Regulatory Pathways for Cough Monitoring: FDA Validation Requirements Explained

March 2025

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Introduction

- 24-hour cough count (or frequency) has emerged as a **key endpoint to measure treatment response** in cough studies.
- Multiple clinical programs using cough counting are ongoing.
- The FDA has yet to approve a treatment based on cough counting results and will likely **require validation** of the end-to-end process for each novel trial.

What does this mean for your study?

Semi-Automated Cough Counting Overview

Semi-Automated Cough Count Explained

Annotators listen to recording files, with **speech obfuscated** and **non-cough portions withheld,** to more efficiently identify and count coughs.

- More efficient than manual method
- Protects patient privacy
- Used in pharmaceutical trials for measuring primary endpoints

- Your cough monitoring partner would likely use a **semi-automated approach** due to a clear regulatory pathway and combination of efficiency and accuracy.[1]
  - Fully manual cough counting is more time-consuming for annotators.
  - Fully automated cough counting offers a less clear regulatory approval pathway and lower accuracy.[2]

- Semi-automated cough counting retains all data while other processing approaches may delete or fail to record data determined by the algorithm to be non-cough.
  - Failing to retain all data eliminates the ability for future review, audit, or algorithm performance tracking.

1. US FDA. Gefapixant FDA briefing document: Pulmonary-Allergy Drugs Advisory Committee Meeting. 17 November 2023: https://www.fda.gov/media/173850/download (accessed 11 March 2024)
2. Lal A et al. Regulatory oversight and ethical concerns surrounding software as medical device (SaMD) and digital twin technology in healthcare. Annals of Translational Medicine 2022;10:950.

Semi-Automated Cough Counting Overview Continued

Three Steps

1. Medical Device

Wearable device records lung sounds (including cough)

2. Data Processing & Speech Obfuscation

Algorithm withholds quiet portions of recording unlikely to contain cough and obfuscates patient speech

3. Cough Counting

Cough counting by trained annotators

- Semi-automated cough counting involves three main steps.
  - **Validation of these steps will likely be expected to be performed on a trial-by-trial basis to ensure accuracy for populations included and disease state.[2]**
  - Some semi-automated approaches have been the subject of prior feedback from the FDA.[2]
- This explainer provides an overview of Strados Labs' semi-automated **validation process** which is based on extensive agency feedback.

2. US FDA. Gefapixant FDA briefing document: Pulmonary-Allergy Drugs Advisory Committee Meeting. 17 November 2023: https://www.fda.gov/media/173850/download (accessed 11 March 2024)

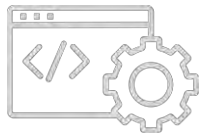
Step 1

Validation of Medical Device for Data Collection

1. Medical Device

Wearable device records lung sounds (including cough)

2. Data Processing & Speech Obfuscation



Algorithm withholds quiet portions of recording unlikely to contain cough and obfuscates patient speech

3. Cough Counting

Cough counting by trained annotators

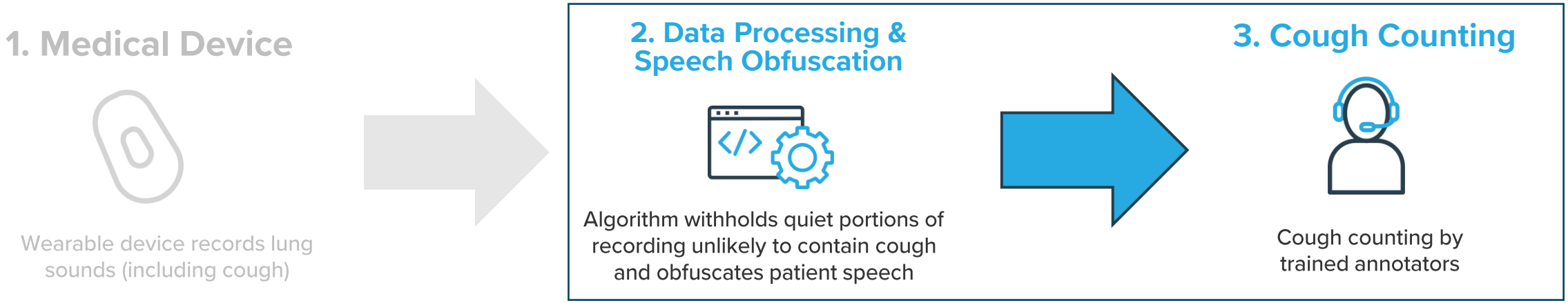
- **Strados Labs' RESP® Biosensor has received FDA 510(k) clearance and a CE mark for the recording of lung sounds (including cough).[3]**

- While not all cough monitoring technologies are medical devices, the regulatory approval pathway for a non-medical device is less clear.
    - It may also present issues with importing in some countries.

3. 510(k) clearance received by Strados Labs for the RESP Biosensor on April 27, 2022

Steps 2 & 3

Validation of Data Processing and Cough Counting



- **Validation of those steps will likely be expected to be performed on a trial-by-trial basis.[2]**
- Ensures accuracy of the process for:
  - Populations included
  - Disease state and range of cough frequencies studied
  - Treatment effect expected

2. United States Food & Drug Administration. Gefapixant FDA briefing document: Pulmonary-Allergy Drugs Advisory Committee Meeting. 17 November 2023. Available at: https://www.fda.gov/media/173850/download (accessed 11 March 2024).

Steps 2 & 3 Cont.

Validation of Data Processing and Cough Counting

With Agency feedback, Strados Labs has developed experience and expertise to help design appropriate validation for cough studies.

2. Data Processing & Speech Obfuscation

Aim: Validate that algorithms & speech-privacy filters do not affect the cough count

- Based on a statistically significant number of 24-hour cough recordings from unique subjects

3. Cough Counting

Aim: Assess the reliability and accuracy of cough counting between annotators (inter-rater variability)

- Based on a statistically significant number of 24-hour cough recordings from unique subjects

Additional details on these steps are available upon request

Will Validation of the Cough Counting Process Be Required In Your Study?

YES, MOST LIKELY:

- The existing 510(k) clearance and CE mark of the RESP® Biosensor for the collection of lung sounds (including cough) will help streamline the validation for your study.
- However, **trial-specific validation of data processing and speech obfuscation will likely be expected by the FDA.**[2]
  - Regardless of the device used, or prior trials, this is to account for differences in population and drug studied.
  - This validation will likely be requested in Phase 2 trials and after (but may vary from study to study)

2. United States Food & Drug Administration. Gefapixant FDA briefing document: Pulmonary-Allergy Drugs Advisory Committee Meeting. 17 November 2023. Available at: https://www.fda.gov/media/173850/download (accessed 11 March 2024).

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