K984530

METRIKA

Metrika, Inc.
510 Oakmead Parkway
Sunnyvale, CA 94086
main 408 524 2255
fax 408 524 2252

# 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is K984530.

**807.92 (a)(1): Name:** Metrika, Inc.
**Address:** 510 Oakmead Parkway
Sunnyvale, CA 94086
**Phone:** (408) 524-2255
**FAX:** (408) 524-2252
**Contact:** Stephen J. Hardt

**807.92 (a)(2): Device name- trade name and common name, and classification**

Trade name: DRx® NTx or Osteomark® NTx Point of Care (POC)

Common Name: urinary assay for quantitative ratio of cross-linked N-telopeptides of type I collagen (NTx) divided by creatinine (nM Bone Collagen Equivalents [BCE]/mM creatinine)

Classification: ratio numerator: 21 CFR 862.1400, Hydroxyproline Test System
ratio denominator: 21 CFR. 862.1225, Creatinine Test System

**807.92 (a)(3): Identification of the legally marketed predicate device**

Osteomark® NTx POC is substantially equivalent to two commercially available predicate devices; Osteomark® NTx EIA (Ostex International Inc., Seattle, WA), is a stand-alone NTx kit, and is the predicate device for the numerator of the ratio. Creatinine Plus (Boehringer-Mannheim Corporation [Roche], Indianapolis, IN) is a creatinine assay, and is the predicate device for the denominator value. Osteomark® NTx POC reports a single corrected result (NTx/creatinine), while Osteomark NTx EIA requires a separate creatinine determination (no method specified) in order to report the final corrected result.

**807.92 (a)(4): Device Description**

The Osteomark® NTx POC device is a single-use, disposable four-channel reflectance photometer integrated with dry reagent chemistry strips and contained within a sealed plastic case. Each unit consists of:

- an optics subassembly that also supports the reagent strips
- electronics, batteries, photodetectors, and light emitting diodes (LEDs).
- plastic parts
- two reagent strips
- a desiccant
- a liquid crystal display (LCD)

The reagent strips capillary transport with various chemical reactions. The first strip is an immunoassay for measuring the NTx, and the second strip is a general chemistry assay for measuring the creatinine. In both strips, a blue color is measured in discrete test zones. The test zones are the areas where the specific reaction occurs and concentrations are measured.

The NTx reaction proceeds as follows: anti-NTx antibody, conjugated to blue microparticles, migrate across the strip upon the addition of urine sample. The amount of blue microparticles captured on the test zones is proportional to the amount of NTx in the sample.

The creatinine reaction proceeds as follows: the addition of the urine sample solubilizes enzymes immobilized in the strip test zones. A cascade of enzymatic reactions mediates the production of hydrogen peroxide from the oxidation of creatinine. In the presence of horseradish peroxidase and a color indicator, a blue color is generated from the hydrogen peroxide with an intensity proportional to the concentration of creatinine in the sample.

The LEDs and silicon photodetectors compare the reflectances of the color intensities before and after the sample addition. Based on the calibration parameters stored in memory, the numerical concentrations of NTx and creatinine are calculated. Assay results are expressed in nM Bone Collagen Equivalents (BCE) divided by mM creatinine (nM BCE/mM creatinine).

**807.92 (a)(5): Intended use**

Osteomark® NTx POC is a urinary assay for the quantitative measure of the excretion of cross-linked N-telopeptides of type I collagen (NTx) normalized to urinary creatinine (nM Bone Collagen Equivalents/mM creatinine). The test is used to monitor bone resorption changes following initiation of antiresorptive therapy (e.g., hormone replacement therapy).

## 807.92 (a)(6): Technological Similarities and Differences to the Predicate

**Similarities Between Osteomark® NTx POC and Osteomark NTx EIA / Creatinine Plus**

| CHARACTERISTIC | Osteomark® POC K984530 | Osteomark® EIA K961562 | CREATININE Plus K854766 |
|---|---|---|---|
| **Intended Use** | DRx® NTx is a urinary assay for the quantitative measure of the excretion of cross-linked N-telopeptides of type I collagen (NTx) normalized to urinary creatinine (nM Bone Collagen Equivalents/mM creatinine). The test is used to monitor bone resorption changes following initiation of antiresorptive therapy (e.g., HRT). | 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. Measurement of NTx is intended for use in the therapeutic monitoring of antiresorptive therapies, and in predicting skeletal response to hormonal antiresorptive therapy. | Creatinine Plus is for the quantitative determination of creatinine in serum. plasma, or urine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, **and as a calculation basis for measuring other urine analytes.** |
| **Analyte(s)** | NTx (nM BCE)/ creatinine (mM) | NTx (nM BCE) | Creatinine conversion of mg/dL to mM: mg/dL ÷ 11.3 = mM |
| **Testing Matrix (Specimen Type)** | urine: second morning void | urine: 24-hour or second morning void | serum. plasma, or urine |
| **Testing Environment** | professional use | professional use | professional use |
| **Risk to Patient** | not a sole discriminate; NTx results are interpreted along with medical histories and other biochemical markers. | not a sole discriminate; NTx results are interpreted along with medical histories and other biochemical markers. | N/A |

**Differences Between DRx® NTx and Osteomark / Creatinine Plus**

| CHARACTERISTIC | Osteomark® POC | Osteomark® EIA | CREATININE Plus |
|---|---|---|---|
| **Methodology/Testing Platforms** | Osteomark® NTx POC is a four channel, "ratioing" reflectance photometer, (plus an internal reference channel), with integral dry chemistry strips (competitive inhibition immunoassay for NTx; enzymatic assay for creatinine). | Osteomark EIA is a standard competitive inhibition enzyme-linked immunosorbent assay (ELISA). | The Creatinine Plus assay consists of enzymatic reactions where creatinine is converted to red benzoquinone imine dye (red) in the presence of creatininase, creatinase, sarcosine oxidase, and peroxidase. |
| **Reportable Ranges** | ratio: 2-350 nM BCE/mM creatinine | NTx: 20-3000 nM BCE | Creatinine (urine, pre-dil. 1/10): 0.03 – 35.4 mM |

The differences in the two testing platforms do not raise new issues of safety and effectiveness.

**807.92 (b)(1): Brief Description of Nonclinical Data**

Studies were conducted that evaluated both NTx and creatinine for analytical sensitivity, analytical specificity, and linearity. The sensitivity of the NTx portion of the device was shown to be 30 nM BCE, while the sensitivity of the creatinine was shown to be 2 mM.

Osteomark® NTx POC results were not affected (differences less than 15%) by the addition of most potential interferents such as biological compounds, therapeutic agents, or microorganisms found routinely in urine. Interference was noted with very high levels of calcium (> 4mg/mL), chloride (> 300 mM), and *C. albicans* and *E. coli* (both $1.5 \times 10^5$).

Linearity studies confirmed dynamic ranges of 30 nM to 1300 nM for NTx, and 2 mM to 25 mM for creatinine.

**807.92 (b)(2): Brief Description of Clinical Data**

Accuracy was evaluated by comparative testing between Osteomark® NTx POC and the two predicate methods (NTx and creatinine). Two hundred thirty-five (235) urine samples were assayed by Osteomark® NTx POC among three "POL-type" clinical sites, and by the predicate methods at the reference laboratory. The data are summarized below (laboratory methods = X-axis).

CLINICAL LINEAR REGRESSION DATA

| | n samples | Linear Regression Equation | Correlation Coefficient |
|---|---|---|---|
| **Osteomark NTx POC** | 235 | y = 1.12x +6 | 0.79 |

Precision testing was performed by three physician office laboratory (POL) sites. Each site tested two levels of NTx/creatinine ratios five times a day over four days. From this testing, the total pooled imprecision was calculated at each of the two levels. The percent coefficient of variation (%CV) at the lower level (approximately 25 nM BCE/mM creatinine) was 13.3% (within-day range 7.5% to 22.1%, n = 5), and the %CV at the higher level (approximately 100 nM BCE/mM creatinine) was 12.8% (within-day range 4.0% to 20.4%, n = 5).

**Use of DRx® NTx to Monitor the Effect of Antiresorptive Therapy (HRT)**
Retained samples from a published study with HRT-treated women (n = 50, 200 samples) were tested with the Osteomark® NTx POC device to determine its ability to measure the expected decrease in NTx concentration following antiresorptive therapy. Prior to HRT initiation, NTx mean baseline values were 67 nM BCE/mM creatinine, significantly higher than the premenopausal mean of 44 nM BCE/mM creatinine. Mean NTx values fell significantly after 6 months of therapy to 33 nM BCE/mM creatinine, a 48% decrease from baseline. Osteomark® NTx POC values were correlated to the laboratory method, Osteomark NTx EIA, throughout the study ($r = 0.66$, at baseline; $r = 0.46$, at 12 months). Significant correlations were also observed between the percent change in spine BMD at 1 year and the percent change in Osteomark® NTx POC from baseline to 6 months ($r = -0.33$).

**807.92 (b)(3): Conclusions from Nonclinical and Clinical Testing**
Studies demonstrated substantial equivalence of Osteomark® NTx POC in terms of accuracy and precision to existing products already being marketed. Sensitivity and linearity studies confirmed the assay's reportable range, and cross reactivity studies confirmed the assay's specificity.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 10 1999

Ms. Erika B. Ammirati, R.A.C., MT(ASCP)
Clinical/Regulatory Consultant
Metrika, Inc.
510 Oakmead Parkway
Sunnyvale, California 94086

Re: K984530
Trade Name: Osteomark® NTx Point of Care
Regulatory Class: II Product Code: JFY
Regulatory Class: I Product Code: JMM
Dated: June 9, 1999
Received: June 10, 1999

Dear Ms. Ammirati:

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 legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). 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/dsma/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: K984530

Device Name: Osteomark® NTx Point of Care

### INDICATIONS FOR USE

Osteomark NTx Point of Care (POC) is a urinary assay for the quantitative measure of the excretion of cross-linked N-telopeptides of type I collagen (NTx) normalized to urinary creatinine (nM Bone Collagen Equivalents/mM creatinine). The test is used to monitor bone resorption changes following initiation of antiresorptive therapy (e.g., hormone replacement therapy).

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K984530

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X
(Per 21 CFR 801.109)

OR

Over-The-Counter Use _____
(Optional Format 1-2-96)