use:

Osteomark is a urinary assay that provides a quantitative measure of the excretion of cross-linked N-telopeptides of type I collagen (NTx) as an indicator of human bone resorption. Elevated levels of urinary NTx indicate elevated human bone resorption. MEasurement of NTx is intended for use in:

A. Predicting skeletal response (bone mineral density) to hormonal anti-resorptive therapy in postmenopausal women

B. Therapeutic monitoring of:
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   3. antiresorptive therapies in individuals diagnosed with Paget's disease of bone
   4. estrogen-suppressing therapies

C. Identifying the probability for a decrease in bone mineral density after one year in postmenopausal women receiving calcium supplement relative to those treated with hormonal antiresorptive therapy.

The measurement range of Osteomark is 20 to 3000 nM Bone Collagen Equivalents (BCE).

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K980518

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

(Optional Format 1-2-96)