July 2, 2024

Tyto Care Ltd.
Stella Raizelman Perry
RA&QA Director
14 Beni Gaon Street
Netanya, 4250803
Israel

Re: K240555
Trade/Device Name: Tyto Insights for Crackles Detection
Regulation Number: 21 CFR 868.1900
Regulation Name: Diagnostic Pulmonary-Function Interpretation Calculator
Regulatory Class: Class II
Product Code: PHZ
Dated: May 31, 2024
Received: May 31, 2024

Dear Stella Raizelman Perry:

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 (the 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 available 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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an

established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Binoy J. Mathews -S

Digitally signed by Binoy J. Mathews -S
Date: 2024.07.02 14:14:26 -04'00'

For

Rachana Visaria
Assistant Director
DHT1C: Division of Sleep Disordered Breathing, Respiratory and Anesthesia Devices
OHT1: Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K240555

Device Name
Tyto Insights for Crackles Detection

Indications for Use *(Describe)*
The Tyto Insights for Crackles Detection is an over-the-counter artificial intelligence (AI) enabled decision support software system used in the evaluation of lung sounds in adults and pediatrics (2 years and older). It automatically analyzes the acoustic signal of the lung as recorded by the FDA 510k cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of "Crackle" is suspected. It is not intended to detect other abnormal or normal lung sounds. A licensed health care professional's advice is required to understand the meaning of the Tyto Insights for Crackles Detection result. Healthcare providers should consider the device result in conjunction with recording and other relevant patient data.

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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510(k) Summary

Submitter Name and Address:	Tyto Care Ltd. 14 Beni Gaon Street Netanya, Israel, 4250803
Contact Person:	Stella Raizelman Perry RA & QA Director Email: stellar@tytocare.com Phone Number: +972 72-2210750 Fax Number: +972 72-2210752
Establishment Registration Number:	3012678246
Date Prepared:	July 02, 2024
Device Trade Name(s):	Tyto Insights for Crackles Detection
Device Common Name:	Tyto Insights for Crackles Detection
Classification:	**Name:** Diagnostic pulmonary-function interpretation calculator **Product code:** PHZ **Regulation No:** 21 CFR 868.1900 **Class**: II **Panel:** Anesthesiology

Primary Predicate Device(s):

Device name	510(k) No.	Date of Clearance
Tyto Insights for Wheeze Detection	K232237	December 13, 2023

Reference Device(s):

Device name	510(k) No.	Date of Clearance
VRIxp	K091732	March 04, 2010

Intended use / indication for use statement

The Tyto Insights for Crackles Detection is an over-the-counter artificial intelligence (AI) enabled decision support software system used in the evaluation of lung sounds in adults and pediatrics (2 years and older). It automatically analyzes the acoustic signal of the lung as recorded by the FDA 510k cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of "Crackle" is suspected. It is not intended to detect other abnormal or normal lung sounds. A licensed health care professional's advice is required to understand the meaning of the Tyto Insights for Crackles Detection result. Healthcare providers should consider the device result in conjunction with recording and other relevant patient data.

Device description

The Tyto Insights for Crackles Detection is a web-based (AI) enabled software system designed to aid in the clinical assessment of lungs auscultation sound data by analyzing recorded lung sounds to determine whether a Crackle is detected within the recorded sound data. The Tyto Insights for Crackles Detection Software is intended to process recordings from the FDA-cleared compatible Tyto Stethoscope (Tyto Stethoscope, K181612). The acquisition of the acoustic data (recordings) is carried out by a professional user in a clinical environment or by a lay- user in a non-medical environment, in compliance with the labeling of the Tyto Stethoscope. The system is composed of the following sub-systems:

1. The Tyto Insights for Crackles Detection Application Server (APS) communicates with the Tyto Insights for Crackles Detection Algorithm Server (ALS) and implements an application programming interface (API) for communication with the telehealth server.
2. The Tyto Insights for Crackles Detection Algorithm Server (ALS) receives an audio file as input and returns an analysis result of positive or negative regarding whether a Crackles was detected as output.
3. The Tyto Insights for Crackles Detection Web Server (WBS) provides a graphic indication whether a Crackles is detected in the recording. It can be utilized both in patient and clinician side.

All the software subsystems (servers and storage) are hosted in the cloud and communicate through IP network.

Substantial Equivalence to Predicate Devices

The following table compares the Tyto Insights for Crackles Detection to the predicate and reference device.

Table 1. Substantial Equivalence Summary

	Device	**Primary Predicate device**	**Reference device**	**Summary**
Device Name	Tyto Insights for Crackles Detection	Tyto Insights for Wheeze Detection	VRIxp	NA
Device Manufacturer	Tyto Care Ltd.	Tyto Care Ltd.	Deep Breeze Ltd.	NA
510(k) Number	TBD	K232237	K091732	NA
Device Class	Class II	Class II	Class II	Same as the predicate device.
Review Panel	Anesthesiology	Anesthesiology	Cardiovascular Diagnostic Devices	Same as the primary predicate device.
Product code	PHZ	PHZ	OCR	Same as the primary predicate device.
Regulation number	21 CFR 868.1900	21 CFR 868.1900	21 CFR 870.1875	Same as the primary predicate device.
Device Classification Name	Abnormal breath sound device	Abnormal breath sound device	Lung sound monitor	Same as the primary predicate device.

	Device	Primary Predicate device	Reference device	Summary
Intended use and indication for use	The "Tyto Insights for Crackles Detection" is an over-the-counter artificial intelligence (AI) enabled decision support software system used in the evaluation of lung sounds in adults and pediatrics (2 years and older). It automatically analyses the acoustic signal of the lung as recorded by the FDA cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of "Crackle" is suspected. It is not intended to detect other abnormal or normal lung sounds. A licensed health care professional's advice is required to understand the meaning of the Tyto Insights for Crackles Detection result. Healthcare providers should consider the device result in conjunction with recording and other relevant patient data.	The "Tyto Insights for Wheeze Detection" is an over-the-counter artificial intelligence (AI) enabled decision support software system used in the evaluation of lung sounds in adults and pediatrics (2 years and older). It automatically analyses the acoustic signal of the lung as recorded by the FDA cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of "Wheeze" is suspected. It is not intended to detect other abnormal or normal lung sounds. A licensed health care professional's advice is required to understand the meaning of the Tyto Insights for Wheeze Detection result. Healthcare providers should consider the device	The VRIxp is intended for monitoring and recording lung sounds and automatic detection of crackles and wheezes. When interpreted by physicians with general medical training and experience, the VRIxp aids in diagnosis and patient management. The VRIxp is intended to be used in healthcare facilities on adults, adolescents, and /or children over the height of 2 feet 9 inches.	Same intended use as the primary predicate device and similar indication for use as the reference device. Both the predicate device and the subject device have the same intended use in that both are intended to detect specific and abnormal breath sounds in the same intended patient population (adult and pediatric) by the same user [Health Care Professional (HCP)] when self-administered by patient and/or the HCPs. Both devices are only intended to be interpreted by HCP and HCP advice is required for the patient to understand their result. Both are labeled OTC. The subject device is indicated to detect

	Device	Primary Predicate device	Reference device	Summary
		result in conjunction with recording and other relevant patient data.		crackles similar to the reference device.
Type of use	Over-The-Counter Use	Over-The-Counter Use	Prescription use	Same as the primary predicate device.
Intended users	Intended to be used by professional users and lay users (18-65 years old).	Intended to be used by professional users and lay users (18-65 years old).	Professional users	Same as the primary predicate device.
Intended patient population	Intended for patients of 2 years and older	Intended for patients of 2 years and older	Adults, adolescents, and/or children over the height of 2 feet 9 inches.	Same as the primary predicate device.
Intended environment	Non-clinical (home) and clinical	Non-clinical (home) and clinical	Clinical setting	Same as the primary predicate device
Form	Stand-alone software system	Stand-alone software system	Hardware (sensors) and software. Use sound sensors to collect lung sounds via dermal contact, which is then converted to a visual display.	Same as the primary predicate device.
Device composition	The following modules compose the Tyto Insights for Crackles Detection: • The Tyto Insights for Crackles Detection Application Server (APS)	The following modules compose the Tyto Insights for Wheeze Detection: • The Tyto Insights for Wheeze Detection Application Server (APS)	The system is composed of: 1. Sound sensors designed to collect lung sounds via dermal contact with human skin 2. Digital Collection Module (DCM) for the	The subject device shares the same structural sub-systems as the primary predicate device: ALS, APS, and WBS. The analytical component of the ALS module, the AI enabled

	Device	Primary Predicate device	Reference device	Summary
	• The Tyto Insights for Crackles Detection Algorithm Server (ALS) • The Tyto Insights for Crackles Detection Web Server (WBS) provides a graphic indication whether a crackle is detected in the recording It can be utilized both in patient and clinician side.	• The Tyto Insights for Wheeze Detection Algorithm Server (ALS) • The Tyto Insights for Wheeze Detection Web Server (WBS) provides a graphic indication whether a wheeze is detected in the recording It can be utilized both in patient and clinician side.	conversion of analog data to digital data 3. a mobile computer workstation to assist in processing, displaying, and/or storing recording information	algorithm, differs between the proposed device and the primary predicate device. The differences in the sub-systems don't raise new questions of safety or effectiveness.
Input	Lung sounds recorded by compatible Tyto Stethoscope	Lung sounds recorded by compatible Tyto Stethoscope	Sound sensors designed to collect lung sounds via dermal contact with human skin	Same as the primary predicate device
Device technology and operating principle	The recordings are created by the compatible Tyto Stethoscope (K181612) and are sent by the third-party point of care app to the clinician app through the telehealth server. The telehealth server sends the set of the lung sound recordings to the Tyto Insights for Crackles Detection web server using its dedicated API. The telehealth server subsequently sends the	The recordings are created by the compatible Tyto Stethoscope (K181612) and are sent by the third-party point of care app to the clinician app through the telehealth server. The telehealth server sends the set of the lung sound recordings to the Tyto Insights for Wheeze Detection web server using its dedicated API. The telehealth server subsequently sends the link	VRIxv uses sound sensors to collect lung sounds via dermal contact, which is then converted to a visual display. During the breathing process, the VRlxp detects lung sounds (i.e., acoustic energy) and converts them into a visual display, which can be viewed via a personal computer (PC) monitor and stored for future	The analytical component of the AI algorithm differs between the proposed device and the primary predicate device. Both the proposed device and the primary predicate device utilize the CRNN (Convolutional Recurrent Neural Network) models,

	Device	Primary Predicate device	Reference device	Summary
	link to results and the relevant UI web view to the point of care app and clinician app. The AI enabled algorithm runs automatically and returns a response for each audio file with the indication of crackles to the telehealth server, which sends a response to both the clinician side and the patient side.	to results and the relevant UI web view to the point of care app and clinician app. The AI enabled algorithm runs automatically and returns a response for each audio file with the indication of wheezes to the telehealth server, which sends a response to both the clinician side and the patient side.	review. The device is designed to record breath sounds based on sensor location. Additionally, the VRlxp has an automated feature for detecting sounds consistent with crackles and wheezes for further clinical evaluation. Lung sounds are viewed collectively as a grayscale image, as well as audibly by sensor.	each network was trained based on the target clinical class: Wheeze for the predicate device and Crackles for the proposed device. The question concerning the ability of software AI Algorithm to accurately detect abnormal breath sound is not new regardless of the particular lung sound algorithm model employed. The primary predicate device raised similar questions. The different AI Algorithm between the subject device and the predicate device does require that the accuracy of the subject device will be substantiated with valid performance data using acceptable methods.

	Device	Primary Predicate device	Reference device	Summary
Signal length	The length of the signal is dictated by the recording process of the compatible Stethoscope. The subject device processes the recordings in segments of up to 12 seconds while signals shorter than 6 seconds will not be processed.	The length of the signal is dictated by the recording process of the compatible Stethoscope. The subject device processes the recordings in segments of up to 12 seconds while signals shorter than 6 seconds will not be processed.	Was not specified.	Same as the primary predicate device
Data transfer and storage	The telehealth server sends the list of the recordings (identified by a unique identifier and time stamp) to the Tyto Insights for Crackles Detection web server using its dedicated API. The server executes the Tyto Insights for Crackles Detection which runs the algorithm and provides the results. Then the Tyto Insights for Crackles Detection web server initiates the web user interface. All the software subsystems (server and storage) are hosted in the cloud and communicate through IP network.	The telehealth server sends the list of the recordings (identified by a unique identifier and time stamp) to the Tyto Insights for Wheeze Detection web server using its dedicated API. The server executes the Tyto Insights for Wheeze Detection which runs the algorithm and provides the results. Then the Tyto Insights for Wheeze Detection web server initiates the web user interface. All the software subsystems (server and storage) are hosted in the cloud and communicate through IP network.	the VRlxp contains a software application that was designed to provide computer-aided recordings with the electronic stethoscope and to store these recordings along with other appropriate patient information.	Same as the primary predicate

	Device	Primary Predicate device	Reference device	Summary
Output	• Positive (Crackles suspected), • Negative (Crackles not suspected), • The Tyto Insights for Crackles Detection was not able to analyze the recording	• Positive (wheeze suspected), • Negative (Wheeze not suspected), • The Tyto Insights for Wheeze Detection was not able to analyze the recording	Lung sounds can be viewed collectively as a grayscale image, as well as audibly by sensor. Additionally, the VRlxp has an automated feature for detecting sounds consistent with crackles and wheezes for further clinical evaluation.	Same as the primary predicate device. Indication whether the abnormal lung sound was detected or not and indication in case the device was not able to analyze the recording.
Performance	The primary study endpoints and hypotheses were met for the intended patient population, the difference in AUC was in favor of Tyto Insights for Crackles Detection compared to the clinical readers. AUC Tyto Insights for Crackles Detection: 0.97 (0.95–0.98). Sensitivity and Specificity were evaluated: Estimate two-sided 95% Cl): Sensitivity: 0.72 (0.63-0.79) Specificity: 0.99 (0.97 - 1.00)	The primary study endpoints and hypotheses were met for the intended patient population, the difference in AUCs was in favor of Tyto Insights for Wheeze Detection compared to the predicate device and in favor of the non-inferiority claim. AUC Tyto Insights for Wheeze Detection: 0.96 (0.94-0.97) Sensitivity and specificity were evaluated: Estimate two-sided 95% Cl): Sensitivity: 0.5465 [0.4304 – 0.6549]	Unknown	The clinical validation path of the predecessor of the predicate device (TytoCare Lung Sounds Analyzer K221614) that established non inferiority with clinical readers was followed. The study endpoints and hypotheses were met for the intended patient population. The difference in AUC was in favor of Tyto Insights for Crackles Detection compared to the clinical readers. The overall diagnostic performance was found

	Device	Primary Predicate device	Reference device	Summary
		Specificity: 0.9895 [0.9684 – 0.9966].		to be substantially equivalent when compared with the primary predicate and reference devices.
User interface for point of care and clinician apps	Web view	Web view	Mobile computer workstation is used for displaying the recording information to the clinician	Same as the primary predicate device
Predetermined Change Control Plan (PCCP)	PCCP is included in the 510k submission	PCCP was not included in the 510k submission	PCCP was not included in the 510k submission	The subject device is substantially equivalent to the predicate device, other than the implementation of an authorized Predetermined Change Control Plan (PCCP) to the Tyto Insights for Crackles detection device.

The Tyto Insights for Crackles Detection like its primary predicate device the Tyto Insights for Wheeze Detection (K232237) have the same intended use, in that both are intended to identify recordings where a specific abnormal lung sound is suspected in the same intended patient population (adult and pediatric 2 years and older) by the same user [Health Care Professional (HCP)] when self-administered by patient and/or the HCPs. Both devices are only intended to be interpreted by HCP and HCP advice is required for the patient to understand their result. Both are labeled OTC.
VRIxp by Deep Breeze Ltd. (K091732) was added as a reference device to support the substantial equivalence of the specific lung sound - crackles, that the subject device is indicated to detect.

Both the Tyto Insights for Crackles Detection and its primary predicate device are stand-alone software systems that deliver the same intended benefit (identify recordings where a specific abnormal lung sound is suspected). For both devices the source of the Lung sounds recordings is the compatible FDA cleared Tyto Stethoscope (K181612).
Similarly, to the primary predicate device, the Tyto Insights for Crackles Detection system is composed of three sub-systems: Application Server (APS), Algorithm Server (ALS) and Web Server (WBS). The APS communicates with the ALS and implements an application programming interface API for communication with the telehealth server. The ALS receives an audio file as input and returns an analysis result of positive or negative regarding whether a Crackles was detected as output.
The code of the APS sub-system is similar to the APS sub-system of the primary predicate device. The only minor adjustments relate to the algorithm's type related parameters. The ALS receives an audio file as input and returns an analysis result of positive or negative regarding whether a crackle was detected as output. The ALS sub-system is composed of an Algorithm and logic wrapper and Interface components. The code of the logic wrapper and Interface component of the ALS component is similar to the ALS component of the primary predicate device, the Algorithm's component is different. The Algorithm of the proposed device is Artificial Intelligence (AI) enabled Algorithm for Crackles detection when the Algorithm of the primary predicate device is AI enabled Algorithm for Wheezes detection. In both devices, the data is being analyzed by AI Machine Learning algorithm to determine the presence of abnormal lung sound in the lungs sound recording. Both the subject device

and the primary predicate device utilize the CRNN (Convolutional Recurrent Neural Network) model for sound event detection, integrating CNNs (Convolutional Neural Networks) and RNNs (Recurrent Neural Networks). Each network is trained based on the target clinical class: Wheeze for the predicate device and Crackles for the proposed device. The question concerning the ability of software AI Algorithm to accurately detect abnormal breath sound is not new regardless of the particular lung sound algorithm model employed. The primary predicate raised similar question. The different AI Algorithm between the proposed device and the primary predicate device does require that the accuracy of the device will be substantiated with valid performance data using acceptable methods.

The WBS provides a graphic indication whether a crackle is detected in the recording. It can be utilized both in the patient and clinician side. The only difference between the WBS sub-systems is in the user interface, which reflects the presence of Crackles instead of Wheeze. The minor differences in the user interface and the software algorithm do not raise new questions of safety and effectiveness, the differences as compared to the primary predicate device did not introduce new usability related critical tasks and didn't impact existing critical tasks.

Standards Conformance

- ANSI AAMI ISO 14971:2019, Medical devices - Application of risk management to medical devices
- ANSI AAMI IEC 62304:2006/A1:2016, Medical device software - Software life cycle processes
- ISO 15223-1 Fourth edition 2021-07, Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements.
- ANSI AAMI IEC 62366-1:2015+AMD1:2020 (Consolidated Text) Medical devices Part 1: Application of usability engineering to medical device.

Performance evaluation:

The Tyto Insights for Crackles Detection was subject to performance evaluation following methodology similar to the ones used to test the primary predicate device. A testing plan was developed and performed to verify that the Tyto Insights for Crackles Detection meets its specifications. The main aspects of the testing plan included:

- SW verification and validation - The software including both custom developed software and OTS software, have been verified and validated and have been

demonstrated to be safe and effective for its intended use. The software documentation level is basic per *Content of Premarket Submissions for Device Software Functions, Guidance for Industry and Food and Drug Administration Staff*, dated June 14, 2023. All required items related to software as required by FDA guidance for Basic Documentation Level have been included in this submission.

- Cybersecurity- all the applicable information to reflect effective cybersecurity management and to address the FDA's recommendations described in *Cybersecurity in Medical Devices: Refuse to Accept Policy for Cyber Devices and Related Systems Under Section 524B of the FD&C Act,* issue date March 2023, *Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions*, issue date September 2023 and in the other FDA's applicable policies have been included in this submission.
- Performance evaluation - retrospective Stand-alone and Clinical performance evaluation of the "Tyto Insights for Crackles Detection" device in detecting crackles in the compatible Tyto Stethoscope lung auscultation recordings respective to ground truth and human level performance.
- Human factors validation – the minor user interface modifications did not introduce new critical tasks and didn't impact existing critical tasks. Therefore, no additional human factors validation was required and the human factors testing for the predicate device was applicable.

The performance of the Tyto Insights for Crackles Detection device in detecting crackles in recordings acquired by the compatible Tyto Stethoscope has been evaluated on a retrospective validation dataset. The retrospective validation dataset is composed of recordings obtained from the real-world use of the Tyto Care FDA-cleared compatible Tyto Stethoscope (K181612). 446 recordings (120 Crackles positive and 326 negative), corresponding to the intended patient population of the Tyto Insights for Crackles Detection Software (a total of 445 patients). The demographics of the validation dataset are presented hereunder:

			N=446 recordings
Age Group (Years)			
	Positive	**Negative**	**Total**
2-12	57 (25.67%)	165 (74.33%)	222 (50.22%)
12-21	10 (18.18%)	45 (81.82%)	55 (12.33%)
>=21	53 (31.36%)	116 (68.64%)	169 (37.45%)
Gender			
	Positive	**Negative**	**Total**
Male	55 (25.82%)	158 (74.18%)	213 (47.6%)
Female	65 (27.89%)	168 (72.11%)	233 (52.24%)

Table 2: Validation data-set demographics

To establish the ground truth, all the recordings were read by three blinded experienced Pulmonologists at random, the binary ground truth was determined by a majority vote of these three Pulmonologists. For the characterization of the stand-alone accuracy, the automated binary result of the software has been compared to ground truth and specificity and sensitivity were calculated. This stand-alone accuracy is presented hereunder in table 3:

Parameter	**Estimate (two-sided 95% CI)**
Sensitivity (Se)	0.72 (0.63–0.79)
Specificity (Sp)	0.99 (0.97–1.00)
Positive Predictive Value (PPV)	0.63 (0.4–0.87)
Negative Predictive Value (NPV)	0.99 (0.98–0.99)

Table 3: The stand-alone accuracy of the Tyto Insights for Crackles Detection

For the characterization of the clinical performance the Area under the Receiver Operating Curve (AUC) for crackles detection by the device was compared to the clinical readers (Physicians non-Pulmonologists). To calculate the AUC the probability score was extracted from the device and compared to a likelihood score that was recorded by the clinical readers independently for every recording.

The primary endpoint was to establish that the lower bound of 95% two-sided CI for the difference in AUCs between the Tyto Insights for Crackles Detection vs. clinical readers is higher than non-inferiority margin of -0.05. The secondary endpoint was the repeatability of the software as compared to the clinical readers.

Parameter	Estimate 95% two sides CI
AUC Clinical readers	0.77 (0.73–0.8)
AUC Tyto Insights for Crackles Detection	0.97 (0.95–0.98)
AUC Tyto Insights for Crackles Detection – clinical readers	0.2 (0.17– 0.23)

Table 4: The clinical accuracy of the Tyto Insights for Crackles Detection as compared to Clinical readers.

For the indicated patient population the difference in AUC (Tyto Insights for Crackles Detection – Readers; higher values in favor of the device) was 0.2 (0.17–0.23) establishing the non–inferiority (0.17 > margin of –0.05) of the device in detecting crackles. Similar results were also shown within the subgroup analysis, as evidence that the device accuracy is consistent with age and gender groups, different types of crackles, additional abnormal lung sounds and recordings generated by clinician or lay-user. The secondary endpoint was repeatability, the device is characterized by with kappa of 1.0 and agreement of 100% compared to readers repeatability with kappa of 0.42 (0.35 -0.49). In summary, non–inferiority of Tyto Insights for Crackles Detection compared to clinical readers was established. Similar effect trend was also shown within the subgroup analysis, as evidence that the device accuracy is consistent with age and gender groups, different types of crackles, additional abnormal lung sounds and recordings generated by clinician or lay-user.

Predetermined Change Control Plan (PCCP)

The subject device is substantially equivalent to the predicate device, other than the implementation of an authorized Predetermined Change Control Plan (PCCP) that specifies anticipated modifications to the Tyto Insights for Crackles detection device.

The table below includes a description of the software modifications that can be made to the algorithms in the device subject to the authorized PCCP as well as a description of the test methods that will be used to support substantial equivalence determination.

Detailed list of changes	Test Methods	Acceptance criteria to establish substantial equivalence
1. <u>Modifications related to quantitative measures of performance specifications:</u> Re-training of the ML model with additional data to improve the performance)of the re-trained algorithm compared to the original device while the same type and range of input signal is used.	• Software verification and validation • Clinical performance Validation. Retrospective study on dataset of the compatible Tyto Stethoscope recordings that are representative of the intended recorded patient population (data will be acquired by the real-world use of the Tyto Stethoscope).	• Software verification and validation meet the requirements • Clinical performance Validation: **<u>Stand-alone:</u>** Accuracy of device – Sensitivity, Specificity, PPV, NPV **<u>Co-Primary endpoints:</u>** • Sensitivity of the modified device calculated on the new validation dataset compared to the results for the original device • Specificity of the modified device calculated on the new validation dataset compared to the results for the original device **<u>Success criteria:</u>** The success is defined if the LCI for Se is higher than 0.6279 AND LCI for Sp is higher than 0.9668. Se and Sp are co-primary endpoints. Meeting both endpoints is required for the modification to be declared successfully. **<u>Secondary Endpoint</u>** The PPV and NPV of the newly trained algorithm compared to the PPV and the NPV of the original device.
2. <u>Modifications related to quantitative measures – technical performance specifications.</u> Modification of data preprocessing methodologies /data augmentation methodologies/ Architecture and hyper-parameters to improve the performance or the efficiency of the	• Software verification and validation • Verification testing will be conducted for the improved computational parameters • Clinical performance Validation. Retrospective study on dataset of the compatible	• Software verification and validation meet the requirements • Verification testing meet the requirements • Clinical performance Validation: **<u>Stand-alone:</u>** Accuracy of device – Sensitivity, Specificity, PPV, NPV

computational resources (running time, memory consumption and CPU utilization).	Tyto Stethoscope recordings that are representative of the intended recorded patient population (data will be acquired by the real-world use of the Tyto Stethoscope)	**Co-Primary endpoints:** • Sensitivity of the modified device calculated on the new validation dataset compared to the results for the original device • Specificity of the modified device calculated on the new validation dataset compared to the results for the original device. **Success criteria:** The success is defined if the LCI for Se is higher than 0.6279 AND LCI for Sp is higher than 0.9668. Se and Sp are co-primary endpoints. Meeting both endpoints is required for the modification to be declared successfully. **Secondary Endpoint** • The PPV and NPV of the newly trained algorithm compared to the PPV and the NPV of the original device.
3. Modifications related to device inputs: Expanding the algorithm to include new sources of the same signal type (different model of FDA compatible Stethoscope with equivalent audio acquisition specifications). Modification is limited to expanding to electronic stethoscopes that have FDA 510k clearance (for over-the-counter use) at the time that the proposed modification is made.	• Software verification and validation • Clinical performance Validation. Retrospective study on dataset of the compatible Stethoscope recordings that are representative of the intended recorded patient population (data will be acquired by the real-world use of the applicable Stethoscope models).	• Software verification and validation meet the requirements • Clinical performance Validation: **Stand-alone:** Accuracy of device – Sensitivity, Specificity, PPV, NPV **Four co-primary endpoints:** Stand-Alone performance: Accuracy of device – Sensitivity, Specificity, PPV, NPV Four Co-Primary endpoints: • Sensitivity of the newly trained algorithm on the new validation dataset (subset collected only with the new stethoscope that have the required FDA 510k clearance at the

		time that the proposed modification is made) compared to the results for the original device. • Specificity of the newly trained algorithm on the new validation dataset (subset collected only with the new stethoscope that have the required FDA 510k clearance at the time that the proposed modification is made) compared to the results for the original device. • Sensitivity of the modified device calculated on the new validation dataset (subset collected only with the currently 510k cleared Tyto Stethoscope) compared to the results for the original device • Specificity of the modified device calculated on the new validation dataset (subset collected only with the currently 510k cleared Tyto Stethoscope) compared to the results for the original device. Secondary Endpoint • The Se, Sp, PPV and NPV of the newly trained algorithm compared the original device on validation dataset combined from cases collected using both new and already cleared stethoscopes**.** **Success criteria:** The success is defined if the LCI for Se is higher than 0.6279 AND LCI for Sp is higher than 0.9668. Se and Sp are co-primary endpoints. Meeting both endpoints is required for the modification to be declared successfully. Se and Sp are co-primary endpoints (a total of four). Success is defined as success of all four co-primary endpoints. **Secondary Endpoint** The Se, Sp, PPV and NPV of the newly trained algorithm compared the original device on validation dataset combined from cases collected using both new and already cleared stethoscopes.

The PCCP includes an algorithm modification protocol describing the verification and validation activities that will support the proposed changes. The modification protocol incorporates impact assessment considerations and specifies requirements for data management, including data sources, collection, storage, and sequestration, as well as documentation and data re-use practices.

Specific test methods are specified in the PCCP to establish substantial equivalence relative to Subject device and include sample size determination, analysis methods, and acceptance criteria. To help ensure validation test datasets are representative of the intended use population, each dataset will meet minimum demographic requirements similarly to the proposed device.

Upon implementation of the change, the change will be communicated to the users and the labeling will be updated to reflect the new device's performance characteristics.

Conclusion

The Tyto Insights for Crackles Detection Software has the same intended use and indication for use as the predicates. The question concerning the ability of software AI Algorithm to accurately detect abnormal breath sound is not new regardless of the particular lung sound algorithm model employed. The primary predicate raised a similar question. Non–inferiority of Tyto Insights for Crackles Detection compared to the clinical readers for intended patient population was established. Thus, we conclude that the Tyto Insights for Crackles Detection is substantially equivalent. i.e. as safe and as effective as the primary predicate device.