

FDA Executive Summary

Prepared for the
July 18, 2013 meeting of the
Dental Devices Panel

Classification for Endosseous Dental Implants
(Blade-form) [21 CFR 872.3640(b)(2)]

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1. Introduction

Per Section 513(b) of the Food, Drug, and Cosmetic Act (the FD&C Act), the Food and Drug Administration (FDA) is convening the Dental Products Advisory Panel (the Panel) for the purpose of obtaining recommendations regarding reclassification of blade-form endosseous dental implants [21 CFR 872.3640(b)(2)].

Blade-form endosseous dental implants intended for the treatment of edentulous sites in the mandible or maxilla for restoration of chewing function as defined under 21 CFR 872.3640(b)(2), hereinafter referred to as “blade-form implants” are one of the remaining preamendments Class III medical devices currently cleared for marketing through the premarket notification [510(k)] pathway.

FDA is holding this panel meeting to obtain comments and recommendations from the Panel regarding whether blade-form implants should remain in Class III (subject to premarket approval application [PMA]) or be reclassified to Class II (subject to premarket notification [510(k)s]). The Panel will be asked to provide input on the risks to health and benefits of blade-form implants. The panel will also be asked to discuss the FDA’s proposed reclassification strategy for blade-form implants based upon the available safety and effectiveness information. FDA believes that these devices can be reclassified into class II (Special Controls) because special controls, in addition to general controls, can be established to provide reasonable assurance of the safety and effectiveness of these devices. If the Panel believes that Class II is appropriate for blade-form implants, the Panel will also be asked to specifically comment on the adequacy of the proposed special controls to mitigate the identified risks to health.

1.1. Current Classification

As currently defined in 21 CFR 872.3640:

(a)*Identification.* An endosseous dental implant is a device made of a material such as titanium or titanium alloy, that is intended to be surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, in order to restore a patient's chewing function.

(b)*Classification.* (1) Class II (special controls). The device is classified as class II if it is a root-form endosseous dental implant. The root-form endosseous dental implant is characterized by four geometrically distinct types: Basket, screw, solid cylinder, and hollow cylinder. The guidance document entitled "Class II Special Controls Guidance Document: Root-Form Endosseous Dental Implants and Endosseous Dental Implant Abutments" will serve as the special control. (See 872.1(e) for the availability of this guidance document.)

(2) Class III (premarket approval). The device is classified as class III if it is a blade-form endosseous dental implant.

It should be noted that this classification regulation is currently split between Class II and Class III. The focus of this panel today is only on part (b)(2) of the classification regulation. Any modifications to part (b)(1) would be subject to a different regulatory process.

Blade-form implants are currently reviewed through the 510(k) pathway, and are allowed onto the market if their indications for use and technological characteristics are determined to be “substantially equivalent” to a legally marketed predicate device. There are 4 total submissions for blade-form implant devices that FDA has found to be substantially equivalent (first in 1979).

1.2. Device Description

1.2.1. Blade-form Endosseous Dental Implants

The blade-form implant is a device placed into the maxilla or mandible and composed of biocompatible material, such as titanium alloy or commercially pure titanium, with sufficient strength to support a dental restoration, such as a crown, bridge, or denture, intended for the purpose of replacing tooth (or teeth) roots and extending a support post through the gingival tissue into the oral cavity to restore chewing function.

The blade-form implant is generally a rectangular shape or rounded corner rectangle shape (in the mesio-distal plane) with a narrow tapered (narrow at the apical edge) edge (in the bucco-lingual plane) similar in shape to a razor blade. Other blade designs, such as square, V-shaped, and triangles have also been used. The blade generally contains open vents of various shapes and various sizes. Traditionally marketed blade-form implants had a blade width of 1 to 3.25mm, a blade depth of 5 to 21mm, and a blade length of 4 to 36mm.

The blade-form implants are either one-piece or two-piece implants designed with one to three cylindrical abutment posts extending from the coronal aspect of the blade through the soft tissue and into the oral cavity. For the two-piece design, the separate abutment post is retained to the blade implant with a screw.

The blade-form implant as described in the four cleared 510(k)s contains only an as-machined titanium surface with no additional surface treatments or modifications.

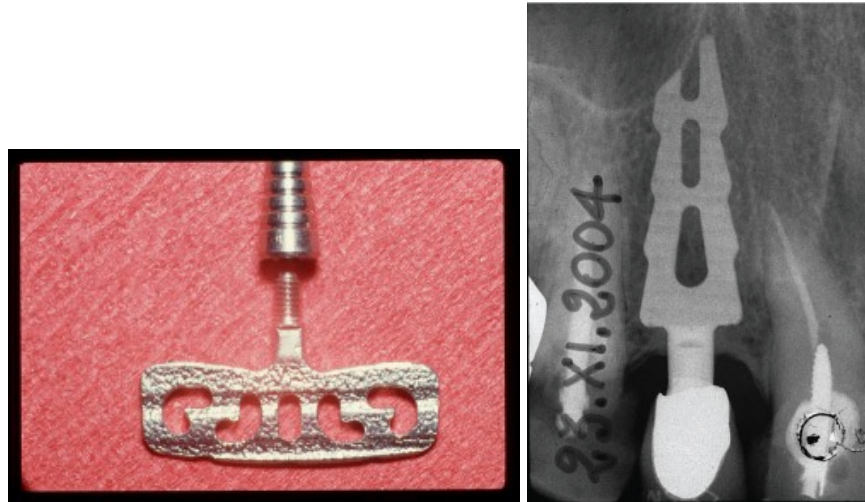


Figure 1 – Examples of blade-form endosseous dental implants (<http://www.dental-vacation.com/wordpress/?p=252>) (<http://www.oapublishinglondon.com/article/390>)

1.2.2. Ramus Frame Blade-form implant

A ramus frame blade-form implant is a sub-set of the blade-form implant specific to the mandible and fully edentulous patients. A ramus frame is a full arch, supra-mucosal bar with an implanted blade at each end which are placed in the retro-molar area of the ramus of the mandible and is supported by a single blade in the anterior of the arch.



Figure 2 – Ramus frame blade-form implant (<http://www.indianhealthguru.com/dental-implants-India-low-cost-benefits.html>)

1.2.3. Distinction between Root-form and Blade-form Endosseous Dental Implants

There are two types of endosseous dental implants: Root-form and Blade-form. Root-form implants is defined in 21 CFR 872.3640(b)(1) as a endosseous dental implant with one of four geometrically distinct types: basket, screw, solid cylinder, and hollow cylinder. All four root-form types are similar in that they

possess a cylinder or conical shape and fill the space left by removed tooth roots in the maxilla or mandible.

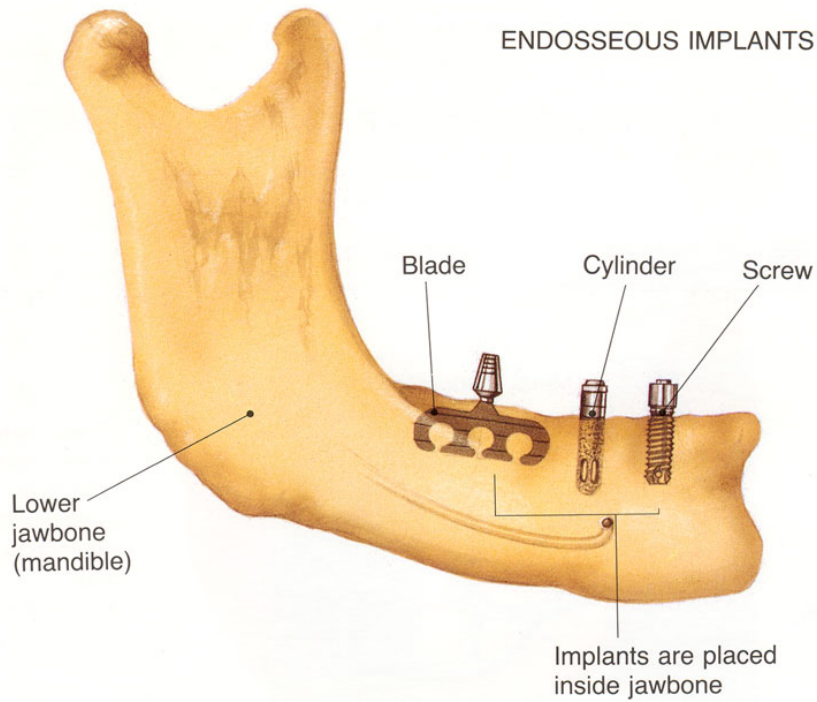


Figure 3 – Comparison of endosseous dental implants
(http://dentalimplants.uchc.edu/images/about_implants/image_page19_endosseous.jpg)

An additional distinction between blade-form and root-form implants is found in the directions for use or surgical manual. The direction for blade-form implants may include specific instructions for bending the abutment post or a one-piece implant design for the purposes of angle correction. Also, the directions for use of previously cleared devices reference cutting or bending the blade portion of the blade-form implant to fit the edentulous site and prepared osteotomy shape, e.g. anterior jaw sites.

Root-form endosseous dental implants are already classified as Class II devices and outside the scope of the panel's discussion today.

2. Regulatory History

A brief summary of the regulatory history for endosseous dental implant (blade-form) devices is provided within this section.

2.1. 1980 Proposed Rule and 1991, 1997 and 1998 Classification Panel Meetings

FDA established several advisory committees to make preliminary recommendations on dental device classification. The 1998 Dental Device Classification Panel, hereinafter referred to as “the Panel,” recommended splitting the classification for Endosseous dental implant devices. Endosseous dental implant devices that are “root-form”, characterized by four geometrically distinct types (basket, screw, solid cylinder, and hollow cylinder), were recommended to be Class II. Endosseous dental implants devices that are “blade-form” were recommended to be Class III. The Panel members at the Panel and Subcommittee meetings of October 24, 1991, November 4, 1997, and January 13, 1998 discussed these devices.

It was stated by the January 13, 1998 Panel that the clinical data demonstrating safety and effectiveness of the blade-form implants had not been presented to the panel to justify reclassification to Class II in contrast to the root-form endosseous dental implants for which a remarkable amount of information had been obtained since the 1991 panel meeting.

2.2. 1980 Classification Proposed Rule, 1991 & 1998 Dental Products Board Reclassification Panel, 2002 Classification Final Rule

Following the classification panel meetings, the FDA published a proposed rule on December 30, 1980 (45 FR 86025) for classification of endosseous dental implants (blade-form as well as root-form) as Class III requiring premarket approval with the following identification:

“An endosseous implant is a device of a material, such as titanium, that is surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, and to restore the patient’s chewing function.”

The panel recommended Class III because the device is implanted in the body and presents a potential unreasonable risk of illness or injury including risks of abnormal spontaneous pain due to nerve impingement and a risk of perforation of the lingual and labial bony plates of the upper and lower jaws.

The Agency agreed with the Panel that insufficient information existed to determine that general controls would provide reasonable assurance of the safety and effectiveness of the device and that insufficient information existed to establish a performance standard to provide this assurance. On August 12, 1987 (52 FR 30082), a final rule was published for endosseous dental implants (without subdividing based on geometry) classifying these devices as Class III.

On December 7, 1989 (54 FR 50592), the FDA published a proposed rule to require PMA submissions for all dental implants. A reclassification petition was subsequently submitted on December 12, 1989, by the Dental Implant Manufacturers

Association (DIMA) requesting reclassification of dental implants. The FDA held reclassification panel meetings on October 24, 1991, and the panel voted to deny the reclassification petition. At the request of the FDA, additional panel meetings were held on November 4, 1997, and January 13, 1998, during which the FDA presented new information regarding root-form endosseous dental implants. During the January 1998 panel meeting, the panel stated that sufficient clinical information was presented to the panel to justify reclassification of root-form implants, implants with special retention features, and temporary implants, as Class II (Special Controls) requiring a premarket notification [510(k)]. However, the panel also stated that sufficient evidence with respect to the blade-form dental implant (including Ramus type implants) had not been presented to the panel even though it was stated by the public that sufficient evidence was available in the literature and from use of the blade-form implant in Europe. The panel did not discuss any specific concerns related to retaining blade-form implants in Class III, but instead stated that sufficient evidence had not yet been presented to reclassify blade-form implants to Class II.

In response to the January 1998 panel statement that sufficient evidence for blade-form dental implants had not been provided, additional information was provided on July 13, 2001 and December 20, 2001, respectively. This information was provided to the FDA outside of the classification docket.

On May 14, 2002 (67 FR 34416) and May 12, 2004 (69 FR 26032) respectively, proposed and final rules were issued reclassifying only root-form implants into Class II. Blade-form endosseous dental implants remained Class III, however, the proposed rule requiring PMA submissions was not finalized, and blade-form implants remained class III 510(k) devices.

2.3. 2009 515(i) Notice for Remaining Class III Preamendments Devices

On April 9, 2009, pursuant to Section 515(i) of the FD&C Act, FDA published a 515(i) notice in the Federal Register that applied to the remaining preamendment Class III 510(k) device types, as the first step in finalizing the classification process. Included in this group of devices were Endosseous Dental Implants (Blade-form) as defined under 21 CFR 872.3640(b)(2). Manufacturers were required to submit information concerning the safety and effectiveness of these devices.

The April 9, 2009 Federal Register Notice [Docket No. FDA-2009-M-0101] requiring safety and effectiveness information from industry, to support either a reclassification of blade-form implants or to require a PMA submission, received responses from one sponsor (TMJ Implants, Inc.). The TMJ Implants, Inc. response stated that the company does not currently manufacture blade-form endosseous dental implant but wanted to provide information regarding four devices marketed before 1976 which the company may market in the near future. These four devices, as described, are not actually blade-form endosseous dental implants. TMJ Implants, Inc. did not provide any information relevant to blade-form endosseous dental implants

2.4. 2013 Proposed Order to Require Premarket Notification for Blade-form implant devices

On January 14, 2013 (78 FR 2647), FDA published a proposed order proposing to reclassify blade-form implant devices. In this order, FDA has proposed

“that the device subject to this proposal be reclassified from class III to class II. In this proposed order, the Agency has identified special controls under section 513(a)(1)(B) of the FD&C Act that, together with general controls applicable to the devices, would provide reasonable assurance of their safety and effectiveness. FDA believes that the identified special controls in this proposed order, if finalized, together with general controls applicable to the device, would provide reasonable assurance of safety and effectiveness. Absent the special controls identified in this proposed order, general controls applicable to the device are insufficient to provide reasonable assurance of the safety and effectiveness of the device.”

3. Responses to the Docket for the 2013 Proposed Order

The proposed order provided for a 90-day comment period that was open until April 14, 2013. FDA received 2 comments to the docket. The comments are available at the following address: <http://www.regulations.gov/#!docketDetail;D=FDA-2012-N-0677>.

If the comments included relevant references, these references were checked against the list of references used in the literature review to determine if they had been considered as part of the Agency’s assessment.

None of the comments openly stated an opinion, but did include statements for the proposed order that could reasonably be interpreted as support for a Class II designation. Both comments were received from dentists.

4. Indications for Use

A necessary component of a device description and labeling is an indication for use (IFU) statement. The IFU identifies the condition and patient population for which the device should be appropriately used, and for which the device has demonstrated a reasonable assurance of safety and effectiveness. 21 CFR 872.3640(a) defines an endosseous dental implant as “*An endosseous dental implant is a device made of a material such as titanium or titanium alloy, that is intended to be surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, in order to restore a patient’s chewing function.*”

There are slight variations on the indications for use of the devices that have been found substantially equivalent through the 510(k) process. It was not until 1996 that FDA began to use an official indications for use page, so it is difficult to ascertain the precise statement for blade-form implant cleared prior to 1996. These 510(k)s for blade-form implants generally describe the device with references which include “for insertion into oral bone”, “for the maxilla or mandible”, “substitute for the roots of the teeth replaced”, or “functions

as an attachment of a dental bridge. There is one blade-form implant cleared by FDA with an official indications for use page which states “Blade-form endosseous dental implants are intended for use in the edentulous sites in the mandible or maxilla for support of a complete denture prosthesis, a terminal abutment or intermediate abutment for fixed or partial dentures, or a single tooth replacement.”

As part of our classification process, we consider all of the devices included within 21 CFR 872.3640(b)(2) that have been found to be substantially equivalent as part of the device type.

5. Clinical Background

5.1. Conditions

5.1.1. Full or Partial Edentulism

Teeth may be lost due to diseases of the periodontium resulting in bone loss and eventual tooth loss; trauma causing exfoliation, fracture, or non-restorable damage to teeth, as well as primary or secondary dental caries rendering the tooth nonrestorable. Teeth may also be congenitally missing.

Teeth transmit masticatory stresses to adjacent alveolar bone. These stresses maintain the alveolar bone in a manner following Wolff’s Law where form follows function. When the alveolar bone is not stressed, or teeth are lost or removed, the alveolar bone loses this stressing and begins to resorb. The parts of the mandible and maxilla that house teeth can resorb to the point where only maxillary and mandibular “basal bone” remains.

Prior to dental implant placement, alveolar bone resorption generally results in a thinner and shorter alveolar process, depending on the amount of time the alveolar process remains unstressed. Thinner alveolar processes are harder to restore functionally and aesthetically because there is less bone present into which dental implants can be placed.

To augment the alveolar process in preparation for dental implant placement, bone grafting may be performed. Bone grafting may be used as a ridge preservation measure and also at the time of implant placement. Implants may transmit occlusal stresses to the alveolar bone, minimizing the amount of alveolar bone lost over time.

5.1.2. Alternative Restorative Measures

The restoration of masticatory function is achieved by prosthetic restoration of missing teeth. This may be accomplished with the placement of fixed or removable partial or full dentures, or endosseous dental implants.

Dental bridgework, also known as fixed bridgework or fixed partial dentures, has been used for many years, and is quite successful. The main drawbacks to

the use of fixed bridges are recurrent caries and the destruction of good tooth structure needed to create space for aesthetic and functional bridge material to be placed. Recorded use of fixed partial dentures date back to the ancient Egyptians. At the present time, the use of partial dentures has been reduced with the advent of dental implants. Partial dentures are removable for daily cleaning and clasp teeth for retention. There is minimal tooth structure removal.

Unlike fixed bridges, removable partial dentures can be removed daily for cleaning and to permit the tissues under them to “breathe”. Less than meticulous cleaning of teeth and removable partial dentures can facilitate recurrent caries, and if not properly made, can cause the loosening of teeth.

Like the use of partial dentures, removable full dentures (tissue supported) have a long history. They are intended to replace all of the teeth in the maxillary or mandibular arches. Full dentures do not transmit masticatory stresses to the alveolar process, and therefore are associated with a progression of bone loss over time. This requires intermittent relining of the dentures. Eventually, full dentures become so loose that they are almost non-functional. Some patients may not adapt well to full dentures.

6. Systematic Literature Review on Blade-form implants

The FDA conducted a systematic literature review to assess the safety and effectiveness of blade-form implant by analyzing the existing clinical literature from 1990 to the present to generate clinical information subsequent to the 1989 classification panel recommendation and FDA’s concurrence to deny a reclassification petition for any form of endosseous dental implant. Some pre-1990 references were also included as they were provided to the FDA independent of the literature search.

We sought to address the following question:

1. What is the evidence for safety and effectiveness of blade-form implant for the treatment of replacing teeth in partially or fully edentulous patients for restoration of chewing function?

6.1. Methods

The following three literature searches were performed, which yielded a total of 95 articles related to blade-form endosseous dental implants:

- On December 20, 2001, 10 citations were provided by to the Dental Devices Branch
- On July 31, 2001, 42 citations were provided to the Dental Devices Branch in support of reclassifying blade-form endosseous dental implant as Class II along with root-form endosseous dental implants.

- In September 2011, a literature search for published clinical data related to blade dental implants was conducted between the years of 1990 and May 2010. The limit of 1990 was set due to the panel meeting in 1989, which rejected the petition to down-classify dental implants (both root-form and blade-form) from Class III to Class II. The primary strategy involved the search of published literature in: PubMed, Academic Search Complete, Alt Health Watch, Cambridge Scientific Abstract, CINAHL, Embase, ScienceDirect, and Web of Science (WOS), using the following terms:
 - “dental blade implant” or “dental blade implants” or
 - “blade implant” or “blade implants”
 - “dental blade endosseous” or “dental endosseous”
 - “surface treatment”
 - “tooth implantation/syn”

The initial search was limited to studies conducted in humans, English language, and publication years from January 1990 to May 2010, which yielded 43 additional citations.

Titles and abstracts were reviewed and screened to identify articles that underwent full-text review ([Figure 4](#) below). Articles were excluded for the following reasons: (i) blade-form implants were not involved; (ii) the article did not contain clinical data; were not human studies; (iii) were not a journal article; and/or (iv) were not in English. Summary assessments were collected for each of the studies and included in [Table 3](#) at the end of this review.

In April 2013, the search was updated using three electronic databases, PubMed, Embase, and WOS, using the same search terms and limitations as the initial search conducted by FDA to support the intent to reclassify blade-form implants as identified in the proposed order that issued on January 14, 2013 (78 FR 2647). The time period for the updated search was from May 1, 2010 to April 18, 2013. The update search yielded 25 additional abstracts, and only two articles were selected for full text review and one was excluded because the study did not examine blade-form implants.

After going through the pre-specified exclusion criteria ([Figure 4](#)) a total of 9 publications were included in this FDA’s literature review as depicted in Figure 3 and identified in Table 1.

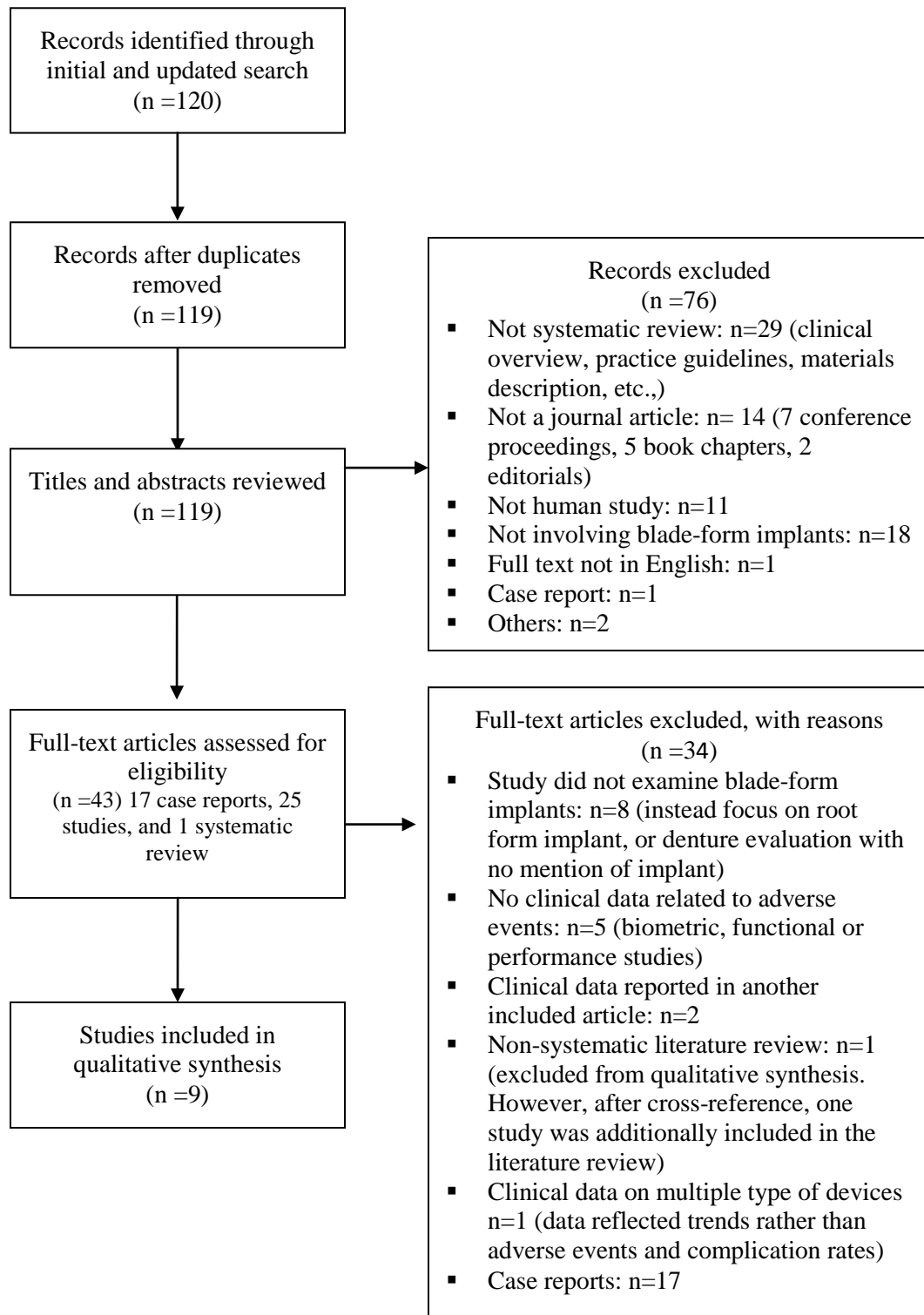


Figure 4 – Diagram of Article Retrieval and Selection

6.2. Summary of Results

A full diagram of the article retrieval and selection process appears in Figure 4 above. In summary, 119 articles were filtered by titles and abstracts. Seventy-six abstracts were excluded due to the following reasons: clinical overview/practice guidelines/materials description (n=29); non-journal article (n=14); non-human study (n=11); not related to blade-form implants (n=18); non-English article (n=1); case report (n=1); and others (n=2). The remaining 43 articles include 17 case reports, 25 studies, and one systematic review. Full-text articles were assessed for eligibility. Thirty-four articles were further excluded due to various reasons listed in the flow chart above. Nine articles were included in the systematic literature review ([Table 2](#)).

Data from eight retrospective studies and one randomized controlled trial were extracted and included in the qualitative analysis ([Table 2](#))

6.3. Study Designs and Methodology

Data from one randomized controlled trial and eight retrospective studies were extracted and included in the qualitative analysis ([Table 2](#)). Success was consistently defined across studies as the device remaining implanted/not being removed.

The sample size for these studies ranged from 7 – 131 patients with blade-form implants. The age range was 50.1- 54 years from two articles [2, 6]. The follow-up period ranged from 3 to 20 years. The success rate and device survivability were the outcome measures for this literature review.

Success rate was defined using the following criteria as explicitly described in Noack, 1999 (based on Buser et al.): (1) absence of persistent subjective complaints, such as pain, foreign body sensation, and/or dysesthesia, (2) absence of recurrent peri-implant infection with suppuration, (3) absence of mobility, and (4) absence of a continuous radiolucency around the implant. However, Kapur et al. defined success rate as the absence of treatment and implant failure. The remaining articles used the term “success rate” but did not define it. In this literature review success rates ranged from 90% to 100% at five years.

Survivability refers to those implants still in function beyond the first five year period [1]. Survivability across the studies ranges from 86%-100% after 5 years. The most common adverse events were: (1) mobility, (2) swelling/pain, (3) implant fracture, and (4) bone loss or bone deterioration.

6.4. Safety/Effectiveness Findings for Tooth Replacement

Randomized Controlled Clinical Trial (N=1)

Kapur KK, et al. (1989) conducted a randomized controlled trial in US in 1987. Male patients in five Veteran Affairs centers in southern California were recruited. The patients' mean age at baseline was 51years old. The study compared two devices:

fixed partial dentures (FPD) supported by blade-vent implants and removable partial dentures (RPD). There were 119 patients with RPD and 114 patients with FPD. FPD has 84.2% five-year success rate (95% confidence interval [CI] 77.7, 97.7) and RPD has 74% five-year success rate (95% CI 66.0, 82.0). This 10.2% difference was not statistically significant. During the five-year period, treatment failures occurred in 19 FPD patients and 30 RPD patients. Ten (10) FPD failures occurred before FPD insertion and 9 failures after FPD insertion. For overall (FPD and RPD combined) bone deterioration at six-years, 29.6% did not have deterioration, slight: 25.4%, moderate: 15.9%, marked: 27%, severe: 2.1%.

Retrospective Observational Studies (N=8)

There were eight retrospective observational studies published from 1987 to 2010. Every study had at least three-years of follow-up. Two studies had three years[2, 6], four studies had five-year follow-up [1, 3, 5, 8]; the study in Germany had 16 year follow-up on average [7]; and Acevedo AL, et al. had up to 20 year follow-up on average.

There were four studies from the US. Sample sizes varied from 31 patients [3] to 131 patients [2]. The baseline clinical status varied between the studies. Patients were treated according to the indications for use.

There are two studies from Japan that examined retrieved devices and described reasons for failure [5, 6]. These two papers used the same dataset, which contained 59 patients with 78 hydroxyapatite-coated blade-form implants. However, the first one published in February 1996, described the entire sample (59), while the second one published in October of the same year, only described seven patients.

The outcome measures under evaluation for this literature review included device survivability and success rate. Acevedo AL also showed survival rate at intervals of 6-10 yrs, 11-15 yrs, and 16-20 yrs. Overall success proportion at five-year was above 90%. After 5 years, Acevedo et al. showed 100% survivability for interdental for mandible; 86% survivability with 50-57% grade I bone loss for interdental for maxilla; 67% survivability with 66% grade I bone loss for free-end for mandible. The Germany study that followed up patients for 16 years showed a 76% success rate.

6.5. Adverse Events Associated with Blade-form Implants

The literature review identified several adverse events reported in the nine assessed articles. Table 1 lists the adverse events and the reporting article.

Table 1. Summary of adverse events reported in publications included in systematic literature review

Author, year	Range of follow-up	Bone loss or Bone deterioration	Swelling/Pain	Infection/Periodontal Disease	Implant fracture	Mobility
Takeshita F, 1996	1 – 8 years	100% * (7/7)	43%* (3/7)	43%* (3/7)	14%* (1/7)	43%* (3/7)
Telsey B, 1991	1 – 15 years	9.1% (6/66)	9.1% (6/66)	9.1% (6/66)	1.5% (1/66)	
Takeshita F, 1996	1 – 6 years		1% (1/78)		2% (2/78)	1% (2/78)
Roberts RA, 1996	1 – 26 years	1.7% (4/235)		0.4% (1/235)	1.3% (3/235)	
Kapur KK, 1989	1 – 5 years	3.9% (6/155)	3.9% (6/155)			1.3% (6/155)
Acevedo AI, 1987	1 – 5 years	18% (16/91)				
Hahn JA, 1990	1 – 3 years					
Noack N, 1999	1 – 16 years					
Strecha J, 2010	1-5 years					

Number of adverse events/number of implants placed

*Proportion of adverse events among seven implants that were removed

FDA has identified several potential risks of blade-form implant. Based on the literature and prior panels, the panel will be asked whether they believe this list is complete and accurate.

A reasonable assurance of safety is defined in 21 CFR 860.7(d)(1) as the probable benefits to health from use of the device outweighing any probable risks for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use. The regulation also states that the evidence shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use.

The panel will be asked whether the evidence demonstrates a reasonable assurance of safety for the indications for use of “surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, in order to restore a patient’s chewing function.”

6.6. Discussion of Limitations of Systematic Literature Review

The one randomized controlled trial available only recruited male veteran patients, therefore gender bias cannot be ruled out and possible effects by gender could not be examined. In addition, the patients were veterans, a subgroup of patients who may differ from non-veterans. The study focused mainly on effectiveness and not safety.

One of the advantages for a RCT is that randomization avoids treatment selection bias, because the investigator does not have control selecting treatments based on the patient's profile. Also, if the patient was randomized and the sample size was large enough, the confounding factors known and unknown may be equally distributed.

Out of eight retrospective studies, most of them had small sample sizes ($n < 50$) and were from single dental offices. Therefore, the power and generalizability of the results to overall patient population are limited. The overall success proportion at five-years was above 90%, this data comes from half of the studies which retrospectively extracted data from radiographic images. Most of the studies reported success/failure rates without providing information describing the reasons for implant failure. Therefore, it is difficult to make determinations about individual adverse events. Additionally, none of the papers systematically reviewed adverse events. The only conclusion to be derived is a general observation of the success rate. Of note, some of the reported studies did not provide information about the gender of the subjects, so the effects of how the device would perform in one gender as compared to the other are less clear.

6.7. Overall Literature Review Conclusions

An important strength of this review is that a systematic literature review reduces uncertainty by a rigorous methodology that is comprehensive, transparent or explicit, leading to minimum bias and providing objective and reproducible results. This process prevents bias in favor or against any unconsciously preferred outcome, providing more balanced answers to the systematic literature review questions. Well-defined methodology, like in this review, prevents bias, although does not protect against publication bias in the primary studies. If studies give consistent results, such as in this review, conclusions can be drawn that there is robust and generalizable evidence about the effectiveness and long-term safety profile of the device. In contrast, a systematic review methodology could be so rigorous that some publications could be excluded. Case reports and articles that were published in other languages were not selected in this review. Such studies may include reports for unusual adverse events. This limitation may prevent from identifying the presence of unusual adverse events.

In summary, nine articles were reviewed systematically for the safety and effectiveness of blade-form endosseous dental implants based on the five year survivability and success rates. Data from these nine articles show the success rate being consistently above 90% with the exception of one study reporting 84.2% success in males only. A long-term 100% device survivability was widely reported, except in one article reporting 90% 5-year survival. Although information about the blade-form implant is limited, and there were few studies that reported adverse events. The available evidence suggests that the device is effective and has a satisfactory long-term safety profile.

6.8. Manufacturer and User Facility Device Experience Database

The Manufacturer and Use Facility Devices Experience (MAUDE) database contains adverse events and reportable product problems with medical devices. The database was fully implemented in August 1996, and contains individual adverse event reports submitted by manufacturers, user facilities, importers, and voluntary reporters. The reports are associated with all legally marketed devices. FDA has not received any adverse events reports associated with blade-form implants as of May 30, 2013.

7. Risks to Health

The 1980 proposed rule for endosseous dental implants (both root-form and blade-form) included the following risks to health as previously identified by the Panel:

- *Tissue degeneration:* Localized tissue degeneration may be caused by endosseous implants due to excessive mobility.
- *Pain:* Nerve impingement by the device may cause pain.
- *Bone perforation:* Improper design of the device may cause excess mobility of the implant following surgical placement and subsequent perforation of the bony plates of the upper or lower jaws.
- *Infection:* Micro-organisms may be harbored between the implant and the gums and cause localized infection.

In the 2013 proposed order, FDA reiterated the concerns of the original classification panels, as well as those identified in the 2004 final rule for endosseous dental implants (root-form) and the systematic literature review. The following are proposed as the risks to health for blade-form implants:

- *Local tissue or existing dentition degeneration:* Localized tissue and existing dentition degeneration may be caused by endosseous implants due to excessive mobility, loss of integration, incompatibility of the device components, or structural failure of the device.
- *Pain:* Nerve impingement by the device may cause pain.
- *Bone or nerve damage:* Improper design or use of the device may cause injury during surgery related to sinus perforation, alveolar plate perforation, or nerve damage resulting in transient or chronic pain/facial nerve paresis.
- *Infection:* Implantable devices may introduce microorganisms that may cause local or systemic infections.

- *Adverse tissue reaction:* Inadequate tissue compatibility of the materials used in this device could cause an immune reaction.
- *Migration or thermal injury:* Incompatibility with magnetic resonance imaging may cause the device to migrate or heat.

The panel will be asked to discuss the risks to health identified by FDA for blade-form implant and whether these risks are appropriate, and/or whether there are additional risks to health that should be considered for these devices.

8. Mitigation of Risks to Health

8.1. Overview of Proposed Special Controls

Based on the safety and effectiveness information provided in the responses to the 515(i) Order, as well as information gathered by the FDA, FDA has recommended the establishment of special controls to adequately mitigate the risks to health as described in Section 7 above for blade-form implants,

When evaluating the adequacy of the special controls, it is important to understand that the FDA correlates the ability of each special control identified to mitigate an identified risk to health.

8.2. Proposed Special Controls

The FDA has proposed special controls be enacted in conjunction with reclassification as identified in FDA's proposed order recommending reclassification that issued on January 14, 2013 (78 FR 2647).

It is important to note that the classification of the device type and the special controls to support Class II must be based on the data that are available now, not the data that could be collected in the future. FDA believes that the following special controls, together with general controls, are sufficient to mitigate the risks to health described in Section 7 of this document:

- The design characteristics of the device must ensure that the geometry and material composition are consistent with the intended use.
- Mechanical performance (fatigue) testing under simulated physiological conditions to demonstrate maximum load (endurance limit) when the device is subjected to compressive and shear loads.
- Corrosion testing under simulated physiological conditions to demonstrate corrosion potential of each metal or alloy, couple potential for an assembled dissimilar metal implant system, and corrosion rate for an assembled dissimilar metal implant system.

- The device must be demonstrated to be biocompatible.
- Sterility testing must demonstrate the sterility of the device.
- Performance testing to evaluate the compatibility of the device in a magnetic resonance (MR) environment.
- Labeling must include a clear description of the technological features, how the device should be used in patients, detailed surgical protocol and restoration procedures, and relevant precautions and warnings based on the clinical use of the device.
- Patient labeling must contain a description of how the devices works, how the device is placed, how the patient needs to care for the implant, possible adverse events and how to report any complications.
- Documented clinical experience must demonstrate safe and effective use and capture any adverse events observed during clinical use.

Blade-form endosseous dental implants are prescription devices restricted to patient use only upon the authorization of a practitioner licensed by law to administer or use the device.

The panel will be asked to discuss the adequacy of these proposed special controls in providing a reasonable assurance of safety and effectiveness in light of the available scientific evidence.

9. Summary

For the purposes of classification (see the Regulatory Reference Sheet for additional information), FDA considers the following items, among other relevant factors, as outlined in 21 CFR 860.7(b):

1. The persons for whose use the device is represented or intended;
2. The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;
3. The probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and
4. The reliability of the device.

Part (g)(1) of this regulation further states that it “is the responsibility of each manufacturer and importer of a device to assure that adequate, valid scientific evidence exists, and to furnish such evidence to the Food and Drug Administration to provide reasonable assurance that the device is safe and effective for its intended uses and conditions of use. The failure of a manufacturer or importer of a device to present to the Food and Drug Administration adequate, valid scientific evidence showing that there is reasonable assurance of the safety and effectiveness of the device, if regulated by general controls alone, or by general controls and performance standards, may support a determination that the device be classified into Class III.”

Based on the available scientific evidence and proposed special controls, the panel will be asked whether a Class II designation is warranted for blade-form implant to be surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, in order to restore a patient’s chewing function.”

10. Tables

Table 2 – Publications included in the systematic literature review (n=9)

Author	Year	Study Design	Location
Acevedo AI[1]	1987	Retrospective	US
Hahn JA[2]	1990	Retrospective	US
Telsey B[3]	1991	Retrospective	US
Roberts RA[4]	1996	Retrospective	US
Takeshita[5]	1996	Retrospective	Japan
Takeshita[6]	1996	Retrospective	Japan
Noack N[7]	1999	Retrospective	Germany
Strecha J[8]	2010	Retrospective	Slovak and Czech Republics
Kapur KK[9]	1989	Randomized controlled clinical trial	US

Table 3 – Description of the Publications Evaluated in the Systematic Literature Review

Source [Author, Citation]	Study Design Level of Evidence	Study Population	Sample Size	Devices Studied	Study Endpoints	Relevant Study Results	Study Strengths and Limitations
Acevedo AI. [1]Success and survivability of endosteal blade implants managed in the practice of Dr. Linkow. J Oral Implantol 13:113-119, 1987.	- Retrospective observational study	-US (New York) -92% of 171 implants were full-arch fixed bridge restoration -Interdental and free-end blade implants only	-81 patients, 171 implants	-Interdental and free-end endosteal blade (brand unknown)	-Implant success/failure within 5 yrs -Implant survivability after 5 yrs (6-10 yrs, 11-15 yrs, 16-20 yrs) -Bone loss (Grade I, II, III)	-Interdental and mandible implant site favorable -91 cases with implant duration within 5 yrs have 91.2% success rate -Interdental for mandible (19 cases): Within 5 yrs, 100% success rate with isolated case of grade II bone loss due to gingival infection; After 5 yrs, 100% survivability -Interdental for maxilla (12 cases): Within 5 yrs, 100% success rate with 50% grade I bone loss; After 5 yrs, 86% survivability, 50%-57% grade I bone loss -Free-end for mandible (30 cases): Within 5 yrs, 93% success rate with 13% grade I bone loss, 7% grade II bone loss; After 5 yrs, 90% success rate with 37% grade I bone loss -(?)Free-end data not specified: Within 5 yrs, 85% success rate with 12% grade I bone loss, 7% grade II bone loss; From 6-10 yrs, 67% survivability, 66% grade I bone loss	<i>Strengths:</i> long follow-up (5-15 years) <i>Limitations:</i> - Small sample size - Single private dental office practice. - The table and chart referred in the text were not included
Telsey B, Oshrain HI, Joodeph NH, Mandel ID.[3] Retrospective radiographic study of blade implants, J Oral Implantol 17:140-145, 1991.	- Retrospective observational study	-US -Blade-implant patients aged 31-72 yrs -20 implants in 11 males and 46 implants in 20 females	-31 patients, 66 implants (25 in maxilla and 41 in mandible)	-13 two-post blades and 53 one-post blades -Implant location: 7 incisor, 17 canine, 42 molar (brand unknown)	-Status of blade implant in use at least 5 yrs	-5-year Implant survival 90%, favorable in mandible site -6 total implants removed in 5 patients (5 maxilla and 1 mandible) located in 1 incisor, 3 canines, 2 molars -1 maxillary molar blade and 1 mandibular molar blade failed -2 implants removed after 3.5 yrs due to pain -1 implant removed after 4 yrs due to an adjacent natural teeth severely decaying -1 implant removed after 6 yrs due to head breakage -1 implant removed after 10 yrs due to operator error (implant not placed deep enough) -1 implant removed after 11 yrs due to suppuration, loss of bone, and pain -11 progressive periodontal disease patients with 23 implants had 5 failures -18 stable periodontal disease patients with 34 implants had 1 failure	<i>Limitations:</i> - Small sample size - Single private dental office practice
Noack et. al.[7]	Retrospective	-Germany	-883	-Branemark	-16-year study	-Linkow blade: 13/53 (24%) failure rate	<i>Strengths</i>

Source [Author, Citation]	Study Design Level of Evidence	Study Population	Sample Size	Devices Studied	Study Endpoints	Relevant Study Results	Study Strengths and Limitations
Long-term results after placement of dental implants: Longitudinal study of 1964 implants over 16 years, 1999	observational study	-530 females, 353 males -Ages 15 to 86 years -Patients with history of uncontrolled diabetes, ongoing chemotherapy, radiation therapy (head and neck), psychologic instability were excluded	patients -1250 IMZ in 527 patients -349 Branemark in 144 patients -286 Frialit-1 and Frialit-2 in 151 patients -79 Linkow blade in 61 patients	-Frialit-1 -Frialit-2 -IMZ -Linkow blade	-Follow-up every 3 months for first 2 years, at least annually thereafter		-Long-term follow-up -1 surgeon performed all implantations and follow-ups <i>Limitations</i> -Some patients received more than one type of implant -74 patients with 153 implants lost to follow-up (refusal to follow-up, death) -Branemark (mandible) -Frialit-2 (maxilla) -IMZ, Linkow (mandible) -Higher failure rates in older implant systems (Frialit-1, Linkow)
Roberts RA[4] Types, uses, and evaluation of the plate-form implant. <i>J Oral Implantol</i> 22:111-118, 1996.	Retrospective observational study	-US - gender not reported	-Ramus Blades (51 SS, 184 Ti) -RA-1 (14 SS) -RA-2 (21 SS, 66 Ti) -RA-3 (66 Ti) -STR (7 SS, 249 Ti)	-Ramus Blades -RA-1 -RA-2 -RA-3 -Single Tooth Replacements (stainless steel and titanium)	-9/1969-3/1995 (SS) -5/1982-3/1995 (Ti)	-8/51 Ramus Blades (SS) failure rate -2/184 Ramus Blades (Ti) failure rate -failure due to mobility, settling, non-resolvable local inflammation, paresthesia, anesthesia, significant pain	<i>Strengths</i> - Kaplan-Meier survival and hazard curves for Ramus Blades <i>Limitations</i> -No mention of number of patients by age, gender etc. -Ti use primary after 1982
Hahn JA.[2] A preliminary clinical evaluation of the steri-oss implant	Retrospective observational study	-US -58 males -73 females -14-83 years	-131 implants -97 (root form)	-Steri-Oss System	-3-year period -4-6 months follow-ups	-0/50 implant failure rate	<i>Strengths</i> -100% success rates

Source [Author, Citation]	Study Design Level of Evidence	Study Population	Sample Size	Devices Studied	Study Endpoints	Relevant Study Results	Study Strengths and Limitations
system. <i>Int J Oral Implan</i> 7:31-36, 1990.			-7 (blade) -27 (root and blade)				<i>Limitations</i> - Small sample size
Takeshita et. al.[6] Fractures of hydroxyapatite-coated blade implants connected with natural teeth. A histological study using SEM, light microscopy, and an image processing system. <i>J Periodontol</i> 67:86-92, 1996	Retrospective observational study	-Japan -of the 5 cases presented -3 males -2 females -45-69 years	-78 HA-coated blade implants in 59 patients	-HA-coated blade-form implants	-Over 3-year period -4-6 months follow-ups	-5 failures occurred due to superstructure mobility, swelling/pain, implant fracture	<i>Strengths</i> - Scanning electron microscopic analysis <i>Limitations</i> -Small sample size
Kapur KK. J [9] <i>Prosthet Dent</i> 59:499, 1987. Part II, 1989	Randomized controlled trial	-5 VA centers in south California, US -dental implants -All male patients -- Mean age: =51 at baseline, age categories: 25-54yr, 55+ yr. - Exclusion criteria : prespecified medical conditions that make patients not suitable for surgery; oral/teeth conditions not suitable for surgery.	-119 patientsts with RPD -114 patientsts with FPD	compare 2 devices: fixed partial dentures supported by blade-vent implants (FPD) and removable partial dentures (RPD)	-Success rate at 5 yrs -Periodontal health -Bone deterioration at 5 yr	-5-yr success rates = 84.2% for FPD and 74% for the RPD - During 5-yr period, treatment failures occurred in 19 FPD patients and 30 RPD patients -10 FPD failures occurred before FPD insertion and 9 failures after FPD insertion - Bone deterioration at 6-yr: - 29.6% No deterioration - 25.4% slight - 15.9% moderate - 27% marked - 2.1% severe	-gender bias was introduced because only male patients were recruited -not clear how age cut-off was selected -mainly focused on effectiveness
Takeshita et. al.[5] A histologic evaluation of retrieved	Retrospective observational study	-Japan -of the 7 cases presented -4 males	-78 HA-coated blade implants	-HA-coated blade form implants	-Over 5-yr period -Time of restoration	-7 failures occurred due to discomfort (swelling), implant fracture, pain (purulent discharge), mobility w/and w/out purulent discharge	<i>Strengths</i> - Scanning electron microscopic

Source [Author, Citation]	Study Design Level of Evidence	Study Population	Sample Size	Devices Studied	Study Endpoints	Relevant Study Results	Study Strengths and Limitations
hydroxyapatite-coated blade-form implants using scanning electron, light, and confocal laser scanning microscopies. J Periodontol 67:1034-1040, 1996		-3 females -33-61 years	-59 patients		between 2-4 months		analysis <i>Limitations</i> -Small sample size
Strecha J et. al.[8] Fixed Bicortical Screw and Blade Implants ans a Non-Standard Solution to an Edentulous (Toothless) Mandible Int J Oral Sci, 2(2): 105-110, 2010	Retrospective observational study	4 Clinics: 3 in the Slovak Republic and 1 in the Czech Republic. - dental implants - Male and female patients were studied - no specific demographics for those implanted with the blade implant	- 84 blade implants	- blade dental implants were made of biocompatible titanium by fy. Martikan from the Slovak Republic (www.martikan.eu)	- implant success/failure in a maximum of 5-year follow-up	- 5-year success rate: 98.8% -Only one failure reported	<i>Strengths:</i> Success rate of blade implants (98.8%) is slightly higher than bicortical implant (98.4%). <i>Limitations</i> Small sample size No specific demographics included Not clear how many patients were followed for 5 years No data analysis methods included No inclusion/exclusion selection criteria included

Abbreviations
Yrs = years

11. References

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