April 7, 2025

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

Re: K243567
Trade/Device Name: Tyto Insights for Rhonchi Detection
Regulation Number: 21 CFR 868.1900
Regulation Name: Diagnostic Pulmonary-Function Interpretation Calculator
Regulatory Class: Class II
Product Code: PHZ
Dated: March 5, 2025
Received: March 5, 2025

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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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,

Rachana Visaria -S

Rachana Visaria, Ph.D.
Assistant Director
DHT1C: Division of Anesthesia,
Respiratory, and Sleep 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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K243567

Device Name
Tyto Insights for Rhonchi Detection

Indications for Use *(Describe)*
The Tyto Insights for Rhonchi Detection is a prescription-use 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 "Rhonchi" 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 Rhonchi 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.

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:	April 07, 2025
Device Trade Name(s):	Tyto Insights for Rhonchi Detection
Device Common Name:	Tyto Insights for Rhonchi Detection
Classification:	**Name:** Diagnostic pulmonary-function interpretation calculator **Product code:** PHZ **Regulation No:** 21 CFR 868.1900 **Class**: II **Panel:** Anesthesiology

Predicate Device(s):

Device name	**510(k) No.**	**Date of Clearance**
Tyto Insights for Crackles Detection	K240555	July 02, 2024

Intended use / indication for use statement

The Tyto Insights for Rhonchi Detection is a prescription-use 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 "Rhonchi" 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 Rhonchi Detection result. Healthcare providers should consider the device result in conjunction with recording and other relevant patient data.

Device description

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

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

The recordings from the compatible Tyto Stethoscope (K181612) 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 Rhonchi Detection web server using its dedicated API. The AI enabled algorithm runs automatically and returns a response for each audio file with the indication of rhonchi to the telehealth server which sends a response to both the clinician side and the patient side.

Substantial Equivalence to Predicate Devices

The following table compares the Tyto Insights for Rhonchi Detection to the predicate device.

Table 1. Substantial Equivalence Summary

	Device	Predicate Device	Comparison
Device Name	Tyto Insights for Rhonchi Detection	Tyto Insights for Crackles Detection	NA
Device Manufacturer	Tyto Care Ltd.	Tyto Care Ltd.	NA
510(k) Number	K243567	K240555	NA
Device Class	Class II	Class II	Same
Review Panel	Anesthesiology	Anesthesiology	Same
Product code	PHZ	PHZ	Same
Regulation number	21 CFR 868.1900	21 CFR 868.1900	Same.
Device Classification Name	Abnormal breath sound device	Abnormal breath sound device	Same
Intended use and indication for use	The Tyto Insights for Rhonchi Detection is a prescription-use 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 510k cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of	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 510k cleared compatible Tyto Stethoscope and identifies recordings where a specific abnormal lung sound suggestive of	Same Both the predicate device and the subject device have the same intended use and indication for 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

	Device	Predicate Device	Summary
	"Rhonchi" 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 Rhonchi Detection result. Healthcare providers should consider the device result in conjunction with recording and other relevant patient data.	"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.	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.
Type of use	Prescription Use	Over-The-Counter Use	Use under prescription (clinical oversight) does not raise different questions of safety and effectiveness
Intended users	Professional users and lay users (18-65 years old).	Professional users and lay users (18-65 years old).	Same
Intended patient population	Patients of 2 years and older	Patients of 2 years and older	Same
Intended environment	Non-clinical (home) and clinical	Non-clinical (home) and clinical	Same
Input	Lung sounds recorded by compatible Tyto Stethoscope (K181612)	Lung sounds recorded by compatible Tyto Stethoscope (K181612)	Same
Signal length	Recordings are processed in segments of up to 12 seconds while signals shorter than 6 seconds will not be processed.	Recordings are processed in segments of up to 12 seconds while signals shorter than 6 seconds will not be processed.	Same

Output	• Positive (Rhonchi suspected), • Negative (Rhonchi not suspected), • The Tyto Insights for Rhonchi Detection was not able to analyze the recording	• Positive (Crackles suspected), • Negative (Crackles not suspected), • The Tyto Insights for Crackles Detection was not able to analyze the recording	Substantially equivalent. Indication whether the abnormal lung sound was detected or not and indication in case the device was not able to analyze the recording.
Performance	AUC: 0.96 (0.92–0.98) Estimate two-sided 95% Cl): Sensitivity: 0.60 (0.50-0.69) Specificity: 0.99 (0.97 - 1.00)	AUC: 0.97 (0.95–0.98) Estimate two-sided 95% Cl): Sensitivity: 0.72 (0.63-0.79) Specificity: 0.99 (0.97 - 1.00)	Substantially equivalent.
User interface	Web view	Web view	Same

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:

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.**

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,* March 2023,

Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions, September 2023.

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.

Clinical Validation- The performance of the Tyto Insights for Rhonchi Detection device in detecting rhonchi 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). 400 recordings (100 Rhonchi positive and 300 negative), corresponding to the intended patient population of the Tyto Insights for Rhonchi Detection Software (a total of 400 patients). The demographics of the validation dataset are presented hereunder:

			N=400 recordings
Age Group (Years)			
	Positive	**Negative**	**Total**
2-18	66 (33.50%)	131 (66.50%)	197 (49.25%)
≥ 18	34 (16.75%)	169 (83.25%)	203 (50.75%)
Sex			
	Positive	**Negative**	**Total**
Male	52 (26.67%)	143 (73.33%)	195 (49%)
Female	48 (23.41%)	157 (76.59%)	205 (51%)

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)	0.60 (0.50–0.69)
Specificity (Sp)	0.99 (0.97–1.00)
Positive Predictive Value (PPV)	0.74 (0.41–1.00)
Negative Predictive Value (NPV)	0.99 (0.98–0.99)

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

For the characterization of the clinical performance the Area under the Receiver Operating Curve (AUC) for rhonchi 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 Rhonchi 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	0.79 (0.75–08 3)
AUC Tyto Insights for Rhonchi Detection	0.96 (0.92–0.98)
AUC Tyto Insights for Rhonchi Detection – clinical readers	0.16 (0.13– 0.21)

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

For the indicated patient population the difference in AUC (Tyto Insights for Rhonchi Detection – Readers; higher values in favor of the device) was 0.16 (0.13–0.21) establishing the non–inferiority (0.13 > margin of –0.05) of the device in detecting rhonchi. Similar results were also shown within the subgroup analysis, as evidence that the device accuracy is consistent with age and sex groups, additional abnormal lung sounds and recordings generated by clinician or lay-user. The accuracy of the device has not been established in obese population (adults with BMI ≥ 30 kg/m² or children at/above the 95th percentile for age and gender). The secondary endpoint was repeatability, the device is characterized by a repeatability (by design) with kappa of 1.0 and agreement of 100% compared to readers repeatability with kappa of 0.57 (0.49 -0.65).

Predetermined Change Control Plan (PCCP)

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 0.500 and LCI for Sp is higher than 0.9749. 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 computational resources (running time, memory consumption and CPU utilization).	• Software verification and validation • Verification testing will be conducted for the improved computational parameters • 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	• 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 **<u>Co-Primary endpoints:</u>** • Sensitivity of the modified device calculated on the new validation dataset compared to
	real-world use of the Tyto Stethoscope)	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>** Success is defined if the LCI for Se is higher than 0.500 AND LCI for Sp is higher than 0.9749. 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.

3. <u>Modifications related to device inputs:</u> 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: **<u>Stand-alone:</u>** Accuracy of device – Sensitivity, Specificity, PPV, NPV **<u>Four co-primary endpoints:</u>** Stand-Alone performance: Accuracy of device – Sensitivity, Specificity, PPV, NPV <u>Four Co-Primary endpoints:</u> • 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. <u>Secondary Endpoint</u> • 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**.** **<u>Success criteria:</u>** Success is defined if the LCI for Se is higher than 0.500 AND LCI for Sp is higher than 0.9749. 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. **<u>Secondary Endpoint</u>** 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.

Conclusion

Tyto Insights for Rhonchi Detection Software has the same intended use and indication for use as the predicate. Non–inferiority of Tyto Insights for Rhonchi Detection compared to the clinical readers for intended patient population was established through clinical validation testing. Thus, we conclude that the Tyto Insights for Rhonchi Detection is substantially equivalent. i.e. as safe and as effective as the predicate device.