November 23, 2021

Insightec, Inc.
Nadir Alikacem, Ph.D.
VP of Global Regulated Clinical Affairs
4851 LBJ Freeway, Suite 400
Dallas, TX 75244

Re: K212150
Trade/Device Name: Exablate Prostate System
Regulation Number: 21 CFR§ 876.4340
Regulation Name: High Intensity Ultrasound System For Prostate Tissue Ablation
Regulatory Class: II
Product Code: PLP
Dated: October 27, 2021
Received: October 28, 2021

Dear Nadir Alikacem:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Mark J. Antonino, M.S.
Assistant Director
DHT3B: Division of Reproductive,
Gynecology and Urology Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K212150

Device Name
Exablate Prostate System

Indications for Use *(Describe)*
The Exablate Prostate System is indicated for endorectal MR-Guided Focused Ultrasound (MRgFUS) ablation of Prostatic Tissue

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

☒ 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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5. 510(k) Summary

Submitter:	Insightec, Ltd. 5 Nachum Heth St. PO Box 2059, Tirat Carmel 39120 Israel	
Regulatory Contact Person:	Insightec, Inc. Nadir Alikacem, PhD VP of Global Regulated Clinical Affairs4851 LBJ Freeway, Suite 400 Dallas TX 75244	
Date Prepared:	November 18, 2021	
Proposed Device:	Manufacturer:	Insightec, Ltd
	Trade Name:	Exablate Prostate System
	Common Name:	High Intensity Focused Ultrasound System
	Classification Name:	High Intensity Ultrasound System for Prostate Tissue Ablation
	Product Code:	PLP
	Regulatory Number:	21 CFR 876.4340
	Regulatory Class:	II
Predicate Device:	510(k) Number:	K160942,
	Manufacturer:	SonaCare Medical, LLC
	Trade Name:	SONABLATE
	Common Name:	High Intensity Focused Ultrasound System
	Classification Name:	High Intensity Ultrasound System for Prostate Tissue Ablation
	Product Code:	PLP
	Regulatory Standard:	21 CFR 876.4340
	Regulatory Class:	II

Device Description:

The proposed Exablate 2100 / 2100V1 Type 3 Prostate System (Trademark Name: **Exablate Prostate System)** is a high intensity Magnetic Resonance ("MR") image- guided focused ultrasound (MRgFUS) system intended for endorectal use that delivers focused ultrasound energy into the prostate in a minimally invasive manner by utilizing anendorectal probe transducer.

The Exablate Prostate System combines a multiple-channel phased-array Focused Ultrasound (FUS) transducer probe and magnetic resonance imaging ("MRI") in a closed-loop treatment for the thermal procedure of Prostatic Tissue while monitoring the procedure in real time.

The Exablate Prostate System is designed to work in conjunction with FDA cleared 1.5Tand 3.0T MRI scanners with phased array torso cardiac coils that is used for guidance andprocedure monitoring and control feedback. The Exablate Prostate System is fully integrated with the MRI scanner used to provide MR images of the patient's anatomy and prepare an appropriate procedure plan. Measured tissue temperature changes provide feedback on the procedure dose in the targeted area and its surroundings, allowing real-time monitoring to achieve safe and effective outcomes.

The intended users for the Exablate Prostate System are trained and certified physicians and/or technicians (clinicians) who are seeking to offer patients an incisionless, focal, and MR guided and controlled prostate tissue ablation and have successfully completed the Insightec Exablate training to operate the device.

The Exablate Prostate System platform is intended to ablate prostatic tissue with focused ultrasound and operates in conjunction with FDA cleared compatible MRI scanners for the purposes of real time procedure planning, MR based guidance of the focused ultrasound energy to the target region, MR thermal imaging and ablation monitoring. The procedure effect of the Exablate Prostate System is achieved by accurately guiding the focus of the ultrasound energy to the target region. The energy is then repeatedly transmitted to the target until the desired outcome is achieved. The targeted area is defined based on MR images taken during the procedure, while patient is in procedure position.

The procedure is constantly monitored in a real-time closed-loop MR thermal feedback. Once the targeting is complete, the outcome is confirmed with adequate post-procedure MR imaging sequences.

Indications for Use:

The Exablate Prostate System is indicated for endorectal MR-Guided Focused Ultrasound (MRgFUS) ablation of Prostatic Tissue.

Summary of Technological Characteristics:

Comparisons with the predicate devise show the technological characteristics of the proposed Exablate Prostate System to be substantially equivalent to the predicate device.The proposed device is functionally identical to the predicate device.

The major differences between the proposed and predicate device are identified in the following table. No other technological changes have been made to the proposed device.

	(New Device)	(Predicate Device)
Model	**Exablate Prostate System**	**SONABLATE**
510(k) Submitter	Insightec	Sonablate Medical, LLC
510(k) Number	K212150	K160942
Product code	PLP	PLP
Indications for Use	The Exablate Prostate System is indicated for endorectal MR-Guided Focused Ultrasound (MRgFUS) ablation of Prostatic Tissue.	The Sonablate® is 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	• Console/Workstation • Patient Table • Exablate Probe • Equipment Cabinet • Water System Cabinet • Cleaning and HLD Cart • Disposable accessories	• Control module • Endorectal probe • Computer and peripherals • Cooling fluid • Probe moment assembly and holder • Disposable accessories
Patient Position	Lithotomy	Lithotomy
Imaging modality for localization, procedure and control	MR Imaging	Ultrasound
Probe Type	Phased Array	Linear Mechanical
Therapy Frequency	2.3±0.2 MHz	4 MHz
Longitudinal Motion	5 cm	4.5 cm
Image Size	28 x 28 cm	4.5 cm x 6.25 cm
Field of View	90°	112°
Ablation Modality	HIFU	HIFU
Ablation Frequency	2.3±0.2 MHz	4.0 MHz
Focal Distance	1.5 – 6.0cm	3.0±0.1 cm 4.0±0.1cm

Probe Length	9.5 cm	5.9cm
Probe Diameter	3.1 cm	3.3 cm
Probe Neck Diameter	1.8 cm	1.8 cm
Duty Cycle	NA (up to the physician)	3 seconds "on" and 5 seconds "off"
HIFU Total Acoustic Power	0-30W	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	0.8 – 4.0 cm	1.0 cm
Longitudinal lesion spacing	3.0 mm	3.0 mm
Transverse lesion spacing	3-4 ^{o}	3^{o}
Ablation planning	In longitudinal and transverse planes	In longitudinal and transverse planes

Summary of Non-Clinical /Testing:

The following non-clinical studies were conducted on the Exablate Prostate System to support substantial equivalence to the predicate device:

- Bioburden testing of the rectal balloon component
- Reprocessing validation studies on the reusable endorectal probe
- Package integrity testing of the kit containing single use components
- Biocompatibility studies on the rectal balloon component were demonstrated in accordance with ISO 10993 standards as follows:
    - Cytotoxicity [ISO 10993-5:2009] [ISO 10993-12:2008]
    - Sensitization [ISO 10993-12:2008]
    - Irritation / Intracutaneous Reactivity [ISO 10993-10-2002] [ISO 10993-12:2008]
- Software verification and validation testing were demonstrated in accordance with the FDA's "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*" guidance documented issued on May 11, 2005
- Electrical safety and electromagnetic compatibility testing were demonstrated in accordance with the following standards:
    - SII, 60601-1-2
    - SII, 60601-2-62
    - SII, 60601-1 + 62304
    - SII, 60601-1-6
- Bench tests to characterize the device's acoustic output, verify MR safety, image quality, targeting accuracy and thermal monitoring,

	and verify the performance of hardware functions
	Animal study (canine prostate model) to demonstrate that the device thermally ablates targeted tissue without thermal injury to adjacent, non-target tissues
Summary of Clinical Data:	The Insightec MRgFUS utilizes a non-invasive thermal ablation integrated with a MRImaging system that allowed real time-controlled ablation of prostate tissue within thestudy. This technology resulted in the successful safety and effectiveness endpoint outcomes reported. The study in support of the submission was conducted as a multi-center in the United States, prospective, single arm where subjects were treated and followed for 12 months. One-hundred and one (101) males over 50 years of age (median age of 63 years) with a single, MRI-visible, hemilateral lesion of biopsy proven Gleason Grade Group 2 (3+4) or 3 (4+3) adenocarcinoma and with a PSA less than or equal to 20 ng/mL were treated with the Exablate 2100 Prostate System. The median prostate lesion volume was 1.7 cm^3. It should be noted the median planned Region of Treatment (ROT) was approximately 3.4 cm^3. The study's primary endpoints are 12 Months for safety and 6 Months for effectiveness. The safety analysis included all subjects who received at least one sonication of Exablate treatment, with Adverse Events documented and reported by the investigational sites throughout the subject's participation in the study. The effectiveness analysis included all subjects who completed at least one Exablate treatment, with the primary effectiveness endpoints being biopsy at 6-months, reduction in PSA value at 6 months, and non-perfused volume (NPV) covering physician targeted prostate tissue at treatment. The clinical study was conducted in accordance with Good Clinical Practice, Insightec Standard Operating Procedures and FDA 21 CFR 50, 54, 56 and 812. **Safety Analysis** There were no Serious Adverse Events (SAEs) or Life-threatening AEs reported in this study, with only 1 AE was categorized as Severe for an UTI event resolving in less than a week. The vast majority (99.5%) of AEs reported were either Mild (n=173, 86.5%) or Moderate (n=26, 13%). Overall, 70 subjects (69.3%) of all subjects reported at least one AE, with 67 subjects (66.3%, 95% CI 56.25-75.44) reporting at least one event that was deemed related to the Exablate procedure or device. Overall, 57 subjects had one or more neurovascular bundle and/or their urethra included within their treatment, while 44 did not have any critical structures included with their treatment volume.

Table 1. Exablate Device- or Procedure-Related AEs				
Coded AE Term	**Number of Events**	**Number of Subjects**	**Unresolved at 12 Months (*Frequency)**	**Unresolved at 12 Months (**Frequency)**
Hematuria	25	24 (24%)	0 (0%)	0 (0%)
Urinary incontinence	21	19 (19%)	7 (3.5%)	7 (7%)
Erectile dysfunction	19	19 (19%)	16 (8.0%)	16 (16%)
Urinary retention	17	15 (15%)	0 (0%)	0 (0%)
Penile/ testicular pain	15	14 (14%)	0 (0%)	0 (0%)
Hematospermia	13	13 (13%)	1 (0.5%)	1 (1%)
Fatigue	10	9 (9%)	0 (0%)	0 (0%)
Ejaculation disorder	9	9 (9%)	2 (1.0%)	2 (2%)
Urinary frequency	9	9 (9%)	2 (1.0%)	2 (2%)
Urinary tract pain	6	6 (6%)	0 (0%)	0 (0%)
Urinary hesitancy	6	6 (6%)	1 (0.5%)	1 (1%)
Urinary urgency	6	6 (6%)	1 (0.5%)	1 (1%)
Constipation/ bloating	3	3 (3%)	0 (0%)	0 (0%)
Diarrhea	3	3 (3%)	0 (0%)	0 (0%)
Groin/pelvic/ suprapubic pain	3	3 (3%)	0 (0%)	0 (0%)
Bladder spasm	3	3 (3%)	0 (0%)	0 (0%)
Edema limbs	2	2 (2%)	0 (0%)	0 (0%)
Urinary tract infection	2	2 (2%)	0 (0%)	0 (0%)
Anal/rectal pain	2	2 (2%)	0 (0%)	0 (0%)
Hemorrhoidal hemorrhage	1	1 (1%)	0 (0%)	0 (0%)
Proctitis	1	1 (1%)	0 (0%)	0 (0%)
Allergic reaction	1	1 (1%)	0 (0%)	0 (0%)
Vertigo	1	1 (1%)	0 (0%)	0 (0%)
Testicular infection	1	1 (1%)	0 (0%)	0 (0%)
Paresthesia	1	1 (1%)	0 (0%)	0 (0%)
Positional pain	1	1 (1%)	0 (0%)	0 (0%)
Prostatic pain	1	1 (1%)	0 (0%)	0 (0%)
Orchitis	1	1 (1%)	0 (0%)	0 (0%)

Prostatic cyst	1	1 (1%)	1 (0.5%)	1 (1%)
Bullous dermatitis	1	1 (1%)	0 (0%)	0 (0%)
Urethra stricture	1	1 (1%)	1 (0.5%)	1 (1%)
Deep vein thrombosis	1	1 (1%)	0 (0%)	0 (0%)
*n= 200 AEs occurred in cohort 2 **N=101 subjects in cohort 2				

Most events resolved in 90 days or less (n=127, 63.5%) with 46 (23%) resolving within a week. There were no ongoing AEs noted as severe or life threatening and 23% of the AEs were transient in nature and resolved within 7 days. There were 121 out of the 187 (**Table 1**) Exablate procedure- or device-related adverse events (64.5% of all Exablate procedure- or device-related events, 95% CI 57.40-71.54) that self-resolved, without any actions taken to date.

There were 32 (16%) Exablate procedure- or device-related adverse events that were unresolved at 12 months. Of these, erectile dysfunction and urinary incontinence were the highest recorded events at 8% and 3.5%, respectively. The rest of the unresolved AEs at 24 months were under 1% which include ejaculation disorder, urinary frequency, hematospermia, urinary hesitancy, urinary urgency, prostate cyst, and urethra stricture.

Additional adverse events have been reported previously in the literature for whole-gland or focal prostate ablation therapies but were not observed in this study through 12 months. These include urinary events such as urinary tract obstruction, bladder neck contracture, urinary fistula, urinary tract or kidney stones, urethral sloughing/discharge/debris in urine, hydronephrosis, and urinoma. Gastrointestinal events that have been reported, but not observed in this study consist of rectal fistula, small intestine obstruction, bowl injury including anal tears, inguinal hernia, upper gastrointestinal hemorrhage, and diverticulitis. Additional reproductive events that have been reported include prostate infection, testicular disorder or epididymitis, and decreased libido. Other general events reported in focal or whole gland prostate ablation therapies include hypotension, hypertension, fever, anemia, syncope, indigestion, and osteomyelitis.

Efficacy Analysis

The first primary effectiveness endpoint is within area of treatment prostate biopsy occurring at 6-months post-treatment. Positive biopsy was defined as any Gleason Grade Group tissue identified within the area of planned Exablate treatment. The majority (n=92, 91.1%) of subject biopsies were negative within the area of treatment. This data is shown in **Table 2** below.

Table 2. Biopsy Results of Any GGG Tissue Within the Planned ROT at 6 Months				
Biopsy Results Within the Planned ROT	**Exablate**		**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**
	N	**%**		
Positive	9	8.9	4.2%	16.2%
Negative	92	91.1	83.8%	95.8%
Total	**101**	**100.0**		

The second primary effectiveness endpoint is reduction in PSA value from baseline to 6-months post-treatment. PSA values that increased or remained the same were considered an increase. The vast majority (n=92, 91.1%) of subjects showed a decrease in PSA at 6-months. This data is shown below in **Table 3**.

Table 3. Reduction in PSA Value at 6 Months				
Reduction in PSA Value at 6 Months	**Exablate**		**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**
	N	**%**		
Yes	92	91.1	83.8%	95.8%
No	9	8.9	4.2%	16.2%
Total	**101**	**100.0**		
Reduction is calculated as change of PSA value at 6 months compared to Baseline Missing data was imputed using LOCF (Last Observation Carried Forward)				

The final primary effectiveness endpoint is Non-Perfused Volume (NPV) coverage of targeted Gleason tissue at treatment. The majority (n=88, 87.1%) of subjects showed that the NPV covered targeted Gleason Grade Group (GGG) tissue following treatment. This data is shown below in **Table 4**.

Table 4. NPV Covered Target Gleason Grade Group (GGG) Tissue at Treatment				
NPV Covered Targeted GGG Tissue	**Exablate**		**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**
	N	**%**		
Yes	88	87.1	79.0%	93.0%
No	13	12.9	7.0%	21.0%
Total	**101**	**100.0**		

The safety profile for this study is favorable on its own as well as compared tothe predicate device. There have been no life threatening nor unanticipated events, and noSAEs reported. Of those events commonly reported with the MRgFUS procedure, the frequency identified for Exablate tends to be lower with most events resolving within 90 days. Moreover, other than one Severe event that was not related to the Exablate device, all others were either Mild or Moderate.

Effectiveness data, especially that of the biopsy results showing a 91% negative result within the area of procedure compared to a 76% negative rate, is considerably betterthan the predicate comparator. On the other hand, the PSA decreased from baseline of 91% compared to 93% at 6-months, which is in-line with the predicate.

In conclusion, it is evident that Insightec's Exablate MR Guided therapy for ablation of prostate tissue is not only comparable, but in most instances' superior to that of data from the predicate device.

Conclusions

This data supports the substantial equivalence of the Exablate Prostate System to its predicate and demonstrates safety and effectiveness of the device for the ablation of prostate tissue.

Conclusion:

The subject and predicate devices have the same intended use. Although there are differences in technological characteristics between the subject and predicate devices, these differences do not raise different questions of safety or effectiveness. The clinical and non-clinical performance data demonstrate that the subject device is substantially equivalent to the predicate device.