DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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November 6, 2015

EDAP Technomed, Inc.
John C. Rewcastle, Ph.D.
Medical Director
2201 Denton Dr., Suite 110
Austin, Texas 78758

Re: K153023
Trade/Device Name: Ablatherm Integrated Imaging
Regulation Number: 21 CFR 876.4340
Regulation Name: High Intensity Ultrasound System For Prostate Tissue Ablation
Regulatory Class: Class II
Product Code: PLP
Dated: October 15, 2015
Received: October 15, 2015

Dear Dr. Rewcastle:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). 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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Benjamin R. Fisher -S

Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

Device Name
Ablatherm Integrated Imaging

Indications for Use *(Describe)*
The Ablatherm® Integrated Imaging device is indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostate tissue.

Type of Use *(Select one or both, as applicable)*

[x] Prescription Use (Part 21 CFR 801 Subpart D) [ ] Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

The following information is provided as required by 21 CFR § 807.87 for Ablatherm Integrated Imaging 510(k) premarket notification. In response to the Safe Medical Devices Act of 1990, the following is a summary of the information upon which the substantial equivalence determination is based.

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Date of Submission: **October 15, 2015**

Proprietary Name: Ablatherm Integrated Imaging

Common Name: High intensity ultrasound system for prostate tissue ablation

Regulatory Class: II

Regulation: 21 CFR 876.4340

Product Code: PLP

Predicate Device(s): Sonablate 450 (DEN150011)

Device Description: The Ablatherm Integrated Imaging is a computer controlled medical device intended to provide High Intensity Focused Ultrasound (also referred as HIFU) to ablate prostate tissue. The system consists of the following main sub-assemblies: Treatment Module, Control Module, Endorectal Probe, and Ablapak. HIFU is a unique process of delivering a large amount of heat energy to a confined space in a highly controlled manner. This energy heats the tissue to ablation levels while minimizing the effect on surrounding structures.

The ultrasound energy is delivered via an endorectal probe, which includes an imaging system. The ultrasound waves propagate through the rectal wall and are focused on a portion of the prostate, generating intense heat and causing the ablation of tissue within the targeted area. The process is then repeated in a stepwise fashion to destroy the targeted tissues within the prostate. The apex, sphincter and rectum are preserved while prostate tissues are ablated.

Intended Use: The Ablatherm® Integrated Imaging device is indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostate tissue.

Non-clinical testing

The following non-clinical testing was provided in support of this submission:

- Sterilization and Shelf Life
- Biocompatibility
- Reprocessing validation
- Software Documentation
- Electrical Safety and Electromagnetic Compatibility
- IEC 60601-2-62: Medical electrical equipment Part 2 62 Particular requirements for the basic safety and essential performance of high intensity therapeutic ultrasound HITU equipment.
- Bench Testing - Technical and performance testing were performed to evaluate the transducer testing and calibration. The objectives of the tests were to calculate measurements for the following parameters: electrical impedance, transducer dimension, ultrasonic beam profile, acoustic intensity, radiation force, reference electrical power, and acoustical power stability verification.
- Animal Studies -Animal studies were conducted on canine and rabbit models, as well as liver.

Conformance to Recognized Standards

The Ablatherm® Integrated Imaging complies with applicable sections of the following recognized consensus standards:

- ISO 10993-1, biological evaluation of medical devices - part 1: evaluation and testing within a risk management process.
- ISO 10993-5, Biological Evaluation of Medical Devices: Test for in vitro cytotoxicity
- ISO 10993-10, Biological evaluation of medical devices - part 10: tests for irritation and skin sensitization
- ISO 10993-11, biological evaluation of medical devices - part 11:tests for systemic toxicity
- IEC 60601-1:2005- Corr 1:2006, Corr 2:2007, Medical Electrical Equipment - Part 1: General Requirements For Safety
- IEC 60601-1-2:2007/AC:2010, Medical Electrical Equipment - Part 1-2: General

Requirements For Safety - Collateral Standard: Electromagnetic Compatibility - Requirements And Test

- IEC 62304: 2006/AC:2006, Medical device software-Software life cycle processes.
- IEC 60601-2-62:1.0 2013-07, medical electrical equipment; part 2-62: particular requirements for the basic safety and essential performance of high intensity therapeutic ultrasound (hitu) equipment.
- AAMI TIR12:2010 – Designing, testing, and labeling reusable medical devices for reprocessing in health care facilities: A guide for medical device manufacturer
- AAMI TIR30:2011 – A compendium of processes, materials, test methods, and acceptance criteria for cleaning reusable medical devices,
- ANSI/AAMI ST81:2004/(R)2010 - Sterilization of medical devices - Information to be provided by the manufacturer for the processing of resterilizable medical devices
- ISO 17664:2004 – Sterilization of medical devices – Information to be provided by the manufacturer for the processing of resterilizable medical devices.

Clinical Data

A clinical study was conducted that included 136 subjects who had not received previous prostate treatment, of which 135 underwent the HIFU procedure. One subject was enrolled but did not undergo HIFU due to calcifications in the prostate, an exclusion criterion, being observed immediately prior to the HIFU procedure. The first subject was enrolled on May 4, 2006 and the last subject was enrolled on June 30, 2010. All subjects underwent whole gland ablation. All adverse events were collected during the IDE study regardless of their relationship to the HIFU procedure. The majority of adverse events resolved within 2 years with the exception of erectile dysfunction and urinary incontinence.

All adverse events observed during the 2 years of follow-up are summarized in table 1, regardless of severity or relation to device or procedure.

Table 1: All adverse events regardless of relationship between device or procedure.

Adverse Event	**Any Occurrence # Subjects (%) (n=135)**
Any	131 (97.0%)

Adverse Event	**Any Occurrence # Subjects (%) (n=135)**
Erectile Dysfunction	91 (67.4%)
Urinary Incontinence	52 (38.5%)
Urinary Tract Infection	46 (34.1%)
Hematuria	44 (32.6%)
Bladder urgency	39 (28.9%)
Perineal/penile/rectal/prostate pain	37 (27.4%)
Urinary Obstruction	33 (24.4%)
Slow stream	33 (24.4%)
Bladder spasms	31 (23.0%)
Dysuria	31 (23.0%)
Urinary Retention not resolved by day 30 or onset ≥ 30 days	28 (20.7%)
Stricture	26 (19.3%)
Urinary frequency	25 (18.5%)
Bladder Neck Contracture	24 (17.8%)
Urethral sloughing	17 (12.6%)
Urinary Retention Resolved by Day 30	12 (8.9%)
Bowel Injury	4 (3.0%)*
Epididymitis	4 (3.0%)
Sepsis	2 (1.5%)**
* Anal tears ** Both cases of sepsis were not considered to be related to either the device or procedure	

The majority of adverse events summarized in Table 2 resolved within 2 years with the exception of erectile dysfunction and urinary incontinence. Persistence of erectile dysfunction was expected due to the intentional targeting of the lateral margins of the prostate. Of the 61 (45.2%) subjects with erectile dysfunction unresolved at 2 years, 12 had a pre HIFU history of erectile dysfunction, and the severity of unresolved erectile dysfunction in 9 subjects was reported as mild. Of the 21 (15.6%) subjects with unresolved urinary incontinence 16 were reported as mild.

The number of subjects with unresolved urinary obstruction, retention stricture, bladder neck contracture and sepsis was observed in 1 (0.7%), 3 (2.2%), 2 (1.5%), 1 (0.7%) and 1 (0.7%), respectively. All urinary tract infections and bowel injuries were resolved within 2 years.

Evidence of prostate tissue ablation is provided through post-HIFU ablation prostate volume reduction, PSA reduction and stability as well as biopsy survival rate.

Prostate Volume Reduction

The prostate volume reduction as measured at the first post-HIFU ablation is evidence of prostate tissue ablation. The mean prostate volume as measured post-HIFU ablation at the first biopsy that included a volume measurement is 9.0 cc (95% CI: 7.9, 10.2) compared to 22.7 cc (95% CI: 20.5, 24.8), at baseline, and the mean volume decrease from baseline was 13.6 cc (95% CI: 10.9, 16.3).

Stability of PSA Following HIFU Procedure

Decreased and subsequently stable PSA post-HIFU provides additional evidence of prostate tissue ablation. PSA decrease and stability is demonstrated by PSA measurements at baseline and at each follow-up visit allowing for determination of PSA nadir, PSA reduction from baseline. Additionally, Phoenix Biochemical Survival provides a context in which PSA can be interpreted. The Phoenix Biochemical Survival is the most frequent definition in the literature used to report biochemical survival post-HIFU ablation and interpret PSA measurements. A subject demonstrates biochemical survival if he did not have any PSA obtained between 6 and 24 months post-HIFU ablation that was greater than or equal to the PSA nadir + 2 ng/ml:

No PSA between 6 and 24 months post-HIFU procedure $\geq$ PSA Nadir + 2

Using a PSA nadir definition of the lowest PSA achieved during the first 6 months of follow-up after HIFU, the mean PSA nadir is 0.53 ng/mL (95% CI: 0.37, 0.69 ng/mL) and the mean reduction from baseline to nadir is 4.07 ng/mL (95% CI: 3.67, 4.47 ng/mL) and the mean % reduction from baseline is 87.97% (95% CI: 84.80, 91.15 %).

Prior to HIFU the mean PSA was 4.60 ng/mL (95% CI: 4.20, 5.00 ng/mL). Table 4 summarizes

the PSA observations at 1-month, 1-year and 2-years and the percentage PSA reductions from baseline which were 78.14%, 80.34% and 82.25%, respectively.

Table 3: PSA reductions at 1-month, 1-year and 2-years

Visit month	n	Mean PSA (ng/mL) (95% CI)	Mean PSA Reduction from Baseline (ng/mL) (95% CL)	Percentage PSA Reduction from Baseline (95% CL)
1	133	0.89±1.23 (0.68, 1.10)	3.71±2.40 (3.30, 4.12)	78.14%±30.28 (72.95, 83.34%)
12	131	0.91±1.56 (0.64, 1.18)	3.65±2.30 (3.25, 4.04)	80.34%±26.44 (75.77, 84.91)
24	107	0.72±1.20 (0.49, 0.94)	3.52±2.20 (3.09, 3.94)	82.25%±24.21 (77.61, 86.89%)

Maintaining biochemical survival post prostate tissue ablation demonstrates the effectiveness of ablation. In the 116 evaluable subjects, 90.5% (95% CI: 85.2, 95.8%) of subjects met the definition of the Phoenix Biochemical Survival.

Biopsy Survival Rate

Fifty-nine percent (59%) of the total cohort of 135 patients had a negative post-ablation biopsy (95% confidence limits = 50, 68). For this ITT analysis, 17 patients who did not have a biopsy performed during the 24-month follow-up period were considered “positive.”

The data supports the substantial equivalence of the Ablatherm Integrated Imaging to the Sonablate 450.

Substantial Equivalence

Both the subject and predicate devices are high intensity focused ultrasound devices and are indicated for the ablation of prostate tissue. Both devices are intended for use by physicians who have completed mandatory didactic and hands-on training for safe operation and use of the devices. Both the subject and predicate devices are intended for prescription use and are performed as minimally invasive, outpatient procedures.

Both the subject and predicate devices use high intensity focused ultrasound (HIFU) to elevate the tissue temperature within a focal zone. Non-clinical performance of the Ablatherm demonstrates that the device performs as intended, with similar to characteristics of the Sonablate 450. Both the subject and predicate devices have similar operating principles. Both use ultrasound to monitor the ablation. Although there are some differences in technological features that could impact safety or effectiveness, they do not raise new types of safety or effectiveness questions. For example, there are some differences in the ultrasound frequency, duty cycle, lesion size and location, etc. The total acoustic power is similar to the predicate but slightly higher power is available. These differences have been assessed through bench, animal, and clinical studies, which demonstrate that the Ablatherm Integrated Imaging performs as intended and is substantially equivalent to the Sonablate 450.

Intended Use and Design

	Ablatherm Integrated Imaging-subject device	**Sonablate 450**
Manufacturer	EDAP	SonaCare
510(k) No.	not yet assigned	DEN150011
Product Code	PLP	PLP
Indications for Use	Indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostate tissue.	Indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostatic tissue.
Prescription use	Yes	Yes
Minimally invasive	Yes	Yes
Outpatient procedures	Yes	Yes
Anesthesia required	Yes	Yes
Physician training required	Yes	Yes
System Components	Control module, computer and peripherals. Treatment module, (patient support), endorectal probe, cooling unit, probe moment assembly and holder, movement detector, ultrasound scanner, Disposable accessories	Control module, endorectal probe, computer and peripherals, cooling fluid, probe moment assembly and holder, Disposable accessories
Patient position	right lateral decubitus	lithotomy

Performance characteristics

	Ablatherm Integrated Imaging	Sonablate 450	
Imaging modality for localization, treatment and control	Ultrasound	Ultrasound	
Probe type	Curved array	Linear Mechanical	
Imaging Frequency	7.5 MHz	4.0 MHz Nominal (3.5-8 MHz Range)	
Longitudinal Imaging frame rate (typical)	NA (Longitudinal image is reconstructed)	2 FPS	
Transverse Imaging frame rate (typical)	5 FPS	3 FPS	
Image size	8.0 x8.0 cm	4.5 x 6.25 cm	
Field of view	130°	112°	
Ablation modality	HIFU	HIFU	
Ablation Frequency	3.0 MHz	4.0 HMz	
Focal Distance	45 mm ± 2 mm	30 mm ± 1 mm	40 mm ± 1 mm
Probe length	60.9 mm	58.7 mm	
Probe diameter	38.4 mm	33 mm	
Probe neck diameter	19.5 mm	18 mm	
Duty cycle	6 seconds “on” and 4 seconds “off”	3 seconds “on” and 6 seconds “off”	
HIFU total acoustic power	35-48 W according lesion length (19 to 24 mm)	0-28 W, 24 W typical (3.0 cm focal length transducer) 0-40 W, 37 W typical (4.0 cm focal length transducer)	
Lesion height	19-24 mm	10 mm	
Longitudinal lesion spacing	1.7 mm	3.0 mm	
Transverse lesion spacing	2.5°	3°	
Ablation planning	In transverse and longitudinal planes	In longitudinal and transverse planes	
Longitudinal motion	8.0 cm max length scanning	4.5 cm	

Conclusion

Any differences between the subject device and predicate do not render the device NSE as the changes do not constitute a new intended use, and any differences in technological characteristics

do not raise new types of safety or effectiveness questions. Data is provided to assess the effects of the technological differences, including bench, animal and clinical data. These data demonstrate that the device performs as intended and support a finding of substantial equivalence.