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APPROVAL ORDER

OOM-0577

AAV 1



Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

JAN 20 2000

Sunlight Ultrasound Technologies, Ltd.  
c/o Johnathan S. Kahan, ESQ.  
Hogan & Hartson, L.L.P.  
555 Thirteenth Street, N.W.  
Washington, DC 20004-1100

Re: P990035  
Omnisense Ultrasound Bone Sonometer  
Filed: June 30, 1999  
Amended: July 2, 13 and 21, August 23, September 22, October 15, and 28,  
November 18, December 22, 1999, and January 7, 2000

Dear Mr. Kahan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Omnisense Ultrasound Bone Sonometer.

The Sunlight Omnisense™ (Omnisense) Ultrasound Bone Sonometer is a non-invasive device that is designed for the quantitative measurement of the velocity of ultrasound waves ("Speed of Sound" or "SOS in m/sec") propagating along the distal one-third of the radius bone. SOS provides a measure of skeletal fragility. The output is also expressed as a T-score and Z-score and can be used in conjunction with other clinical risk factors as an aid to the physician in diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk.

The SOS measured by Omnisense has a precision error low enough in comparison with the expected annual change in a patients' measurement to make it suitable for monitoring bone changes which occur in the early years following menopause (i.e., age range approximately 50-65 years).

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (*enclosed*). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of Section 520(e) of the Federal, Food, Drug and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Page -2 - Mr. Kahan

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. As part of our reengineering effort, the Office of Device Evaluation is piloting a new process for review of final printed labeling.

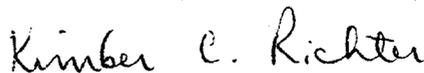
The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment. Please see the CDRH Pilot for Review of Final Printed Labeling document at <http://www.fda.gov/cdrh/pmat/pilotpmat.html> for further details.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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

If you have any questions concerning this approval order, please contact Joseph S. Arnaudo at (301) 594-1212.

Sincerely yours,



Kimber C. Richter, M.D.  
Deputy Director for Clinical  
and Review Policy  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

Issued: 3-4-98

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mix-up of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Medical Device Reporting  
PO Box 3002  
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

SUMMARY OF SAFETY AND  
EFFECTIVENESS DATA (SSED)

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

**Device Generic Name:** Ultrasound Bone Sonometer

**Device Trade Name:** The Sunlight Omnisense™ Ultrasound Bone Sonometer

**Applicant's Name and Address:** Sunlight Ultrasound Technologies Ltd.  
Weitzmann Science Park Building #3  
P.O. Box 2513  
Rehovot 76100 ISRAEL

**Applicant's U.S. Representative:** Jonathan S. Kahan, Esq.  
Hogan & Hartson L.L.P.  
Columbia Square  
555 Thirteenth Street, N.W.  
Washington, D.C. 20004-1109

**PMA Number:** P990035

**Date of Notice of Approval to the Applicant:** January 20, 2000

### II. INDICATIONS FOR USE

The Sunlight Omnisense™ (Omnisense) Ultrasound Bone Sonometer is a non-invasive device that is designed for the quantitative measurement of the velocity of ultrasound waves ("Speed of Sound" or "SOS in m/sec") propagating along the distal one-third of the radius bone. SOS provides a measure of skeletal fragility. The output is also expressed as a T-score and Z-score and can be used in conjunction with other clinical risk factors as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk.

The SOS measured by Omnisense has a precision error low enough in comparison with the expected annual change in a patient's measurement to make it suitable for monitoring bone changes which occur in the early years following menopause (i.e., age range approximately 50-65 years).

### III. CONTRAINDICATIONS

None Known.

### IV. WARNINGS AND PRECAUTIONS

**Warnings:**

Never attempt to operate the Omnisense unit if it is plugged into an outlet that does not meet all electrical code requirements.

Make sure that there is proper grounding in the wall outlet.

The Omnisense is not suitable for use in the presence of a flammable anesthetic mixture containing air, oxygen or nitrous oxide.

Always shut down the system using the switch at the rear panel before plugging or unplugging the Main unit.

Precautions:

The Omnisense probe should not be used on subjects with breached skin or open sores on the skin area that comes with contact with the probe.

Use the Omnisense only indoors, in a clean, dry environment.

To prevent fire or electric shock, do not open or expose the Omnisense Main Unit to rain or moisture.

Do not operate or store the Omnisense near a heat source or air conditioner and always store the System Quality Verification (SQV) phantom near the Omnisense Main Unit.

The system is not sterile. Thus, the probe must be cleaned and disinfected before each patient session. The correct cleaning and disinfection procedure is described in the Omnisense User Guide, "Cleaning and Disinfecting the Omnisense", in Chapter 11.

The Omnisense provides no protection against the harmful ingress (entry) of liquids. Hence, when cleaning the unit, avoid applying liquid near probe connections and the sockets.

SQV phantom and probes should not be immersed in liquid of any kind. Alcohol-free, dry or pre-moistened wipes may be used to clean them.

Use Sunlight recommended and approved ultrasound coupling gels with the Omnisense sonometer to generate and maintain acoustical contact of the probe with the skin.

Sunlight ultrasound gel is for external use only.

When applying ultrasound coupling gel, do not use a Q-tip, an examination glove treated with talc, or any other applicator that may introduce fibers or other foreign matter into the probe.

Do not expose the SQV phantom and the monitor screen to direct sunlight.

When conducting the System Quality Verification procedure, avoid touching the temperature indication strip on the phantom with the fingers, as this affects the phantom temperature reading required for correct interpretation of the procedure results.

When conducting System Quality Verification, be sure that no air bubbles are trapped in the gel between the phantom and probe, as this affects the acoustic contact of the probe with the phantom.

Refer all service problems to qualified Sunlight representative only.

Monitors, printers and other interfacing accessories used with the Omnisense bone sonometer must meet IEC 601-1, IEC 950, UL 2601 or equivalent safety standards.

**V. DEVICE DESCRIPTION**

The Sunlight Omnisense™ (Omnisense) Ultrasound Bone Sonometer is a noninvasive PC-based device that employs a hand-held probe designed to measure SOS values. The probe is connected by a cable to the Omnisense Main Unit. During measurement, the probe is applied directly to the skin at the distal one-third of the radius. A thin layer of Sunlight Ultrasound Gel is applied between the probe surface and the skin to facilitate good acoustic coupling. Inaudible high frequency acoustic waves, at a center frequency of

1.25MHz, are produced by two transducers (called ultrasound signal generators or transmitters) in the probe. The ultrasound waves are conducted along the bone and then detected by two different transducers (called ultrasound signal detectors or receivers) in the same probe.

The device's software compares the SOS result with the SOS of a young healthy population, as well as an age-matched population, using an embedded reference database ("normative database"), and reports the comparison in the form of a T-score and a Z-score. A T-score is the difference between the measured SOS value of the subject, and that of the average value of the young healthy population, described in units of standard deviation (SD) of the young healthy population. A Z-score is defined as the difference between a patient's SOS result and the mean SOS of the age and gender-matched normal population, given also in units of standard deviation of the population. Thus, if a patient has a T-score of -1.5, the patient's SOS is one and one-half SDs below the average SOS of the young healthy population, and if a patient has a Z-score of +0.5, the patient's SOS is one-half SD above the age-matched mean.

#### A) DEVICE COMPONENTS

The Omnisense is a noninvasive PC-based device that consists of: (1) a desktop personal computer-based Main Unit; (2) a Video Display monitor; (3) a keyboard with integrated trackball; (4) a small hand-held probe; (5) a System Quality Verification phantom; (6) a foot pedal; (7) a positioning gauge; (8) a cushion hand rest; (9) a set of earphones; and (10) a User Guide. The Omnisense is also supplied with a Startup Kit that consists of: (1) three bottles of acoustic contact gel (Sunlight Ultrasound Gel); (2) a 100 MB high capacity Zip™ diskette; (3) a 1.44 MB floppy diskette; (4) a skin marker pencil; (5) a screw driver; and (6) two replacement line power fuses.

The user interface with the Omnisense is comprised of the keyboard and the integrated trackball, the video display monitor, the foot-pedal and an optional printer (which is not supplied with the Omnisense). The operator uses these accessories mainly to input patient information into the PC. These accessories are also used for entering other administrative input required in order to operate the system, such as operator's I.D. and password, or the names of new operators or physicians. The software displays to the operator the list of previously measured patients, enables the user to edit a patient information record, and follows the progress of the measurement procedure.

An off-the-shelf printer may be used to generate a record of the patient information entered and the SOS Measurement Result, as well as the corresponding T-scores and Z-scores. The printer may also be used to print Patient History data and SQV History data.

The System Quality Verification (SQV) procedure and a phantom, which is supplied with the system, are used to verify that the entire system is working properly. The phantom, which is designed to be a substitute for bone, is composed of a homogenous hard polymeric material that transmits ultrasound signals at known speeds of approximately 2750 m/sec at room temperature. As a daily routine, the operator is requested to perform the SQV procedure. The SQV measurement procedure is performed in a manner similar to the measurement of the SOS of the radius and the same equations are used to compute the SOS value.

Two aids are supplied with Omnisense: a radius measurement gauge, and a hand rest. The gauge is made of a spring-loaded measuring band, connected at one end to a flat platform. The operator then uses the gauge to measure the distance from the elbow to the tip of the third finger. Using a skin marker, which is provided with the Starter Kit, a mark is drawn around the forearm at exactly the mid-point from the elbow to the third finger tip, which is the distal border of the Region of Interest.

Other accessories provided with Omnisense include a set of earphones for listening to the On-Line Measurement Methodologies, and a screw driver for tightening the probe connector in its socket. The supplies Starter Kit includes a skin marker, three 250cc bottles of Ultrasound Gel, manufactured for Sunlight by Parker Laboratories, Inc, Orange NJ 07050, one 100MB high capacity Zip™ Disk and one 1.44MB floppy diskette, and two line voltage replacement fuses.

## B) DEVICE OPERATION

The procedure for taking measurements with the Omnisense is performed according to the following steps: (1) opening a patient file; (2) marking the measurement position on the limb; (3) preparing the probe and the skin surface; (4) performing the actual bone measurements; and (5) reading and printing the measurement results.

The measurement results are displayed on the monitor. Omnisense reports the bone SOS, together with the T-score and Z-score values, which are computed by the system's software using the patient's measured representative SOS value and the reference database. These values appear, together with a graphical display of the measurement results relative to the normative reference data, on the *Measurement Results* screen. A printout of the results can be obtained if a printer is connected to the Main Unit, and the *Print* button on the screen is pressed. The physician may use these results in conjunction with other clinical risk factors as an aid in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk. In order to monitor bone changes, the physician may recall the record of past measurements (*Measurement History*) on the Video Display monitor or print them out.

Other operations can be performed with the help of the graphic user interface of the Omnisense. These include the System Quality Verification (daily procedure to insure proper operability of the Omnisense), database management operations, defining system parameters, and other management operations.

## C) PRINCIPLES OF OPERATION

Ultrasound is well established in the medical community as a method, used in its qualitative mode, to obtain in-vivo views of many internal structures. Ultrasound can also be used in a quantitative mode, by measuring various parameters associated with the propagation of a signal through the medium of interest. Quantitative Ultrasound (QUS) is an accepted method for the assessment of bone status, primarily because it offers quick, relatively low cost results without the radiation associated with other traditional techniques such as radiography, x-ray absorptiometry and computed tomography.

Sound energy consists of alternating cycles of compression and rarefaction of the medium through which it is transmitted. Audible sound for humans is in the range of approximately 20 Hz to 20,000 Hz (20 kHz). Ultrasound refers to a range of frequencies that begins at the high-frequency end of the audible range and extends into the Megahertz range.

The propagation of ultrasound through a medium, its speed, its dispersion and the attenuation of signal strength are strongly influenced by the physical properties of that medium. For example, the speed of propagation increases with the density of the medium and its modulus of elasticity (Young's Modulus). Moreover, the microstructure of the medium, as well as macro-structures on the order of a wavelength of the ultrasound, affects the speed. The QUS measure, which is used by the Omnisense, is the *speed of sound transmission* through bone, also known as Speed of Sound (SOS).

The SOS propagation depends, among other factors, on the density of the medium through which it is travelling. At the center frequency used by Omnisense, 1.25MHz, an ultrasound signal travels much faster through the relatively dense, cortical layer of the bone than through the trabecular layer, e.g., approximately 4000 m/s vs. 1800 m/s. The signal travels through soft tissue much more slowly than through either type of bone, at a speed of about 1540 m/s.

Sound waves propagate in all directions from the transmitting transducer of the Omnisense probe. Every molecule in the medium acts as a new transmitter, thus propagating the signal again in all directions. Thus, there are many paths that the signal can follow from transmitter to receiver. The Omnisense detects the *first signal to arrive* at the receiving transducer. The time taken by the signal to travel between the transmitter and the receiver is the parameter measured by Omnisense. This propagation time is a function of: (1) the bone SOS; (2) the soft tissue SOS; (3) the average distance between the transducers and the bone; and (4)

the angle of inclination between the surface of the bone and the line connecting the two transducers. The Omnisense software uses a proprietary algorithm to analyze these variables and to calculate the patient's SOS measurement. The device's software then compares the SOS result with the SOS of a young healthy population, as well as an age-matched population, using an embedded reference database ("normative database"), and reports the comparison in the form of a T-score and a Z-score.

## **VI. ALTERNATIVE PRACTICES/PROCEDURES**

### **A) BONE DENSITOMETRY (BMD)**

Different absorptiometric techniques have been established to date as a useful tool for skeletal assessment. Methods of measurement include single energy and dual energy x-ray absorptiometry with x-ray tube sources (SEXA, and DEXA), and spinal and peripheral quantitative x-ray computed tomography (QCT and pQCT). All are capable of evaluating bone mineral density (BMD) as the test parameter. The result is given as an absolute scale, and also relative to population reference values. All of these methods expose the patient and operator to x-ray radiation.

### **B) BIOCHEMICAL BONE MARKERS**

Bone markers estimate the rate of bone resorption and/or bone formation; as such they are considered as an indirect measurement for bone assessment. Nevertheless, they can be used for estimating the rate of change and evaluating response to treatment.

## **VII. MARKETING HISTORY**

Omnisense is being marketed in Israel, the United Kingdom, Italy, Switzerland, Norway, Denmark, Portugal, South Korea, China, Turkey, Egypt, and Brazil, for use at one or more of the following sites: the radius, the metatarsal, and the phalanx. Additionally, Sunlight Ultrasound Technologies Ltd. has authorization to display the CE Marking of Conformity on the Omnisense and the probes accompanied by the KEMA Notified Body Identification number 0344. Omnisense has not been withdrawn from any international market for any reason, including reasons related to safety and/or effectiveness.

## **VIII. POTENTIAL ADVERSE EFFECTS OF DEVICE ON HEALTH**

There are no known potential adverse effects of the Omnisense bone sonometer on a patient's health.

## **IX. SUMMARY OF PRECLINICAL STUDIES**

### **A) PRECISION**

Sunlight conducted two different in vivo precision tests for the Omnisense device. Included in these precision tests were: (1) a reproducibility study which involved the assessment of in vivo precision between different instruments, connecting slot configurations and probes; and (2) a reproducibility study which measured the in vivo precision between different operators and probes.

The objectives of both studies were to estimate the variability, between device components and between operators, of SOS measurements of the distal one-third of the radius. The in vivo precision (reproducibility), expressed by the coefficient of variation (CV), ranged from 0.60% to 0.73%.

### **B) ACCURACY**

Accuracy tests were performed as part of the Omnisense testing to verify compliance with the device's specifications that allow for line voltage variations as well as a range of environmental operating conditions. Two phantoms were measured under different environmental and line voltage conditions while changing the ultrasound probes and probe slot positions. The measured accuracy of the Omnisense was found to comply

with the Omnisense Specification requirement of better than  $\pm 0.2\%$  at both extremes of the SOS measurement range. The CV of the SOS results, computed from five successive measurements, was less than 0.1% in all of the different tests performed using either of the phantoms over a range of environmental conditions and operating line voltages tested.

#### C) ACOUSTIC OUTPUT TESTING

The Omnisense device was tested to verify compliance of the device with acoustic output limits and requirements in accordance with: (1) the International Standard IEC 61157, "Requirements for declaration of the acoustic output of medical diagnostic ultrasonic equipment" (1993); (2) FDA's 510(k) Guidance: "Measuring and Reporting Acoustic Output of Diagnostic Ultrasound Medical Devices" (1985); and (3) FDA's 510(k) Guidance: "Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers" (September 30, 1997). The acoustic output test was performed based on the definitions and methods recognized by the National Electrical Manufacturers Association (NEMA), "Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment", UD-2 revision 2, NEMA (1997).

The measured acoustic output levels of the Omnisense are summarized below, and are compared well below the limits specified in FDA's Guidance: "Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers" (September 30, 1997).

$I_{(SPTA.3)}$ [ $mW/cm^2$ ]	6.5
$I_{(SPPA.3)}$ [ $W/cm^2$ ]	3.7
MI	0.24
$W_{(0)}$ [ $mW$ ]	1.1

#### D) ELECTRICAL SAFETY

A series of electrical safety tests of the Omnisense was performed to verify the compliance of the Omnisense with the limits and requirements of medical electrical equipment general safety requirements IEC 601-1 (EN 60601-1, 1988), including Amendments 1 (1991) and 2 (1995). The Omnisense device was found to be in conformity with IEC 601-1 (1988) and Amendments 1 and 2.

#### E) ELECTROMAGNETIC COMPATIBILITY

A series of electromagnetic compatibility tests on the Omnisense was performed and the Omnisense was found to be in compliance with the limits and requirements of the United State Federal Communication Commission (FCC) regulations at 47 C.F.R. Part 15 for radio frequency devices, Subpart B: Unintentional radiators, as well as the requirements of IEC 601-1-2 (EN 60601-1-2), Medical Electrical Equipment - Part 1: General Requirements for Safety, Electromagnetic Compatibility Requirements and Tests, and the associated IEC standards, IEC 801-1 (EN 55011/ANSI C63/4/1992), IEC 801-2, IEC 801-3, IEC 801-4 and 801-5.

#### F) BIOCOMPATIBILITY

The polyurethane material of the Omnisense probe is the only material that comes into contact with the user and patient. This contact material was tested for biological effects in accordance with Biological Evaluation of Medical Devices - Part 1: Guidance on Selection of Tests First Edition, ANSI/AAMI/ISO-10993-1 that apply to surface devices that contact skin for limited duration (i.e.,  $\leq 24$  hours). For these types of devices, biocompatibility is demonstrated through testing for sensitization, irritation or intracutaneous reactivity, and cytotoxicity. The results from these tests demonstrated that the Omnisense patient contact material meets all applicable biocompatibility requirements.

## G) CLEANING AND DISINFECTION

The Omnisense ultrasound probe is considered a non-critical, reusable medical device which is applied only to intact skin, and therefore, only low-level disinfection is required. Results from testing to determine the effects of disinfection methods on the probe characteristics demonstrated that a wiping method using Sporidicin Disinfectant Towelettes does not affect the probe parameters and the SOS measurement results and is, therefore, an acceptable method for low-level disinfection procedure. The Omnisense Operator's Manual includes a recommendation that users conduct disinfection procedures of the Omnisense probe using Sporidicin Disinfectant Towelettes. These towelettes have FDA 510(k) clearance for disinfection of medical devices (K904579), are EPA registered for "Hospital Disinfection" with AOAC testing protocols (Reg. No. 8383-7), and comply with OSHA *Bloodborne pathogen Standard* (29 CFR 1910.1030).

## X. SUMMARY OF CLINICAL STUDIES

Five clinical studies were conducted to achieve the following objectives:

- Create normative reference databases of speed of sound ("SOS") in a Caucasian female population. Two clinical studies were conducted, one multicenter study in North America and one single center study in Israel, to collect the necessary information for creating normative databases.
- Assess the ability of the Sunlight Omnisense™ to discriminate osteoporotic fracture subjects from age-matched non-fracture subjects and healthy young subjects, and estimate the risk of osteoporotic fracture. Two studies were conducted to meet this objective; the first study examined only subjects that had hip fractures and a second study enrolled subjects with hip, wrist, or vertebral fractures. A separate analysis also was performed on data pooled from the two studies with respect to the hip fracture subjects.
- Determine the precision of the Sunlight Omnisense™ in a clinical setting. The precision was measured by comparing results obtained from multiple readings taken by different operators on the same subjects to determine whether the SOS measurements are reproducible.
- Evaluate the safety of the Sunlight Omnisense™ Ultrasound Bone Sonometer.

### A) NORMATIVE DATABASE STUDIES

#### 1. NORTH AMERICA NORMATIVE DATABASE (STUDY 4205):

*Study design and subject population:* Study 4205 was conducted in Caucasian females between the ages of 20 and 90 years old by five investigators at five geographically diverse investigational sites in North America (4 in the U.S. and 1 in Canada). Potential subjects were identified by placing advertisements in the newspaper, contacting potential subjects from drivers license listings, recruiting at college and university campuses, and recruiting at nursing homes. Eligible women had a negative history of osteoporotic fracture or chronic conditions affecting bone metabolism, and were not taking medications that affect bone metabolism. Of the 573 subjects recruited, 545 subjects were found eligible according to the inclusion/exclusion criteria of the study and 521 had SOS measurements of the distal one-third radius that were analyzed in this study.

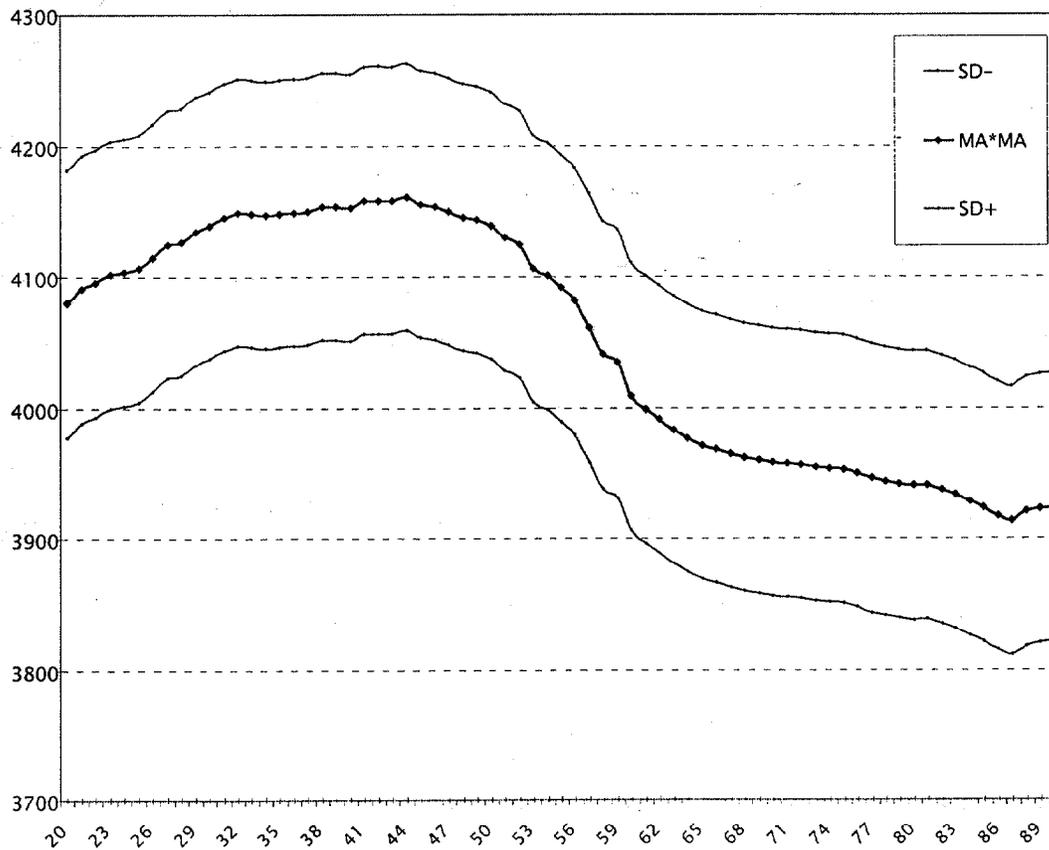
*Results:* The mean SOS was  $4083 \pm 146$  m/sec with a range of 3532 to 4490. About 90% of the SOS measurements were between 3800 and 4300 m/sec. Over half of the measurements (52%) were between 4000 and 4200 m/sec.

Table 1 presents mean SOS results by age decade. Figure 1 depicts the moving average of the SOS results as a function of age. The moving average SOS increases to a peak of 4158 m/sec at the age of 41, with population standard deviation of 102 m/sec, and declines thereafter. The largest decline, about 15 m/sec/year, is observed around the age of 58, about eight years past the mean age of menopause. At older ages, 65 to 90, the decline slows down to about 2-5 m/sec/year. Linear regression models show that both a straight line and quadratic fit are highly significant ( $p < 0.0001$ ).

Table 1: SOS Measurements by Age - Study 4205

Age	Mean±SD
20-29	4103±107
30-39	4150±93
40-49	4161±130
50-59	4095±131
60-69	3971±141
70-79	3949±125
80-90	3921±149
All	4083±146

Figure 1: Moving Average SOS by Age - Study 4205



The moving average for the age of 41, and a representative standard deviation taken at the age decade around the peak SOS area, are used to calculate T-scores for each SOS measurement. The mean T-scores by age decade are shown in Table 2. The mean T-score of the entire eligible population in the study was  $-0.75 \pm 1.43$  with a range of -6.16 to 3.24. Mean T-score reached a low of -2.45 at age 80-89. This table also indicates the percent of subjects in each age decade that had T-scores less than -2.5 (WHO criteria for osteoporosis) and those that had T-score between -2.5 and -1.0 (WHO criteria for osteopenia). Among subjects aged 60-90 years, 35.0% had T-scores less than -2.5 and 42.3% had T-scores between -2.5 and -1.0.

**Table 2: SOS T-Scores by Age - Study 4205**

Age	N	Mean $\pm$ SD	T<-2.5 n (%)	-2.5<T<-1.0 n (%)
20-29	92	-0.56 $\pm$ 1.05	4 (4.3)	24 (26.1)
30-39	100	-0.10 $\pm$ 0.92	1 (1.0)	15 (15.0)
40-49	102	0.01 $\pm$ 1.28	2 (2.0)	15 (14.7)
50-59	90	-0.64 $\pm$ 1.28	7 (7.8)	29 (32.2)
60-69	64	-1.84 $\pm$ 1.38	22 (34.4)	24 (37.5)
70-79	48	-2.07 $\pm$ 1.23	16 (33.3)	23 (47.9)
80-90	25	-2.34 $\pm$ 1.46	10 (40.0)	11 (44.0)
<b>All</b>	<b>521</b>	<b>-0.75<math>\pm</math>1.43</b>	<b>62 (11.9)</b>	<b>141 (27.1)</b>
<b>Range</b>		<b>-6.16 to 3.24</b>		

No adverse events of any kind were reported in the course of this clinical study.

*Conclusion:* The North America normative database for Caucasian female population follows the classical curvature of bone densitometry, with minor variations, since bone properties other than mineral density are probed. The peak SOS value is observed at about the age of 41. A rapid decrease in SOS is further observed on or about the mean age of menopause, 51, reaching a maximal slope of about 15 m/sec/year at the age range of 56 to 62. This change per year should be compared to the measurement precision (see Section 4. below) of about 17 m/sec. Being at about the same value, the Omnisense is shown to have a high sensitivity to change, thus making it suitable for measuring bone status in the first years after menopause when bone changes are most pronounced. At older ages, the change per year moderates to a level of about 2-5 m/sec/year.

The prevalence of osteoporosis (in accordance with the World Health Organization definition) as measured by the SOS in the North American female population at the age of 60-69 was found to be about 35.5% which is comparable to the prevalence observed using axial DXA measurements.

## 2. ISRAEL NORMATIVE DATABASE (STUDY 205)

*Study design and subject population:* Study 205 was conducted in Caucasian females between the ages of 20 and 90 years old by a single investigator at Asaff Harophe Medical Center, Zerifin, Israel. The eligibility criteria were met by 1,132 subjects who had their SOS measurements of the distal one-third radius taken.

The mean age of the study subjects was  $49.3 \pm 17.6$  years with a range of 20 to 89 years. Each decade was roughly comparable in size except for the decade 40-49, in which there were 266 subjects. Sixty percent of the subjects in this study were pre-menopausal.

**Results:** Table 3 presents mean SOS results by age decade. The mean SOS was  $4082 \pm 151$  m/sec with a range of 3510 to 4602. Ninety percent of the SOS measurements were between 3800 and 4300 m/sec. Over half of the measurements (52.5%) were between 4000 and 4200 m/sec.

The moving average SOS increases to a peak of 4173 m/sec at the age of 39, with population standard deviation of 99 m/sec, and declines thereafter. The largest decline, 15 m/sec/year, is observed around the age of 55, about four years past the mean age of menopause. At older ages, 65 to 90, the decline slows to about 5 m/sec/year. Linear regression models show that both a straight line and quadratic fit are highly significant ( $p < 0.0001$ ).

**Table 3: SOS Measurements by Age - Study 205**

Age	Mean $\pm$ SD
20-29	4108 $\pm$ 95
30-39	4161 $\pm$ 101
40-49	4167 $\pm$ 98
50-59	4115 $\pm$ 128
60-69	3989 $\pm$ 151
70-79	3931 $\pm$ 129
80-90	3879 $\pm$ 159
<b>All</b>	<b>4082<math>\pm</math>151</b>

The mean T-scores by age decade are shown in Table 4. The mean T-score for the study was  $-0.92 \pm 1.53$  with a range of -6.70 to 4.33. Mean T-score reached a low of -2.97 at age 80-89. This table also indicates the percent of subjects in each age decade that had T-scores less than -2.5 (WHO criteria for osteoporosis) and those that had T-score between -2.5 and -1.0 (WHO criteria for osteopenia). Among subjects aged 60-90, 44.9% had T-scores less than -2.5 and 34.5% had T-scores between -2.5 and -1.0.

**Table 4: SOS T-Scores by Age - Study 205**

Age (years)	N	Mean $\pm$ SD	T<-2.5 n (%)	-2.5<T<-1.0 n (%)
20-29	182	-0.65 $\pm$ 0.96	4 (2.2)	60 (33.0)
30-39	185	-0.12 $\pm$ 1.02	3 (1.6)	28 (15.1)
40-49	266	-0.06 $\pm$ 0.99	2 (0.8)	37 (13.9)
50-59	145	-0.58 $\pm$ 1.30	12 (8.3)	34 (23.4)
60-69	160	-1.86 $\pm$ 1.53	58 (36.2)	56 (35.0)
70-79	145	-2.44 $\pm$ 1.31	68 (46.9)	54 (37.2)
80-90	49	-2.97 $\pm$ 1.61	33 (67.3)	12 (24.5)
<b>All</b>	<b>1132</b>	<b>-0.92<math>\pm</math>1.53</b>	<b>180 (15.9)</b>	<b>281 (24.8)</b>
<b>Range</b>		<b>-6.70 to 4.33</b>		

No adverse events of any kind were reported in the course of this clinical study.

**Conclusions:** The Israel normative database for Caucasian female population follows the classical curvature of bone densitometry similar to that of the North America normative database. Peak SOS value is observed at about the age of 39. A rapid decrease in SOS is further observed on or about the mean age of menopause, 51, reaching a maximal slope of

about 15 m/sec/year at the age range of 54 to 57. Similar to the North America case previously described, this change per year may be compared to the measurement precision (see Section 4. below) of about 17 m/sec. Being at about the same value, the Omnisense is again shown to have a high sensitivity to change, thus confirming the findings of the North American study that the Omnisense is suitable for measuring bone status in the first years after menopause when bone changes are most pronounced. At older ages, the change per year moderates to a level of about 5 m/sec/year.

The prevalence of osteoporosis (in accordance with the World Health Organization definition) as measured by the SOS in the Israeli female population at the age of 60-69 was found to be about 32% which is comparable to the prevalence observed using axial DXA measurements.

## A) CROSS SECTIONAL STUDIES

### 1. ASSESSMENT OF HIP FRACTURE RISK (STUDY 201)

*Study design and subject population:* Study 201 was a cross-sectional case-control study performed at one investigational site in Israel. The objective of this study was to determine the ability of Omnisense SOS measurements to discriminate osteoporotic hip fracture subjects from age matched non-fracture subjects and young healthy subjects, and to determine the fracture risk estimate.

Three different groups of subjects were recruited and analyzed in this study: 50 low trauma hip fracture (HF) subjects, 130 age matched non-fracture subjects (NF) and 185 young healthy subjects (YF). The mean age for the hip fracture group was  $76.1 \pm 6.0$  years with a range of 65 to 85 years. The mean age for the non-fracture group was  $71.5 \pm 5.2$  with a range of 65 to 85 years. The mean age for the young healthy group was  $40.6 \pm 3.0$  with a range of 35 to 45 years.

*Results:* As seen in Table 5, hip fracture subjects had a mean SOS of  $3861 \pm 149$  m/sec, while non-fracture subjects had a mean SOS of  $3966 \pm 145$  m/sec. The difference between the two groups was statistically significant ( $p < 0.0001$ ). Young healthy subjects, on the other hand, had a mean SOS of  $4165 \pm 96$  m/sec, which was greater than the mean SOS of both hip fracture subjects and elderly non-fracture subjects ( $p < 0.0001$  for both). The SOS distributions for the three study groups are also illustrated in Figure 2. While there is a clear difference in the SOS distributions between the two elderly groups, there is an overlap as well in the range of 3800-3900 m/sec, since it is likely that a significant proportion of the elderly subjects in the non-fracture group might also be osteoporotic.

Table 5: SOS Measurements by Study Group - Study 201

Speed of Sound (m/sec)	Hip Fracture n (%)	Elderly Non-Fracture n (%)	Young Healthy n (%)
<3800	18 (36.0)	15 (11.5)	0 (0.0)
3800-3899	12 (24.0)	32 (24.6)	0 (0.0)
3900-3999	11 (22.0)	35 (26.9)	11 (5.9)
4000-4099	5 (10.0)	22 (16.9)	33 (17.8)
4100-4199	4 (8.0)	19 (14.6)	75 (40.5)
4200-4299	0 (0.0)	6 (4.6)	52 (28.1)
4300+	0 (0.0)	1 (0.8)	14 (7.6)
<b>Total</b>	<b>50 (100.0)</b>	<b>130 (100.0)</b>	<b>185 (100.0)</b>
<b>Mean±SD</b>	<b>3861±149</b>	<b>3966±145</b>	<b>4165±96</b>
<b>Range</b>	<b>3490 - 4177</b>	<b>3582 - 4359</b>	<b>3901 - 4407</b>
<b>T-test p-value (vs. non-fracture)</b>	<b>&lt;0.0001</b>	----	<b>&lt;0.0001</b>
<b>T-test p-value (vs. young healthy)</b>	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	----

Figure 2: SOS Distribution by Study Group - Study 201

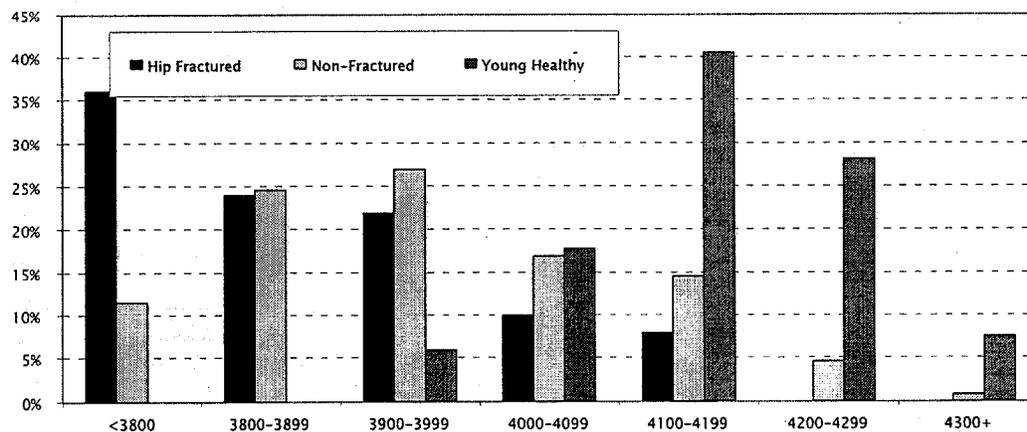


Table 6 shows the distribution of SOS T-scores for hip fracture and non-fracture subjects. Among hip fracture subjects, 70% (35/50) had T-scores less than -2.5, while 39% (51/130) of non-fracture subjects and 1% (2/185) of young healthy subjects had T-scores less than -2.5. Conversely, 10% (5/50) hip fracture subjects had T-scores greater than -1.0, while 24% (31/130) of non-fracture subjects and 85% (158/185) of young healthy subjects had T-scores greater than -1.0.

**Table 6: SOS Measurement T-Scores by Study Group - Study 201**

T-Score	Hip Fracture n (%)	Elderly Non- Fracture n (%)	Young Healthy n (%)
< -2.5	35 (70.0)	51 (39.2)	2 (1.1)
-2.5 to -1.0	10 (20.0)	48 (36.9)	25 (13.5)
> -1.0	5 (10.0)	31 (23.8)	158 (85.4)
<b>Total</b>	<b>50 (100.0)</b>	<b>130 (100.0)</b>	<b>185 (100.0)</b>
<b>Mean±SD</b>	<b>-3.11±1.52</b>	<b>-2.06±1.47</b>	<b>-0.02±0.98</b>
<b>Range</b>	<b>-6.91 to 0.10</b>	<b>-5.97 to 1.96</b>	<b>-2.71 to 2.45</b>

The logistic regression analysis for hip fracture discrimination (*i.e.*, comparing hip fracture subjects with elderly non-fracture subjects) presented in Table 7 indicates that the area under the ROC curve ("AUC") is 0.63 (95% CI: 0.61-0.79) and the fracture odds ratio is 2.16 (95% CI: 1.46-3.19). The age- and BMI-adjusted AUC is 0.79 (95% CI: 0.73-0.84) and the age-adjusted odds ratio is 1.75 (95% CI: 1.15-2.65).

**Table 7: SOS Fracture Discrimination - Area Under ROC Curve and Odds Ratio Study 201**

BMI & Age adjusted			BMI adjusted		
ROC (95% CI)	Odds ratio (95% CI)	p-value	ROC (95% CI)	Odds ratio (95% CI)	p-value
0.79 (0.73-0.84)	1.92 (1.22-3.02)	0.005	0.77 (0.70-0.83)	2.29 (1.49-3.54)	0.0002
Age adjusted			Unadjusted		
ROC (95% CI)	Odds ratio (95% CI)	p value	ROC (95% CI)	Odds ratio (95% CI)	p value
0.75 (0.66-0.84)	1.75 (1.15-2.65)	0.009	0.69 (0.61-0.79)	2.16 (1.46-3.19)	0.0001

Table 8 shows the results of a logistic regression with fracture status as the dependent variable (excluding young healthy subjects) and SOS as the independent variable, adjusting for age and BMI. This analysis shows that for every 100 m/sec decrease in SOS the odds of fracture increase by about 50% and that for every decrease of 162 m/sec in SOS the odds of fracture double. Age and BMI are independent predictors of fracture risk: for every additional decade of age the risk of fracture increases by nearly 2.5 times, and for every decrease of one kg/m<sup>2</sup> in BMI, the risk of fracture increases by more than 25%.

**Table 8: Results of Multivariate Logistic Regression - Study 201**

Variable	Parameter Estimate	Standard Error	Chi-Square	p-value
Intercept	-14.96	7.53	3.95	0.05
Age	-0.09	0.04	6.72	0.01
BMI	0.23	0.06	14.27	0.0002
SOS	0.004	0.0015	7.94	0.005

No adverse events of any kind were reported in the course of this clinical study.

*Conclusions:* This case-control based study has shown that the Omnisense can significantly discriminate between young and healthy subjects, who are at very low risk of any osteoporotic fracture, and a group of elderly subjects, who are known to be, on the average, at high risk of fracture. Moreover, the Omnisense was also found to significantly discriminate between osteoporotic hip fracture subjects and age-matched elderly non-fracture subjects. This finding is noted despite a high likelihood that there are a significant number of osteoporotic subjects in the non-fracture group. The odds ratios found in this study, which can be considered fracture risk estimates, are comparable to those of other bone assessment devices.

These study results show that the SOS, as measured by the Omnisense, can be considered as an important factor in aiding the physician when diagnosing a patient for osteoporosis and determining the patient's risk of fracture.

## 2. ASSESSMENT OF HIP, WRIST AND VERTEBRAL FRACTURE RISK (STUDY 202)

*Study design and subject population:* The objective of Study 202 was to determine the ability of Omnisense SOS measurements to discriminate osteoporotic hip, vertebral, and wrist fracture subjects from non-fracture subjects, and to determine the fracture risk estimate. Thus, four groups of subjects were enrolled and found eligible to be analyzed in the study: 94 hip fracture subjects (HF), 50 vertebral fracture subjects (VF), 41 wrist fracture subjects (WF), and 89 elderly non-fracture subjects (NF). All subjects were in the age range of 55 to 85. The study was conducted by one investigator at Rambam Medical Center, Haifa, Israel.

*Results:* As seen in Table 9, hip fracture subjects had a mean SOS of  $3873 \pm 154$  m/s, vertebral fracture subjects had a mean SOS of  $3877 \pm 144$  m/s, wrist fracture subjects had a mean SOS of  $3880 \pm 154$  m/s, and non-fracture subjects had a mean SOS of  $3953 \pm 138$  m/s. All fracture subjects had a mean SOS of  $3878 \pm 154$ . All of the differences between the mean SOS of each of the fracture group and the mean SOS of the non-fracture group were statistically significant ( $p < 0.01$ ). The SOS distributions for the study groups are illustrated in Figure 3. While there is a clear difference in the SOS distributions between the fracture groups and the non-fracture group, there is considerable overlap as well in the range of 3800-3900 m/sec.

Table 9: SOS Measurements by Study Group - Study 202

Speed of Sound (m/sec)	Hip Fracture n (%)	Vertebral Fracture n (%)	Wrist Fracture n (%)	All Fracture n (%)	Elderly Non-Fracture n (%)
<3800	32 (34.0)	16 (32.0)	14 (34.1)	51 (32.1)	15 (16.9)
3800-3899	21 (22.3)	8 (16.0)	7 (17.1)	32 (20.1)	21 (23.6)
3900-3999	20 (21.3)	16 (32.0)	10 (24.4)	42 (26.4)	22 (24.7)
4000-4099	16 (17.0)	7 (14.0)	8 (19.5)	24 (15.1)	16 (18.0)
4100-4199	4 (4.3)	3 (6.0)	1 (2.4)	8 (5.0)	12 (13.5)
4200-4299	1 (1.1)	0 (0.0)	1 (2.4)	2 (1.3)	2 (2.2)
4300+	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
<b>Total</b>	<b>94 (100.0)</b>	<b>50 (100.0)</b>	<b>41 (100.0)</b>	<b>159 (100.0)</b>	<b>89 (100.0)</b>
<b>Mean±SD</b>	<b>3873±154</b>	<b>3877±144</b>	<b>3880±154</b>	<b>3878±154</b>	<b>3953±138</b>
<b>Range</b>	<b>3326-4246</b>	<b>3577-4149</b>	<b>3415-4206</b>	<b>3326-4246</b>	<b>3718-4325</b>
<b>T-test p-value (compared to non-fracture)</b>	<b>&lt;0.0001</b>	<b>0.003</b>	<b>0.01</b>	<b>0.0001</b>	<b>----</b>

Figure 3: SOS Distribution by Study Group - Study 202

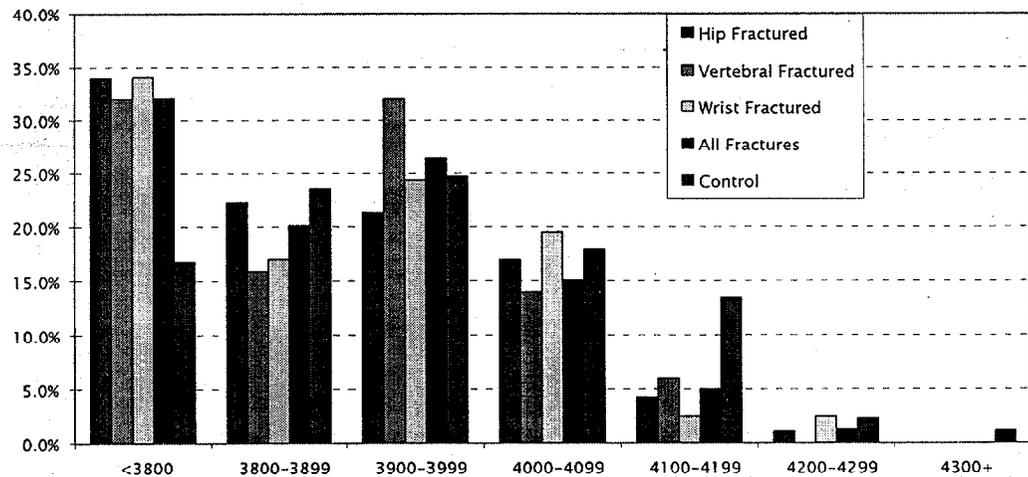


Table 10 shows the distribution of SOS T-scores for each of the fracture groups and the non-fracture subjects. Among the different fracture groups: 60% of the hip fracture subjects, 52% of the vertebral fracture subjects and 54% of the wrist fracture subjects had T-scores less than -2.5, as did 46% of non-fracture subjects. Conversely, less than 10% of each of the fracture groups had T-scores greater than -1.0, while 24% of non-fracture subjects had T-scores greater than -1.0.

Table 10: SOS Measurement T-Scores by Study Group - Study 202

T-Score	Hip Fracture n (%)	Vertebral Fracture n (%)	Wrist Fracture n (%)	All Fracture n (%)	Elderly Non- Fracture n (%)
< -2.5	56 (59.6)	26 (52.0)	22 (53.6)	87 (54.7)	41 (46.0)
-2.5 to 1.0	31 (33.0)	20 (40.0)	16 (39.0)	59 (37.1)	27 (30.3)
> 1	7 (7.4)	4 (8.0)	3 (7.4)	13 (8.2)	21 (23.6)
<b>Total</b>	<b>94 (100.0)</b>	<b>50 (100.0)</b>	<b>41 (100.0)</b>	<b>159 (100.0)</b>	<b>89 (100.0)</b>
<b>Mean±SD</b>	<b>-3.03±1.55</b>	<b>-2.99±1.45</b>	<b>-2.96±1.56</b>	<b>-2.98±1.55</b>	<b>-2.22±1.39</b>
<b>Range</b>	<b>-8.56 to 0.74</b>	<b>-6.02 to -0.24</b>	<b>-7.66 to 0.33</b>	<b>-8.56 to 0.74</b>	<b>-4.60 to 1.54</b>

The logistic regression analysis for fracture discrimination (*i.e.*, comparing all fracture subjects with elderly non-fracture subjects) presented in Figure 11 indicates that the area under the ROC curve (“AUC”) is 0.63 (95% CI: 0.56-0.70) and the fracture odds ratio is 1.72 (95% CI: 1.29-2.30). The age- and BMI-adjusted AUC is 0.70 (95% CI: 0.63-0.77) and the age-adjusted odds ratio is 1.41 (95% CI: 1.04-1.93).

Table 11: SOS Fracture Discrimination Area Under ROC Curve and Odds Ratio - Study 202

BMI & Age adjusted			BMI adjusted		
ROC (95% CI)	Odds ratio (95% CI)	p-value	ROC (95% CI)	Odds ratio (95% CI)	p-value
0.70 (0.63-0.77)	1.43 (1.04-1.95)	0.03	0.63 (0.56-0.70)	1.74 (1.29-2.33)	0.0002
Age adjusted			No adjustment		
ROC (95% CI)	Odds ratio (95% CI)	p-value	ROC (95% CI)	Odds ratio (95% CI)	p-value
0.70 (0.63-0.77)	1.41 (1.04-1.93)	0.03	0.63 (0.56-0.70)	1.72 (1.29-2.30)	0.0003

Table 12 shows the results of a logistic regression with fracture status as the dependent variable and SOS as the independent variable, adjusting for age and BMI. This analysis shows that the odds of hip, vertebral, wrist or any fracture increase by 50% for a decrease in SOS of 241 m/sec, 127 m/sec, 142 m/sec and 174 m/sec respectively. Furthermore the odds of hip, vertebral, wrist or any fracture double when the SOS decreases by 412 m/sec, 217 m/sec, 242 m/sec and 297 m/sec, respectively.

**Table 12: Results of Multivariate Logistic Regression**

Variable	Parameter Estimate	Standard Error	Chi-Square	p-value
Intercept	-3.11	4.72	0.43	0.51
Age	-0.09	0.02	16.67	0.0001
BMI	-0.02	0.04	0.19	0.66
SOS	0.0023	0.0011	4.91	0.03

No adverse events of any kind were reported in the course of this clinical study.

*Conclusions:* This case-control based study has shown that the Omnisense can significantly discriminate between subjects having any of the most common osteoporotic fractures (*i.e.*, hip, vertebral and wrist fractures) and age matched non-fracture controls, even though the control group, being also formed of elderly subjects, is likely comprised of a significant number of osteoporotic subjects. A significant discrimination was similarly observed between each of the fracture subjects grouped according to their type of osteoporotic fracture, and the control group. The odds ratios found in this study, which can be considered fracture risk estimates, are comparable to those found in Study 201, and also to those of other bone assessment devices.

These study results confirm once again, while widening the spectrum of the type of fractures, that the SOS as measured by the Omnisense can be used by physicians when diagnosing a patient for osteoporosis and determining the patient's risk of fracture.

### 3. COMBINED CROSS-SECTIONAL STUDIES

The 201 and 202 cross-sectional studies were very similar in many respects. Both studies had similar patient populations and recruited hip fracture subjects and healthy non-fracture subjects in the same age groups. Since hip fracture is the most important osteoporotic fracture from a personal, public health and economic point of view, it is important to obtain estimates of Omnisense hip fracture discrimination ability that are as accurate as possible. To this end, the hip fracture and healthy non-fracture groups in these two studies have been pooled in order to arrive at a more precise estimate of the Omnisense capabilities.

The combined hip fracture group consists of 144 subjects, 50 from Study 201 and 94 from Study 202. The combined non-fracture group consists of 219 subjects, 130 from Study 201 and 89 from Study 202.

*Results:* Table 13 shows the distribution of SOS measurements for the combined hip fracture group and the combined non-fracture group. Hip fracture subjects had a mean SOS of  $3869 \pm 152$  m/sec, while non-fracture subjects had a mean SOS of  $3960 \pm 142$  m/sec ( $p < 0.0001$ ). As seen in this table, there is considerable overlap between the two groups in the range of 3800-4000 m/sec, since elderly subjects in the non-fracture group might also be osteoporotic.

**Table 13: SOS Measurements by Study Group - Pooled Study  
201+202**

Speed of Sound (m/sec)	Hip Fracture n (%)	Elderly Non- Fracture n (%)	p-value
<3600	3 (2.8)	2 (0.9)	
3600-3699	10 (6.9)	0 (0.0)	
3700-3799	37 (25.7)	28 (12.8)	
3800-3899	33 (22.7)	51 (23.3)	
3900-3999	31 (21.5)	59 (26.9)	
4000-4099	21 (14.6)	38 (17.3)	
4100-4199	8 (5.6)	30 (13.7)	
4200-4299	1 (0.7)	9 (4.1)	
4300+	0 (0.0)	2 (0.9)	
<b>Total</b>	<b>144 (100.0)</b>	<b>219 (100.0)</b>	
<b>Mean±SD</b>	<b>3869±152</b>	<b>3960±142</b>	<b>&lt;0.0001</b>
<b>Range</b>	<b>3326 - 4246</b>	<b>3582 - 4359</b>	

Table 14 shows the distribution of SOS T-scores for the combined group of hip fracture subjects, as well as the combined group of non-fracture subjects. Among hip fracture subjects, 63% had T-scores less than -2.5, while 42% of non-fracture subjects had T-scores less than -2.5. Conversely, 8% of hip fracture subjects had T-scores greater than -1.0, while 24% of non-fracture subjects had T-scores greater than -1.0.

**Table 14: SOS Measurement T-Scores by Study Group - Pooled Study  
201+202**

T-Score	Hip Fracture n (%)	Elderly Non- Fracture n (%)
< -2.5	91 (63.2)	92 (42.0)
-2.5 to -1.0	41 (28.5)	75 (34.2)
> -1.0	12 (8.3)	52 (23.7)
<b>Total</b>	<b>144 (100.0)</b>	<b>219 (100.0)</b>
<b>Range</b>	<b>-8.56 to 0.10</b>	<b>-5.97 to 1.96</b>

The logistic regression analysis for hip fracture discrimination (*i.e.*, comparing hip fracture subjects with elderly non-fracture subjects) presented in Table 15 indicates that the area under the ROC curve ("AUC") is 0.67 (95% CI: 0.61-0.73) and the fracture odds ratio is 1.95 (95% CI: 1.53-2.49). The age- and BMI-adjusted AUC is 0.76 (95% CI: 0.70-0.82) and the age-adjusted odds ratio is 1.54 (95% CI: 1.18-2.00).

**Table 15: SOS Fracture Discrimination Area Under ROC Curve and Odds Ratio  
Pooled Study 201+202 Age Range 55-85**

BMI & Age adjusted			BMI adjusted		
ROC (95% CI)	Odds ratio (95% CI)	p-value	ROC (95% CI)	Odds ratio (95% CI)	p-value
0.76 (0.70-0.82)	1.50 (1.15-1.96)	0.003	0.70 (0.64-0.76)	1.91 (1.49 – 2.46)	0.0001
Age adjusted			Unadjusted		
ROC (95% CI)	Odds ratio (95% CI)	p-value	ROC (95% CI)	Odds ratio (95% CI)	p-value
0.75 (0.70-0.81)	1.54 (1.18-2.00)	0.001	0.67 (0.61-0.73)	1.95 (1.53-2.49)	0.0001

Table 16 shows the results of a multivariate logistic regression with fracture status as the dependent variable and SOS as the independent variable, adjusting for age and BMI. This analysis shows that for every 135 m/sec decrease in SOS the odds of fracture increase by about 50% and that for every decrease of 231 m/sec in SOS the odds of fracture doubles.

**Table 16: Results of Multivariate Logistic Regression**

Variable	Parameter Estimate	Standard Error	Chi-Square	p-value
Intercept	-4.79	4.27	1.26	0.26
Age	-0.11	0.02	29.6	<0.0001
BMI	0.12	0.04	10.3	0.001
SOS	0.0027	0.0009	8.68	0.003

*Conclusions:* The results from combining the two fracture studies show that the Omnisense can significantly discriminate between osteoporotic hip fracture subjects and age-matched non-fracture subjects even after controlling for age and BMI. The odds ratios found in this analysis are comparable to those of other bone assessment devices.

#### 4. PRECISION STUDY

The objective of this study was to determine the precision of the Omnisense, as measured by the coefficient of variation ("CV"). The distal one-third radius SOS of each subject was measured twice by three different operators. Probes were repositioned between each measurement. The CV was calculated using the SAS ANOVA procedure, which reports the overall mean, the mean square error (using subject-operator combination as a blocking factor) and the coefficient of variation (the mean square error divided by the mean). The CV was reported for all measurements, as well as stratified by operator and by menopausal status. The variance of each CV was also calculated so that 95% confidence intervals could be reported. Fifteen subjects were measured, 10 premenopausal women and 5 postmenopausal women.

A total of 45 pairs (15 subjects times 3 operators) of SOS measurements were used to compute the CVs. The overall CV was 0.40% (95% CI: 0.39% to 0.41%). For premenopausal women the CV was 0.29% and for postmenopausal women the CV was 0.57%.

A total of six different operators performed SOS measurements in this study. Their CVs ranged from 0.27% to 0.66%.

The coefficient of variation can also be calculated in two different “standardized CV” forms,  $SCV_1$  and  $SCV_2$ .  $SCV_1$  is computed by dividing the measured mean square error by 95% of the individual range, which is taken from the North America Normative Database (Section 3.10.1.1 above).  $SCV_1$  was found to be 1.8%.  $SCV_2$  is computed by dividing the mean square error by the difference of the young healthy mean SOS (taken from the North America Normative Database, section 3.10.1.1) and that of the osteoporotic fracture mean SOS (the mean of the “All Fracture” group in the 202 Study, section 3.10.2.2).  $SCV_2$  is higher than  $SCV_1$ , and equals 5.9%.

No adverse events of any kind were reported in the course of this clinical study.

*Conclusions:* The *in vivo* precision of the Omnisense, as measured by the coefficient of variation, is 0.40%. There were some relative differences in CV between premenopausal and postmenopausal subjects. Differences in precision between premenopausal subjects and postmenopausal subjects have been found in DXA measurements (postmenopausal CV higher than premenopausal CV) as well as in QUS measurements of the calcaneus (postmenopausal CV lower than premenopausal CV). There were also differences between CVs measured by different operators. Nevertheless, all CVs were well below 1%, indicating good precision for all subgroups, and thus allowing for a meaningful assessment of patient status relative to the reference range.

The mean square error, about 17m/sec, is similar in magnitude to the average change per year which is observed during the first years of sharp decline in SOS post menopause, as described in section 3.10.1 above. Thus, the Omnisense can provide precise estimates of bone status during this important time when bone changes are most pronounced.

## XI. CONCLUSIONS DRAWN FROM STUDIES

### A) RISK/BENEFIT ANALYSIS

The Sunlight Omnisense provides useful quantitative measurements of bone fragility via the velocity of acoustic ultrasound waves (“speed of sound” or “SOS”) propagating along the distal one-third of the radius bone. The SOS data, when used in conjunction with other clinical risk factors, can aid physicians in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk. The clinical effectiveness of the Omnisense compares to that or rivals that of established densitometry (BMD), but without exposure to ionizing radiation. Due to the low power levels used, the risks posed by the Omnisense are also significantly lower than the already minimal risks posed by medical ultrasound devices used for other indications such as imaging. It is reasonable, therefore, to conclude that the benefits of the Omnisense outweigh the risk of illness or injury when used in accordance with the directions for use.

### B) SAFETY

There were no complications, adverse events, or side effects reported for patients participating in the clinical studies investigating the Omnisense.

### C) EFFECTIVENESS

Two Omnisense studies determined SOS values in a clinically normal population. Studies also demonstrated the ability of Omnisense SOS measurements to discriminate osteoporotic fracture subjects from age-matched non-fracture subjects, and young and healthy subjects, and thus to

enable determination of fracture risk estimates. A precision study also was conducted and demonstrated that the SOS measurements are reproducible.

## **XII. FDA DECISION**

The applicant's manufacturing facility was inspected on August 25, 1999 and was found to be in compliance with the Quality System regulations. FDA issued an approval order on January 20, 2000.

## **XIII. APPROVAL SPECIFICATIONS**

Directions for use: See attached labeling.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Hazards to Health From Use of the Device. See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the attached labeling.

## **XIV. REFERENCES**

1. D. Hans, T. Fuerst, F. Duboeuf: "Quantitative ultrasound bone measurement", *Eur Radiol* 1997 7 (suppl. 2): S43-S50; S.S. Mehta, O.K. Oz and P.P. Antich: "Bone elasticity and ultrasound velocity are affected by subtle changes in the organic matrix", *JBMR* 1998 13:114-121; Hans D, Gluer C, Njeh C, 1998 Ultrasonic evaluation of osteoporosis. In: Meunier PJ (ed.) *Osteoporosis: Diagnosis and Management*, Martin Dunitz, London U.K., pp. 59-78.
2. D. Hans, P. Dargent-Molina, A.M. Schott, J.L. Sebert, C. Cormier, P.O. Kotzki, P.D. Delmas, J.M. Pouilles, G. Breart and P.J. Meunier: "Ultrasonographic heel measurements to predict hip fracture in elderly women: the EPIDOS prospective study", *Lancet* 1996 348: 511-514.
3. D.C. Bauer, C.C. Gluer, J.A. Cauley, T.M. Vogt, K.E. Ensrud, H.K. Genant and D.M. Black: "Broadband Ultrasound Attenuation Predicts Fractures Strongly and Independently of Densitometry in Older Women: A Prospective Study", *Archives Internal Medicine* 1997 157: 629-634.
4. J.A. Kanis, L.J. Melton III, C. Christiansen, C.C. Johnston and N. Khaltaev: "The Diagnosis of Osteoporosis", *JBMR* 1994, 9:1137-1141.
5. H. Sievanen: "QUS Derived Speed of Sound and Cortical Bone Structure", an abstract submitted to the ASBMR 21<sup>st</sup> Annual Meeting meeting in St. Louis, MI, September 1999.
6. R. Barkmann, E. Kantorovich, C. Singal, D. Hans, H.K. Genant, M. Heller and C.C. Gluer: "A New Method for Quantitative Ultrasound Measurement at Multiple Skeletal Sites – First Results of Precision and Fracture Discrimination", submitted and accepted for publication in the *Journal of Clinical Densitometry*.
7. K. Knapp, C. Singal, G.M. Blake, I. Fogelman: "Preliminary Results of the Sunlight Omnisense™ Bone Sonometer: In-vivo and In-vitro Precision and Correlation with DXA", presented at the ASBMR 20<sup>th</sup> Annual Meeting, *Bone* 1998 23: S524.

8. M. Bouxsein, P.H.F. Nicholson, D.M. Rossler, S. Ashkenazi and I. Yaniv: "Prediction of Femoral Load from Femoral BMD and Ultrasonic Velocity at the Femur, Radius and Phalanx", submitted to the ASBMR 21<sup>st</sup> Annual Meeting meeting in St. Louis, MI, September 1999.
9. K.M. Knapp, G.M. Blake, T.D. Spector and I. Fogelman: "Ultrasound Measurements at the Radius Predict Vertebral Fractures in Postmenopausal Women", an abstract submitted to the ASBMR 21<sup>st</sup> Annual Meeting in St. Louis, MI, September 1999.
10. K.M. Knapp, G.M. Blake, I. Fogelman and T.D. Spector: "Ultrasound Measurements at the Radius Predict Wrist Fractures in Postmenopausal Women", an abstract submitted to the Annual Meeting of the Bone and Tooth Society in Bristol, UK, June 1999.
11. D. Hans, S.K. Srivastav, C. Singal, R. Barkmann, C.F. Njeh, E. Kantorovich, C.C. Gluer and H.K. Genant: "Does Combining the Results from Multiple Bone Sites Measured by a New Quantitative Ultrasound Device Improve Discrimination of Hip Fracture?" *JBMR* 1999; 14:644-651.
12. K.M. Knapp, C. Singal, G.M. Blake, I. Fogelman and T.D. Spector: "Quantitative Ultrasound Measurements Detect Skeletal Changes in Cortical Bone Following HRT Use", presented at the 11<sup>th</sup> International Workshop on Calcified Tissues, Eilat, Israel, 1999.

# LABELING

## 1. Essential Prescribing Information

The Sunlight Omnisense™ Ultrasound Bone Sonometer (Omnisense) is an accurate and easy to use tool for assessing the condition of bone. This chapter provides an introductory overview of the Omnisense System and the Information for Prescribers.

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

### 1.1 Device Description

The Sunlight Omnisense™ (Omnisense) Ultrasound Bone Sonometer is a non-invasive ultrasound device capable of measuring bone speed of sound (SOS) at one or more skeletal sites. It is comprised of a Main Unit and small hand held probes, each designed to measure SOS at one or more specific skeletal sites. The basic system is offered with one probe and the reference database for measurement of the distal one-third radius. See "How Supplied" section for a complete list of accessories.

A brief description of SOS measurement at the distal one-third radius follows. First, the patient personal information is entered, using Windows 95® graphic user interface. The CM probe is used to measure SOS along the distal one-third of the radius. In particular, the arm is marked at the midpoint between the elbow and the tip of the third finger, and the probe is positioned adjacent to the mark on the proximal side. After marking the precise measurement site the operator enters measurement mode. A uniform layer of Sunlight Ultrasound Gel is then applied to the hand-held probe and the measurement area. The probe is positioned parallel to the bone axis and is held at the base. The probe is moved around the circumference of the radius, with its longest dimension approximately in parallel to the axis of the bone. The measurement consists of three consistent measurement cycles, each of which is comprised of several bone scans.

Results are expressed in meters per second (m/sec), reflecting the upper 95th percentile of the SOS values. Sunlight Omnisense™ reports the bone SOS, together with the T-score (units of standard deviations relative to population reference values of healthy young caucasian female adults) and Z-score values (units of standard deviations relative to age matched

The United States (U.S.) version of the Omnisense is approved for SOS measurements at the distal 1/3 radius and as such is provided with measurement and database capabilities for this skeletal site. The use of the device to perform SOS measurements at other skeletal sites has not yet been approved by the FDA.

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population reference values), computed using the patient's SOS value and a reference database.

No calibration is required. Daily system verification is accomplished using the System Quality Verification (SQV) phantom supplied with the device.

### **1.2 Intended Use/Indications**

The Sunlight Omnisense™ (Omnisense) Ultrasound Bone Sonometer is a non-invasive device that is designed for the quantitative measurement of the velocity of ultrasound waves ("Speed of Sound" or "SOS in m/sec") propagating along the distal one-third of the radius bone. SOS provides a measure of skeletal fragility. The output is also expressed as a T-score and Z-score and can be used in conjunction with other clinical risk factors as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk.

The SOS measured by Omnisense has a precision error low enough in comparison with the expected annual change in a patients' measurement to make it suitable for monitoring bone changes which occur in the early years following menopause (i.e., age range approximately 50-65 years).

### **1.3 Contraindications**

None known.

### **1.4 Warnings**

- ◆ Never attempt to operate the Sunlight Omnisense™ unit if it is plugged into an outlet that does not meet all electrical code requirements.
- ◆ Make sure that there is proper grounding in the wall outlet.
- ◆ The Sunlight Omnisense™ is not suitable for use in the presence of a flammable anesthetic mixture containing air, oxygen or nitrous oxide.
- ◆ Always shut down the system using the switch at the rear panel before plugging or unplugging the Main unit.

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## 1.5 Precautions

- ◆ The Omnisense probe should not be used on subjects with breached skin or open sores on the skin area that comes with contact with the probe.
- ◆ Use the Sunlight Omnisense™ only indoors, in a clean, dry environment.
- ◆ To prevent fire or electric shock, do not open or expose the Sunlight Omnisense™ Desktop Unit to rain or moisture.
- ◆ Do not operate or store the Sunlight Omnisense™ near a heat source or air conditioner and always store the System Quality Verification (SQV) phantom near the Sunlight Omnisense™ Desktop Unit.
- ◆ The system is not sterile. Thus, the probe must be cleaned and disinfected before each patient session. The proper cleaning and disinfection procedure is described in this User Guide, "Cleaning and Disinfecting the Omnisense", in Chapter 11.
- ◆ The Sunlight Omnisense™ provides no protection against the harmful ingress (entry) of liquids. Hence, when cleaning the unit, avoid applying liquid near probe connections and the sockets.
- ◆ SQV phantom and probes should not be immersed in liquid of any kind. Alcohol-free, dry or pre-moistened wipes may be used to clean them.
- ◆ Use Sunlight recommended and approved ultrasound coupling gels with the Omnisense sonometer to generate and maintain acoustical contact of the probe with the skin.
- ◆ Sunlight ultrasound gel is for external use only.
- ◆ When applying ultrasound coupling gel, do not use a Q-tip, an examination glove treated with talc, or any other applicator that may introduce fibers or other foreign matter into the probe.
- ◆ Do not expose the SQV phantom and the monitor screen to direct sunlight.
- ◆ When conducting the System Quality Verification procedure, avoid touching the temperature indication strip on the phantom with the fingers, as this affects the phantom temperature reading required for correct interpretation of the procedure results.

- ◆ When conducting System Quality Verification, be sure that no air bubbles are trapped in the gel between the phantom and probe, as this affects the acoustic contact of the probe with the phantom.
- ◆ Refer all service problems to qualified Sunlight representative only.
- ◆ Monitors, printers and other interfacing accessories used with the Sunlight Omnisense™ bone sonometer must meet IEC 601-1, IEC 950, UL 2601 or equivalent safety standards.

### **1.6 Adverse Events**

No adverse events were reported in the course of the clinical studies performed, in which a total of approximately 4000 subjects underwent Omnisense measurement.

There are no known potential adverse effects of the Omnisense on health.

### **1.7 Clinical Studies**

Five clinical studies were performed involving a total of 2,059 women. These studies are briefly summarized below.

#### **1.7.1 North America Normative Database**

*Objective:* To construct a geographically representative database of mean distal one-third radius SOS values by age for Caucasian women in North America.

*Methods:* Caucasian females between the ages of 20 and 90 years old were recruited from the general population. Data were collected from five sites at different geographic locations in North America (4 in the US and 1 in Canada). Participating subjects had a negative history of osteoporotic fracture or chronic conditions affecting bone metabolism, were not taking medications known to alter bone metabolism, and none had experienced premature menopause.

*Results:* SOS measurements of the distal one-third radius were obtained from 521 subjects. The mean SOS was  $4083 \pm 146$  m/sec with a range of 3532 to 4490. **Table 1** presents mean SOS results by age decade.

**Figure 1** depicts the moving average of the SOS results as a function of age. The moving average SOS increases to a peak of 4158 m/sec at the

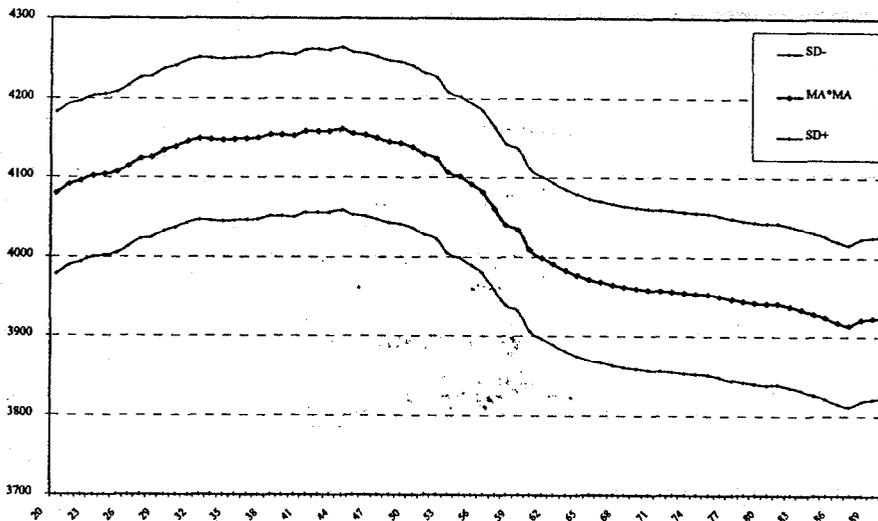
The United States (U.S.) version of the Omnisense is approved for SOS measurements at the distal 1/3 radius and as such is provided with measurement and database capabilities for this skeletal site. The use of the device to perform SOS measurements at other skeletal sites has not yet been approved by the FDA.

age of 41, with population standard deviation of 102 m/sec, and declines thereafter. The peak mean and standard deviation results are used for generating T-scores. The largest decline, about 15 m/sec/year, is observed around age 58, eight years past the mean age of menopause. At older ages, 65 to 90, the decline slows to about 2-5 m/sec/year. The mean T-score of the population was  $-0.75 \pm 1.43$  with a range of -6.16 to 3.24. Among women aged 60-90, 35% had T-scores less than -2.5 and 42% had T-scores between -2.5 and -1.0.

**Table 1: SOS Measurements by Age  
North America Normative Database**

Age (years)	N	Mean±SD
20-29	92	4103±107
30-39	100	4150±93
40-49	102	4161±130
50-59	90	4095±131
60-69	64	3971±141
70-79	48	3949±125
80-90	25	3921±149
<b>All</b>	<b>521</b>	<b>4083±146</b>

**Figure 1: Moving Average SOS by Age  
North America Normative Database**



The United States (U.S.) version of the Omnisense is approved for SOS measurements at the distal 1/3 radius and as such is provided with measurement and database capabilities for this skeletal site. The use of the device to perform SOS measurements at other skeletal sites has not yet been approved by the FDA.

**Conclusion:** The study provides a representative sample of Caucasian women in North America for use as a reference population and for computing T-scores and Z-scores.

### **1.7.2. Israel Normative Database**

**Objective:** To construct a database of mean distal one-third radius SOS values by age for Caucasian women in Israel.

**Methods:** Caucasian females between the ages of 20 and 90 years old were recruited from the general population of a large metropolitan area in Israel. Participating subjects had a negative history of osteoporotic fracture or chronic conditions affecting bone metabolism, were not taking medications known to alter bone metabolism, and none had experienced premature menopause.

**Results:** SOS measurements of the distal one-third radius were obtained from 1,132 subjects. The mean SOS was  $4082 \pm 151$  m/sec with a range of 3510 to 4602. The moving average SOS increases to a peak of 4173 m/sec at the age of 39, with population standard deviation of 99 m/sec, and declines thereafter. The largest decline, about 15 m/sec/year, is observed around age 55, four years past the mean age of menopause. At older ages, 65 to 90, the decline slows to about 5 m/sec/year. The mean T-score of the population was  $-0.92 \pm 1.53$  with a range of -6.70 to 4.33. Among women aged 60-90, 45% had T-scores less than -2.5 and 34% had T-scores between -2.5 and -1.0.

**Conclusion:** The study provides a representative sample of Caucasian women in Israel for use as a reference population and for computing T-scores and Z-scores.

### **1.7.3. Cross-Sectional Study of Hip Fracture Risk**

**Objective:** To determine the ability of the Omnisense to discriminate osteoporotic hip fracture subjects from age matched non-fracture subjects and young healthy subjects, and to determine the fracture risk estimate.

The United States (U.S.) version of the Omnisense is approved for SOS measurements at the distal 1/3 radius and as such is provided with measurement and database capabilities for this skeletal site. The use of the device to perform SOS measurements at other skeletal sites has not yet been approved by the FDA.

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**Methods:** The study was carried out by one investigator at two investigational sites in Israel. A total of 365 Caucasian women were recruited into three groups. Hip fracture subjects were 65 to 85 years of age and were not taking medications having a positive effect on bone metabolism. Elderly non-fracture subjects were age matched to hip fracture subjects. Young healthy subjects were 35 to 45 years of age.

**Results:** **Table 2** contains a summary of SOS results for each study group. All pairwise differences between the three groups were statistically significant ( $p < 0.0001$ ).

**Table 2: SOS Results by Study Group**

	<b>Hip Fracture N=50</b>	<b>Non-Fracture N=135</b>	<b>Young Healthy N=180</b>
SOS Mean±SD	3861±149	3966±145	4165±96
T-Score <-2.5 (%)	70%	39%	1%
T-Score >-1.0 (%)	10%	24%	85%

Logistic regression for hip fracture discrimination indicates that the area under the ROC curve, unadjusted for age, is 0.63 (95% CI: 0.61-0.79). The fracture odds ratio, unadjusted for age, is 2.16 (95% CI: 1.46-3.19) and the age-adjusted odds ratio is 1.75 (95% CI: 1.15-2.65). For every 100 m/sec decrease in SOS the odds of fracture increase by about 50% and for every decrease of 162 m/sec in SOS the odds of fracture doubles.

**Conclusions:** This case-control based study has shown that the Omnisense can significantly discriminate between osteoporotic hip fracture subjects, age-matched elderly non-fracture subjects, and young healthy subjects. This finding is noted despite a high likelihood that there are a significant number of osteoporotic subjects in the non-fracture group.

The odds ratios found in this study can be considered fracture risk estimates, and are comparable to those of other bone assessment devices.

#### **1.7.4. Cross-Sectional Study of Hip, Vertebral and Wrist Fracture Risk**

The United States (U.S.) version of the Omnisense is approved for SOS measurements at the distal 1/3 radius and as such is provided with measurement and database capabilities for this skeletal site. The use of the device to perform SOS measurements at other skeletal sites has not yet been approved by the FDA.

**Objective:** To determine the ability of Omnisense Speed of Sound measurements to discriminate subjects with major osteoporotic fractures from non-fracture subjects, and to determine the fracture risk estimate.

**Methods:** The study was carried out by one investigator in Israel. A total of 274 Caucasian women were recruited into three fracture groups (hip, vertebral and wrist) and an elderly non-fracture group. All subjects were 55 to 85 years of age and fracture subjects were not taking medications having a positive effect on bone metabolism.

**Results:** Table 3 contains a summary of SOS results for each study group. All differences between the three fractures groups and the non-fracture group were statistically significant ( $p < 0.01$ ).

**Table 3: SOS Results by Study Group**

	<b>Hip Fracture N=94</b>	<b>Vertebral Fracture N=50</b>	<b>Wrist Fracture N=41</b>	<b>Non-Fracture N=89</b>
SOS Mean±SD	3873±154	3877±144	3880±154	3878±154
T-Score <-2.5 (%)	60%	52%	54%	46%
T-Score >-1.0 (%)	7%	8%	7%	24%

Logistic regression for fracture discrimination indicates that the area under the ROC curve, unadjusted for age, is 0.63 (95% CI: 0.56-0.70). The fracture odds ratio, unadjusted for age, is 1.72 (95% CI: 1.29-2.30) and the age-adjusted odds ratio is 1.41 (95% CI: 1.04-1.93). For every 174 m/sec decrease in SOS the odds of fracture increase by about 50% and for every decrease of 297 m/sec in SOS the odds of fracture double.

**Conclusions:** This case-control based study has shown that the Omnisense can significantly discriminate between subjects having any of the most common osteoporotic fractures and age matched non-fracture controls. This finding is noted despite a high likelihood that there are a significant number of osteoporotic subjects in the non-fracture group.

The odds ratios found in this study can be considered fracture risk estimates, and are comparable to those of other bone assessment devices.

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### **1.7.5. Pooled Cross-Sectional Studies**

**Background:** The two cross-sectional studies were very similar in many respects. Both studies recruited hip fracture subjects and both studies recruited healthy non-fracture subjects in the same age groups. Both studies had similar eligibility criteria, the population characteristics of these groups in the two studies were similar, and the Omnisense measurements were performed using identical procedures. Since hip fracture may be the most important osteoporotic fracture, it is important to obtain estimates of Omnisense hip fracture discrimination ability that are as accurate as possible. Thus, the hip fracture and healthy non-fracture groups in the two cross-sectional studies have been pooled in order to arrive at a more precise estimate.

**Results:** Hip fracture subjects had a mean SOS of  $3869 \pm 152$  m/sec, while non-fracture subjects had a mean SOS of  $3960 \pm 142$  m/sec; this difference was statistically significant ( $p < 0.0001$ ).

Among hip fracture subjects, 63% had T-scores less than -2.5, while 42% of non-fracture subjects had T-scores less than -2.5. Conversely, 8% of hip fracture subjects had T-scores greater than -1.0, while 24% of non-fracture subjects had T-scores greater than -1.0.

Logistic regression for hip fracture discrimination indicates that the area under the ROC curve, unadjusted for age, is 0.67 (95% CI: 0.61-0.73). The fracture odds ratio, unadjusted for age, is 1.95 (95% CI: 1.53-2.49) and the age-adjusted odds ratio is 1.54 (95% CI: 1.18-2.00). For every 150 m/sec decrease in SOS the odds of fracture increase by about 50% and for every decrease of 257 m/sec in SOS the odds of fracture doubles.

**Conclusions:** Pooling of data from the two cross-sectional studies is justified on the basis of the similarities between the two studies. The results from combining the two studies show that the Omnisense can significantly discriminate between osteoporotic hip fracture subjects and age-matched non-fracture subjects even after controlling for age and BMI.

### **1.7.6. Precision Studies**

Three *in vivo* precision studies were performed to evaluate various aspects of reproducibility of SOS measurements. The objective of all

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three studies was to estimate the variability of SOS measurements of the Distal 1/3 Radius of a human subject between device components, different operators and with repeated measurements. In each study reproducibility is measured by the coefficient of variation (CV), which is the standard deviation divided by the mean.

#### REPRODUCIBILITY OF INSTRUMENTS AND PROBES

In this study three PC-based main units, four CMX probes, and three operators were evaluated to determine the reproducibility of each. All possible combinations of each element (system unit, slot number, and probe) were tested, for a total of 36 SOS measurements (3 system units x 3 slots x 4 probes). The reproducibility (CV) of the probes, for a given combination of system and slot ranged from 0.36% to 0.90% (0.29% overall). The reproducibility of the system units, for a given combination of slot and probe, ranged from 0.21% to 1.01% (0.13% overall). The reproducibility of the slots, for a given combination of system and probe, ranged from 0.18% to 1.01% (0.25% overall).

#### REPRODUCIBILITY OF OPERATORS AND PROBES

In this study three operators and four CMX probes were evaluated. Each operator measured the subject three times with each probe. As before, all possible combinations (probe and operator) were tested, for a total of 36 measurements (3 operators x 4 probes x 3 repeats). The reproducibility of the probes, for a given combination of operator and repetition number, ranged from 0.13% to 1.04% (overall 0.52%). Combining all repetitions for a single operator into one group, the probe CV for different operators ranged from 0.60% to 0.83%. The reproducibility for the operators, for a given combination of probe and repetition number, ranged from 0.19% to 0.80% (overall 0.35%). Combining all repetitions for a single operator into one group, the probe CV for different operators ranged from 0.54% to 0.64%.

#### REPRODUCIBILITY OF REPEATED MEASUREMENTS

In this study the distal one-third radius SOS of each subject was measured twice by three different operators. Probes were repositioned between each measurement. The CV was reported for all measurements, as well as stratified by operator and by menopausal status. The variance

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of each CV was also calculated so that 95% confidence intervals could be reported. Fifteen subjects were measured, 10 premenopausal women and 5 postmenopausal women.

Since there were 15 subjects measured by three different operators, a total of 45 pairs of repeated SOS measurements are available to assess the reproducibility of repeated measurements. The overall CV was 0.40% (95% CI: 0.39% to 0.41%). For pre-menopausal women the CV was 0.29% and for postmenopausal women the CV was 0.57%. A total of six different operators performed SOS measurements in this study. Their CVs ranged from 0.27% to 0.66%.

The coefficient of variation can also be calculated in two different "standardized CV" forms,  $SCV_1$  and  $SCV_2$ .  $SCV_1$  is computed by dividing the measured mean square error by 95% of the individual range, which is taken from the North America Normative Database (Section X.A.1 above).  $SCV_1$  was found to be 1.8%.  $SCV_2$  is computed by dividing the mean square error by the difference of the young healthy mean SOS (taken from the North America Normative Database) and that of the osteoporotic fracture mean SOS (the mean of the "All Fracture" group in the 202 Study).  $SCV_2$  is higher than  $SCV_1$ , and equals 5.9%.

Another measurement of precision is the standard deviation of the T-score (TSD), defined as the mean square error divided by the young health SOS standard error (taken from the North America Normative Database). In this study the TSD is 0.16 (16%).

## CONCLUSIONS

The *in vivo* precision (reproducibility), expressed by CV, for the Omnisense system when performing repeated SOS measurements of the Distal 1/3 Radius of the forearm was very good regardless of the ultrasound probe, the system, the probe connecting slots within each main unit, or the operator used to perform the measurement. Results indicated a high level of reproducibility regardless of the hardware used or the operator performing the measurements, and demonstrated a very narrow dispersion of the SOS measurement results.

The *in vivo* precision of repeated Omnisense measurements in the same subject is also extremely high, with a CV of 0.40%. There were some relative differences in CV between premenopausal and postmenopausal

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subjects. Differences in precision between premenopausal subjects and postmenopausal subjects have been found in DXA measurements (postmenopausal CV higher than premenopausal CV) as well as in QUS measurements of the calcaneus (postmenopausal CV lower than premenopausal CV). There were also differences between CVs measured by different operators. Nevertheless, all CVs were well below 1%, indicating good precision for all subgroups, and thus allowing for a meaningful assessment of patient status relative to the reference range.

The mean square error, about 17m/sec, is similar in magnitude to the average change per year which is observed during the first years of sharp decline in SOS post menopause. Thus, the Omnisense can provide precise estimates of bone status during this important time when bone changes are most pronounced.

### **1.8 Individualization of Treatment**

The Omnisense measures the Speed of Sound (SOS) in m/sec of an ultrasound wave that propagates along the bone. These results may be used by the physician, along with other factors such as laboratory test results, radiographs, life style, and family history in the diagnosis of osteoporosis and other conditions leading to reduced bone strength and bone fragility.

The following detailed information is intended to guide the physician on how to interpret the Omnisense results and its relationship to the currently accepted densitometry methods.

### **SOS RESULT, T-SCORE AND Z-SCORE - DEFINITIONS**

Any patient measurement result consists of three different parameters:

The absolute result of the measured Speed of Sound (SOS) expressed in units of meters per second (m/sec). For the purposes of the following definitions, the term young healthy population is defined as that age group in which bone mineral density (BMD) is at its peak (Kanis *et al.* 1997). For devices that show BMD to be constant between ages 20 to 40 it is typical to use the average value for ages 20 to 40 as the young healthy population reference value. However, Sunlight found that SOS was not constant between ages 20 and 40, but instead gradually increases starting at age 20 and reaches a peak at around age 40. Thus, the "young healthy population" mean is taken as the "peak bone SOS",

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which occurs at age 41 in the company's US Normative Database Study, based on averaging the population SOS values within a window 5 years above and below each age point. T and Z-scores are defined as follows:

- ◆ T-score - The difference between the patient's SOS result and the peak average SOS of young healthy population, in units of population standard deviation. Positive value means that the measured result is above the peak average SOS, while negative value represents a value which is lower than the peak average SOS. A value of  $T = -2$  means that the SOS of the patient is two population standard deviations below the peak average SOS.
- ◆ Z-score - The difference between the patient's SOS result and the average SOS of a population of the same age and gender in units of population standard deviation. A value of  $Z = +0.5$  means that the SOS of the patient is half a population standard deviation above the mean of her age-matched peers.

T and Z-scores provide additional information for bone assessment because they take into account both the mean and statistical distribution of population reference values. Those results, together with the patient's clinical profile, provide the physician with useful data on which therapeutic decisions can be based.

On the next page is an example of a patient report, showing the above results as measured by the Omnisense.

**[NOTE: The Sunlight Omnisense Measurement Report is not included in this file due to the diskette space required for the graphics. If required, this graphic will be supplied separately.]**

### **Bone Ultrasonometry and Fracture Risk**

The Omnisense-reported T-scores can be used to assess a patient's risk of osteoporotic fracture in a manner similar to that used in X-ray absorptiometry.

In 1994, a Study Group commissioned by the World Health Organization (WHO) has proposed clear guidelines for physicians diagnosing osteoporosis, based on T-scores:

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- a. Normal. T-score above -1.0.
- b. Osteopenia. T-score between -1.0 and -2.5.
- c. Osteoporosis. T-score below -2.5.

These cut-off values related initially to Bone Mineral Density (BMD) measured at the forearm. Nevertheless, they were shortly adopted for axial BMD measurements, including BMD of the spine and the hip, whereby the lowest value reported is usually considered for diagnostic purposes (Kanis *et al.* 1994).

The Omnisense sensitivity and categorization capability was found in various studies to be similar to those of hip and spine BMD, and it is therefore suggested that the WHO criteria be adopted and applied to the Omnisense-measured T-scores. The physician should, of course, consider other risk factors, such as low body weight, fracture history, family history, corticosteroids use, etc. in patient evaluation.

Concerning risk of fracture, research shows that the odds ratio of osteoporotic hip fractured to non-fractured subjects measured by the Omnisense is about 1.5. That means that a decrease of 1.5 T-score units corresponds to a 50% increase in the odds of hip fracture while a decrease of about 2.5 T-score units doubles the odds of hip fracture.

### **1.9 Patient Counseling Information**

Information for Patient Brochures are supplied with the Omnisense Bone Sonometer. These brochures give a brief summary of the importance of bone density testing and information about the Omnisense Bone Sonometer.

### **1.10 Conformance to Standards**

The Sunlight Omnisense™ Bone Sonometer conforms to U.S. and international standards, as described below, for safety, electromagnetic compatibility and acoustic output relative to ultrasound devices. The Sunlight Omnisense™ Bone Sonometer generates and emits ultrasonic energy. Emissions have been tested and found to be in conformance with the accepted standard limits for medical diagnostic devices of this type.

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Non-clinical testing demonstrated conformance to the following international standards:

IEC 60601-1 (EN 60601-1) Medical electrical equipment, Part 1: General requirements for safety.

IEC 60601-1-2 (EN 60601-1-2) Medical electrical equipment electromagnetic compatibility - Requirements and tests.

IEC 61157: 1993 Requirements for the declaration of the acoustic output of medical diagnostic ultrasonic equipment

NEMA, ID-2, revision 2: 1997 Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment

FDA Guide 510(k) Track 1 Measuring and Reporting Acoustic Output of Diagnostic Ultrasound Medical Devices (1985); and FDA 510(k) Guidance: "Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers" (September 30, 1997)

ISO 10993: 1992 "Biological evaluation of medical devices"

ISO 10993-1:1992 "Guidance on selection of tests"

ISO 10993-5:1993 "Test for cytotoxicity: in vitro methods"

ISO 10993-10:1994 "Test for irritation and sensitization"

The Sunlight Omnisense™ Bone Sonometer meets the provisions of the Medical Device Directive 93/42/EEC and has been certified by KEMA EC Notified Body (Identification number 0344) for CE Marking of Conformity of Medical Devices. Certificate number 87757CE01 issued by KEMA July 10, 1998.

Monitors, printers and other interfacing accessories used with the Sunlight Omnisense™ bone sonometer must meet IEC 601-1, IEC 950, UL 2601 or equivalent safety standards.

### **1.11 How Supplied**

The basic Omnisense packaging includes the following:

- ◆ Main Unit (230VAC or 115VAC),

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- ◆ Keyboard with integrated trackball,
- ◆ 14" color display monitor,
- ◆ Ultrasound probes according to order specification (each probe contains a set of transducers, some acting as transmitters and the others acting as receivers, housed tightly together in a compact holder),
- ◆ Foot Pedal,
- ◆ System Quality Verification Phantom,
- ◆ User's Guide,
- ◆ Power supply cable,
- ◆ Gauges for marking the region of measurement (according to the skeletal site order specification),
- ◆ Measurement accessories (according to the skeletal site order specification),
- ◆ Earphones,
- ◆ Starter Kit (see below).

Also, included as a Starter Kit:

- ◆ Multimedia Presentation including training,
- ◆ Acoustic contact gel bottles (250 cc each),
- ◆ Zip and 1.44MB Diskettes,
- ◆ Skin Marker,
- ◆ Screw Driver.

### ***1.12 Operators Manual***

Refer to Chapters 2 through 14 for the complete directions for use and maintenance of the Omnisense Bone Sonometer.

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### **1.13References**

Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, and Khaltsev N.  
"The Diagnosis of Osteoporosis." J Bone Miner Res 1994 Aug; 9(8):  
1137-1141.

Kanis JA, Delmas P, Burckhardt C, Cooper C, and Torgerson D.  
"Guidelines for Diagnosis and Management of Osteoporosis." Osteoporos  
Int 1997; 7:390-406.

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