

K954030

NOV 14 1997

SUMMARY

OF

SAFETY AND EFFECTIVENESS

Summary of Safety and Effectiveness

Indications and Inclusion Criteria

General Indications:

Bone-Lock implants may be used for every indication generally prescribed for dental implants; in fact, the design and materials of the Bone-Lock implants were chosen, after extensive study, for successful use in even the most difficult patients, such as tumor patients with grafted and/or irradiated bone.

Principally, every patient receiving implants should be integrated in a treatment concept that entails restoring the entire dentition. Implantation should only be carried out in motivated, cooperative patients with good oral hygiene. There is no limit in terms of age; in fact, better results can be achieved with older than with younger patients (Tetsch 1991, as referenced in Exhibit A, "Indication, Planning, and Clinical Procedure," p. 4). Young patients should not be given dental implants until the jaw has ceased to grow. Other alternatives should be considered for young patients, such as orthodontic gap closure, replantation, or modern prosthetic treatment (e.g. adhesive bridges). The minimum age for implantation should be set at 16 years. Prosthesis intolerance, regardless of age, is an important inclusion criterion. If despite proper functioning, conventional dentures jeopardize one's profession (e.g. speakers, singers, actors, and musicians), this aspect should also be taken into account in indicating implant treatment.

Local Indications:

A prerequisite for local indications is the vital and intact periodontium with good oral hygiene. The particular indications for the Bone-Lock system are those recognized by all the consensus conferences:

1. single-tooth replacement
2. insertion of additional posts
3. free-end situations
4. edentulous patients

Conditions that reinforce these indications include severe nausea or allergy to the plastic used for external prostheses.

Conditions for implant placement are considered ideal when the implants are covered on the lingual and buccal sides with a more than 1 mm thick layer of bone. Bone height under 1 cm in the interforaminal region is a contraindication for implantation as the sole treatment.

Contraindications or Exclusion Criteria

A distinction must be made between absolute and relative general contraindications and absolute

and relative local contraindications. Here it must be taken into account that very different combinations can arise in each particular case, which can strengthen the exclusion criteria, but also weaken them.

General absolute contraindications include

- age under 16 years
- disturbances of the hematopoiesis, of blood clotting, and of the endocrine system that cannot be compensated or substituted for
- therapy resistant cardiovascular disease
- malignant tumors with negative or fatal prognosis
- severe rheumatoid illnesses
- permanent disorders of the immune system (HIV, immunosuppression)
- severe changing or psychopathic personality

General relative contraindications or temporary exclusion criteria include

- allergies
- compensatable disease
- mild rheumatoid or psychological diseases
- general local infection
- acute disease
- convalescence
- pregnancy
- addition to drugs, tobacco, alcohol
- existing or anticipated psychological and physical stress

Local Absolute Contraindications

Implantation is prohibited in diseased segments of the jaw and when there is pain in the maxillofacial region of unknown origin. Implants are also contraindicated in the case of unclarified myoarthropathy, oral dyskinesia and hyperkinesia, as well as in patients with habitual occlusal and/or soft tissue parafunctions such as pressing or cheek-biting. Absolute contraindications also include acute or chronic maxillary osteomyelitis, therapy-resistant or progressive periodontopathy, bone deficits and maxillary defects that cannot be compensated for, unfavorable and unalterable topographic and anatomic conditions, and a lack of motivation to exercise good oral hygiene.

Local Relative Contraindications

Local relative contraindications include temporary bone deficits such as extraction wounds or cystic cavities, maxillary defects or topographically and anatomically unfavorable conditions such as a high emergence of a nerve or deficient alveolar bone in the maxilla which can be corrected by surgery. This also includes untreated occlusal, articulation, and bite anomalies, as well as drug-induced or treatable periodontopathy. Radiotherapy in the craniofacial region can carry certain risks when the implantation site is in the field of radiation. In such cases the implantations should be undertaken in special centers.

Device Description

Function

The Bone-Lock dental implant is a tapered screw with a cone angle of $2^{\circ} 30'$ that simulates the shape of the root of the tooth. Under axial load applied to the Bone-Lock dental implant, a greater load is seen on the anchoring bone in the area of the screw tip. However, because the screw is rounded, it transfers the mechanical forces over the entire surface area of the tip, and not just at certain points (see Exhibit A, "Basic Concept and Scientific Information," p. 7 and Exhibit E, Engineering Drawings). The optimized cone angle reinforces this effect (Bossler 1981, as referenced in Exhibit A, "Basic Concept and Scientific Information," p. 7).

Photoelastic analysis illustrates the load-bearing conditions of the Bone-Lock system compared to other dental implants under axial load. Starting from the tip, the load on the anchoring bone towards the screw neck region decreases by one ordinal number per thread pitch (ibid., p. 7, fig. 4). The isochromatic lines illustrate a thread pattern with decreasing ordinal numbers starting at the thread crest towards the core of the screw. In contrast to the Heinrich screw, for example, the strain decreases 0.5 to 3 ordinal numbers at the most, depending on the stress, but without showing load-free anchor zones. This yields the following state in the area of the thread: the anchoring material at the crest of the thread is subjected to strong mechanical load. Though inside the thread this mechanical load is only slightly weaker (decreasing), shear forces are far weaker than with implants with load-free zones on the threads or steps (ibid., p. 7, fig. 5). Due to the special design of the screw thread, the axial pressure is transferred not only over the tip of the implant and the outer edges of the thread, but also over its entire surface. This can be seen by the course of the isochromatic lines in the threads. They course at an angle that opens upwards towards the core of the screw. Placing a secant on the thread profile parallel to the isochromatic lines results in a point of minimal load within one thread pitch. If a line is placed through this point perpendicularly to the isochromatic lines, the approximate direction of stress can be depicted, which runs from the body of the screw diagonally downwards and outwards. The base of the thread is thus subjected to load such that it can be supported by the outside anchoring tissues and its load-bearing properties are not overtaxed. Shear strains occur parallel to the secant, the existence of which are indicated by the decreasing isochromatic ordinal number in the threads. The special form of the thread, however, prevents shearing forces from dominating, since there are no load-free spaces with low ordinal numbers (ibid).

If the force is induced at an angle of 45° , the neck region is subjected to the most mechanical load. A zone of uniform load on the two sides of the screw is noticeable, however, the ordinal number on the compression side of the screw is higher (7) than on the tensile side (2), which is subjected to only minimal mechanical load. The tip of the screw is subjected to less load than at the axial pressure point. The center of load is located at the point where the first thread pitch starts. Most of the horizontal tensile load is transferred from the implant to the neck region. The remainder of the screw profile is subjected to almost uniform load over its entire contour. No similar balance of compression and tensile stress was achieved with any other implant in the study.

In summary, it can be said that the Bone-Lock implant in its final form exhibits the most balanced photoelastic behavior of all screw-shaped implants tested. A full description of the mechanical design of the Bone-Lock dental implant can be found in the product brochure entitled "Basic Concept and Scientific Information", Exhibit A.

Materials and Coating

Leibinger's Bone-Lock endosseous implant system is pure titanium. The endosteal section, i.e. the root and subgingival portion of the transgingival section, is coated with semi-conductive titanium-zirconium-oxide (Ti, Zr) O, and the supragingival part of the connecting component (transgingival section) is coated with titanium-niobium-oxinitride (Ti, Nb) ON. The (Ti, Zr) O layer - aside from surface deviations - is composed approximately of 35 atomic percent (at%) titanium, 15 at% zirconium, and 50 at% oxygen. Similarly, the (Ti, Nb) ON layer is approximately 33 at% titanium, 23 at% niobium, 41 at% nitrogen, and 3 at% oxygen. The advantage of the addition of Niobium and Zirconium is the high formation enthalpies of the oxides, which are higher for Niobium and Zirconium than for titanium and contribute to the chemical long-term stability of the coating material. A full description and the benefits of these coating materials is given in the product brochure entitled "Scientific Documentation", Exhibit A. A listing of all components and materials can be found in Exhibit D.

Manufacturing

The Bone-Lock Implant is manufactured and packaged at Leibinger GmbH, Bötzingen Straße 41 D-79111 Freiburg Germany. The facility is ISO 9001 certified; all processing and storage practices are executed in accordance with a comprehensive quality system (see Exhibit G).

Alternative Practices and Procedures

Single tooth replacement, free end situations, partially edentulous and edentulous patients can in most instances be treated with traditional prostheses such as bridges, partial dentures and full dentures. Conditions that contraindicate these more traditional approaches include severe nausea or allergy to the plastic used in the construction of these prostheses and clinical situations, such as lack of ridge height for stability of the denture. In addition, the lack of other stable teeth as abutments will in some cases mandate the use of implants to fully reconstruct the area. Also, many patients simply prefer the security and appearance of endosseous implants.

Marketing History of the Device

Bone-Lock has received the CE mark (see Exhibit G) and is currently marketed in the following countries and has not been withdrawn from these markets at any time:

Germany	Austria
Ireland	Italy
Belgium	U.A.E.
France	South Korea
Switzerland	Australia
Portugal	Russia

To date, the published scientific articles concerning the Bone-Lock dental implant have shown favorable results with the use of this implant (see Exhibit C).

Summary of the Nonclinical Laboratory Study

Photoelastic analysis comparing the Bone-Lock implants with IMZ implants, Frankfurt extension implants, and Linkow blades was used to investigate the distribution of forces by the implants. The Bone-Lock implants exhibited the most balanced photoelastic behavior of all screw-shaped implants in the study. (For further details see Exhibit A, "Basic Concept and Scientific Information, pp. 5-8).

Reference Exhibit C for the study "Biomechanical Testing of the Bone-Lock Implants to Evaluate the Stability of the Bone-Implant Bond," describing mechanical performance.

Summary of Animal Experimental Investigation

A two year study was conducted in six 14 month old beagle dogs using 48 implants, 16 each of titanium, vitallium, and Al_2O_3 ceramic placed under identical functional load-bearing conditions.

The macroscopic analyses revealed no essential differences among the various implant bodies. Microscopic analysis (microradiography) showed that the surrounding bone tissue had grown closely to the surface of all implants. Scanning electronmicroscopy and transmission electron microscopy of the unpolished surface of the titanium screw showed an even structure with single cells adhered evenly to the metal surface. The concave area of the thread was covered with a closed layer without any intermediate soft tissue.

In general, the implanted screws healed without complication, with direct contact between bone and fixture at the tip of the thread. Cellular elements are present on the implant shoulder and more at the concavity of the thread. Fiber formation can be seen in some places. Increased resorption processes in the anchoring bone were not observed with any of the implants examined. In the comparison of the various materials, only subtle graduations could be perceived, which were purely subjective. (For further details, see Exhibit A, "Basic Concept and Scientific Information," pp. 9-13).

Summary of Clinical Investigations

Within the scope of a regular three-month recall carried out between July 1988 and December 1993 at the Department of Oral-Maxillofacial Surgery at the University of Würzburg, inserted implants were subjected to follow-up examinations. The study encompassed 174 patients with a total of 585 implants. Particular attention was paid to parameters for the assessment of periimplant soft tissues and their influence on the chances of success for endosseous implants. Study details are presented in Exhibit A, "Scientific Documentation," pp. 28-36.

Case Material

During the specified period, 174 patients were fitted with a total of 585 implants. 13 patients with 48 implants were lost to follow up, 8 patients with a total of 32 implants have since died. The regular recall scheme thus encompasses 153 patients with a total of 505 implants. 50.6% of patients were female, the average age at the time of implantation was 53.6 years (minimum age 16.6 years, maximum age 78.5 years). The quantitative distribution according to indication fields is indicated by the graph below (Fig. 1, as presented in Exhibit A, "Scientific Documentation," p. 28).

Single tooth:	41 implants (7.0 %)
Tooth gap:	73 implants (12.8 %)
Toothless jaw:	393 implants (67.2 %)
Free end:	78 implants (13.3 %)

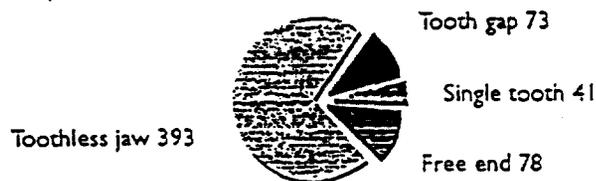


Fig. 1: Quantitative distribution according to indication fields

492 implants (84.1%) had a diameter of 4.5mm, 93 (15.9%) a diameter of 3.5mm. On average, the patients received 3 implants each. 481 (82.3%) implants were inserted in the lower jaw, 104 (17.8%) in the upper jaw. 47 patients (27.0%) of the entire case material were treated with a total of 201 implants (34.4%) as part of a rehabilitation program to restore chewing capability following tumor treatment. Fig. 2 (as presented in Exhibit A, "Scientific Documentation," pp. 28-29) provides a survey of the quantitative distribution of inserted implant length.

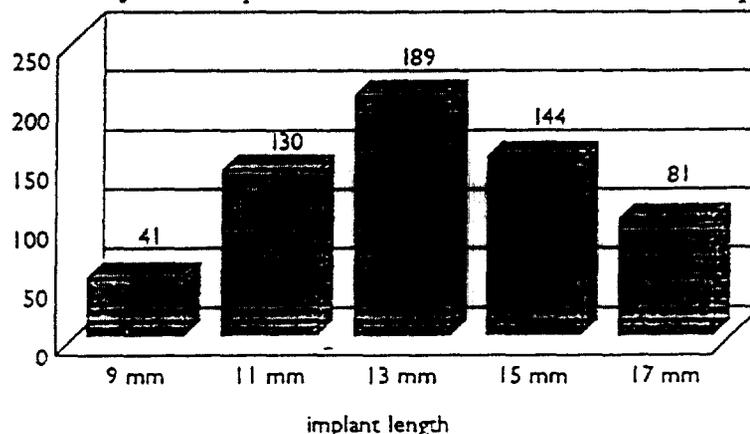


Fig. 2: Quantitative distribution according to implant length

The basis for the study of the periimplant soft tissue situation following the implant of endosteal Bone-Lock implants is formed by data taken from the 118 patients fitted with a total of 375 prosthetic implants over a period of 1, 2, 3, 4 and 5 years within the framework of follow-up examinations. The remaining thirty-five patients either were not prosthetically treated or had their prosthetics in place less than one year at the time the study was compiled.

Duration of Exposure

40 patients (33.9%) were fitted with prostheses for one year, 27 patients (22.9%) for two years and 22 (18.6%) for three years, 12 patients (10.2%) for four years and 17 patients (14.4%) for five years.

Tumor Patients

32 patients (27.1%) of the study-specific case material were tumor patients. 25 had suffered an epithelioma in the mucous membrane of the oral cavity, while 1 patient had cystic ameloblastoma of the lower jaw and 1 patient suffered a malignant degenerated giant-cell granuloma in the area of the basis mandible. Following resection of the tumor, reconstruction was carried out in 19 patients using a free iliac crest graft, in 3 patients using a microvascularly reanastomized scapula graft and in 1 patient with a rib graft. In 20 of these patients, defects in the mucous membrane of the oral cavity were covered using a graft taken from the small intestine. A cutaneous muscle graft from the Pectoralis major was used on three occasions to cover intraoral defects, while on one occasion a split skin graft was used. Insertion of the dental implants was effected using secondary surgery either during removal of the metal fixation for the bone grafts or in a separate operation. On average, 4 implants were inserted per patient. Rehabilitation of the chewing function was carried out in 16 patients using a telescopic double-crown prosthesis, in 8 patients using a dolder-bar prosthesis, in 7 patients with a detachable bridge, and in 1 patient with a ball-attached prosthesis.

Comparison of Periimplant Parameters in Tumor and Non-tumor Patients

The mean parameter values of the two patient groups were statistically evaluated using the U test according to MANN and WHITNEY. Tumor patients demonstrated significantly poorer values in the Hygiene, Gingiva and Sulcus Index as well as the Pocket Probing Depth. Despite the overall less favorable periimplant situation in tumor patients, conditions among this group from the point of view of bone resorption were slightly more favorable than among non-tumor patients.

This experience was backed up by the success rate, which in tumor patients with an implantation time of at least 365 days was 95.1% as against 90.6% in normal patients. Fig. 9 (as presented in Exhibit A, "Scientific Documentation," p. 35) provides a comparison of mean periimplant soft tissue parameter values for tumor and non-tumor patients (observation period 3 years).

Parameter	Tumour	Non-Tumour	Probability
Hygiene Index	69.0 ± 38.9%	19.8 ± 31.4%	p = 0.002***
Gingiva Index	1.2 ± 0.8	0.3 ± 0.6	p = 0.003***
Sulcus Bl. Index	0.9 ± 0.5	0.3 ± 0.6	p = 0.008***
Pocket probing depth	5.1 ± 2.6 mm	3.4 ± 1.3 mm	p = 0.006***
Bone resorption	0.6 ± 0.4 mm	0.7 ± 0.5 mm	p = 0.01***

Fig. 9: Comparison between periimplant parameters in tumour and non-tumour patients

Success Rate

Data taken from the 346 implants which underwent regular follow-up examinations in the recall scheme was evaluated to ascertain the success rate. The average success rate over all indication groups was 92.2%, as shown in Figure 10 (as presented in Exhibit A, "Scientific Documentation," p. 35).

Indication	Implants (Normal/tumour)	Explants (Normal/tumour)	Success rate (Normal/tumour)
Individual prosthesis	19 (19/0)	3 (3/0)	84.2% (84.2/-)
Free end	37 (27/10)	2 (2/0)	94.6% (92.6/100)
Tooth gap	41 (19/22)	2 (1/1)	95.2% (94.7/95.5)
Toothless jaw	249 (158/91)	20 (15/5)	92.0% (90.5/94.5)
Total	346 (223/123)	27 (21/6)	92.2% (90.6/95.1)

Fig. 10: Indicates the breakdown of this success rate according to indication fields and according to tumour and non-tumour patients

Discussion

Assessment of the oral hygiene situation according to O'LEARY'S Hygiene Index resulted in a good average standard of oral hygiene of HI 28.9% among our case material. Over the course of the 5-year observation period, oral hygiene by the patient demonstrated a tendency towards improved care. Corrosion and wear-resistant implant materials demonstrate a less pronounced plaque deposit. The positive oral hygiene situation among our case material is a confirmation of the plaque deposit-inhibiting effect of Titanium Niobium Oxynitride in the supragingivally positioned section of the transgingival intermediate element of Bone-Lock implants. Deposits of microbiological plaque lead to inflamed alterations of the soft tissue surrounding implants as in

natural teeth. Our study revealed a highly significant correlation between plaque accumulation (HI) on the one hand and the degree of inflammation in the periimplant soft tissue (GI, SBI) on the other hand. With a mean Gingiva Index of 0.52 and Sulcus Bleeding Index of 0.81, our patients demonstrated a good, inflammation-free mucous membrane situation. Within 5 years, the values demonstrated a tendency toward increasing indices, underlining the demand for constant re-motivation and re-instruction.

The mean pocket probing depth was 3.7 ± 1.8 mm. Enlarged pocket depths were related in our study to pronounced symptoms of inflammation and greater bone resorption. Within the 5-year observation period, the probing depth increased significantly. Significantly greater pocket probing depths were detected where no or only small proportions of attached gingiva were available. The average width of attached gingiva in our study was 2.4 ± 1.6 mm. However, no correlation was discovered between the width of the attached gingiva and bone resorption. With very good oral hygiene levels, therefore, a positive long-term result can be achieved despite the absence of keratinized gingiva. The average values for periimplant bone resorption (1st year 1.2mm, 2nd year 0.7mm, 3rd year 0.4mm) are comparable to specifications for other implant systems.

With the exception of bone resorption, tumor patients in our study demonstrated poorer values overall for the periimplant parameters. The often lower socioeconomic level combined with lack of cooperation and poor oral hygiene tend to inhibit oral rehabilitation. The explanation for the more favorable resorption values for the periimplanted bone may be connected with the "physiological" stress on the transplanted bone sections. A surprising result is the markedly improved expectation of success among tumor patients at 95.1% as against 90.6% in normal patients.

The mean success rate of 92.2% following an implantation time of >365 days is consistent with expectations familiar from other well documented implant systems.

Discussion of Other Studies and Published Scientific Articles Concerning Bone-Lock

Included in our product brochure is the Scientific Documentation from the University Hospital and Polyclinic for Dental, Oral-Maxillofacial Surgery, University of Würzburg, which describes both the clinical evaluation of the Bone-Lock implant, and the research of the properties of (Ti, Zr) O and (Ti, Nb) ON coatings on titanium (Exhibit A, "Scientific Documentation").

In addition, the following published articles are included, describing the Bone-Lock implant both in terms of clinical usage and biomechanical evaluation:

- A) "Biomechanical Testing of the Bone-Lock Implants to Evaluate the Stability of the Bone-Implant Bond." M. Erbe, R. Kettner, H.J. Schmitz - Zahnärztl. Implantol. 10, 32-36 (1994). (see Exhibit C)
- B) "Masticatory Rehabilitation with the Bone-Lock Implant System in Mandibular Defects Caused by Tumors." H.P. Howaldt, A. Kovacs. (see Exhibit C)

- C) "Evaluation Regarding the Sterilizability of the Newly - Developed Endosteous Implant System." B. Guggenheim. Department of Oral Microbiology and General Immunology, Dental Institute, University of Zurich, June 1990. (see Exhibit F)

A complete bibliography list in German and English can be found in Exhibit H.

Substantial Equivalence

The Bone-Lock Endosseous Implant is substantially equivalent to the following systems that are currently marketed in the United States:

- 1) Steri-Oss Threaded Titanium Implants
- 2) Bud Dental Implants
- 3) Nobelpharma/Branemark Dental Implants

Comparison Table

	<u>Material</u>	<u>Diameter</u>	<u>Length</u>	<u>Design</u>
<u>Steri-Oss</u>	Titanium	3.8-4.5mm	8-18mm	Threaded
<u>Bud</u>	Titanium	3.25-3.75	4-15mm	Threaded
<u>Branemark</u>	Titanium	3.75-4.0	7-20mm	Threaded
<u>Bone-Lock</u>	Titanium	3.5-4.5	9-17mm	Threaded

See Exhibit B for predicate device labeling.

Concerning the usage of niobium and zirconium coatings on the transgingival and implant portions of the Bone-Lock Endosseous Implants applied with a physical vapor deposition, we feel that these do not present any new safety issues as both the materials and method of application are documented in the scientific literature referred to in the Attachments, and their safety and efficacy have been extensively tested as described herein.



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Kristyn R. Waski
Quality Assurance & Regulatory Affairs Engineer
Howmedica Leibinger Incorporated
Pfizer Hospital Products Group
14540 Beltwood Parkway East
Dallas, Texas 75244

NOV 14 1997

Re: K954030
Trade Name: Bone-Lock® Endosseous Implant
Regulatory Class: III
Product Code: DZE
Dated: August 15, 1997
Received: August 18, 1997

Dear Ms. Waski:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does

not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4618. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



Timothy A. Ulatowski
Director
Division of Dental, Infection Control
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure